ALCOR LIFE EXTENSION FOUNDATION

CRYONICS

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DONOR CHALLENGE

ALCOR LIFE EXTENSION FOUNDATION 1972 - 2022 50TH ANNIVERSARY

ALCOR
LIFE EXTENSION FOUNDATION
The World's Leader in Cryonics
www.alcor.org

CRYONICS

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ALCOR LIFE EXTENSION FOUNDATION

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To:	*General Public*
From:	Patrick Harris, Sr.
Date:	November 30, 2021
Subject:	**Alcor's 50th Birthday – Donor Challenge**

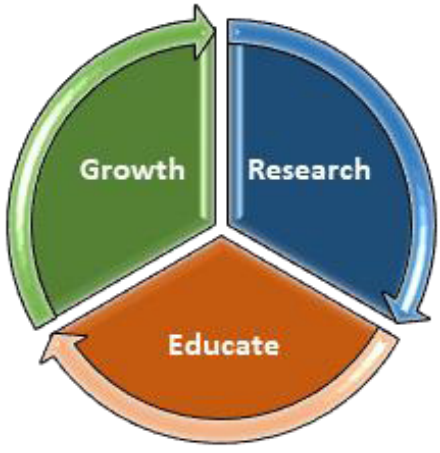
I have worked diligently with Alcor's Board and my leadership team to develop our 2022 roadmap prioritizing Alcor's strategic investments. Alcor's mission statement (LINK):

To save lives through the following prioritized principles:

1. *Maintain the current patients in biostasis.*
2. *Place current and future members into biostasis (if and when needed).*
3. *Eventually restore to health and reintegrate into society all patients in Alcor's care.*
4. *Fund research into developing more cost effective and reliable means for 1-3 above.*
5. *Provide public education as a means of fostering growth to support the goals of 1, 2, 3, 4 above.*

Alcor's longstanding Mission will be implemented and fulfilled by focusing on three (3) strategic pillars: ***Research, Education, and Growth***. These three pillars guide Alcor's Board and my decision-making as we develop strategies, and each one supports the next.

Investing in Research leads to discoveries and innovations, which supports Education. Investing in Education raises public awareness and acceptance of cryonics, supporting Growth. Investing in Growth increases fiscal resources and attracts high caliber people, thus supporting Research capabilities. These strategic pillars are the basic foundation underlying Alcor's Mission.



I am confident Alcor's foundational pillars, in conjunction with our strategic roadmap, will lead to unprecedented growth in FY2022. We are investing in strategic initiatives to take Alcor to the next level, and I am very optimistic about the future.

Alcor has a lot of work ahead of us to achieve our Mission. I am hopeful everyone will enter the **Donor Challenge!** As you consider your pledge, please forward this to your friends. If you wish to "throw down the gauntlet," I look forward to speaking with you. Thank you for supporting the most aspirational and noble goal in history.

Respectfully,

Patrick Harris, Sr.
President & CEO
Alcor Life Extension Foundation

Enter Alcor's 50th Anniversary Donor Challenge!

Alcor was incorporated on February 23, 1972, which means our **50th Anniversary** is next year! To mark this historic event, new strategic initiatives will be announced on our anniversary.

November 30, 2021 is Giving Tuesday, which is touted as a "*global generosity movement unleashing the power of people and organizations to transform their communities and the world.*" Transforming communities and the world is a hallmark of cryonics. Each year, charitable organizations compete for Giving Tuesday donations, providing many opportunities to generously support non-profits. Rather than *ask* for financial support, Alcor wants to **earn** your contribution by running a **Donor Challenge**!

Alcor's **Donor Challenge** focuses on growing membership and awareness of cryonics. Entering the Challenge is easy, and the rules are simple:

***Entry*:**

- Choose a **Pledge Level** from the table below
- Send an email to Donate@Alcor.org and register your **Pledge Level**
- Your pledge must be submitted **by February 22, 2022**

***Rules*:**

1) On **February 23, 2022**, Alcor will announce the FY2022 strategies
2) Each month during 2022, Alcor will report the current **Member Count**
3) When the **Member Count** reaches your **Pledge Level**, Alcor will contact you for your donation
4) All Donors will receive a Commemorative Lapel Pin* and be part of the **50th Anniversary Club**
5) **The Donor Challenge ends on December 31, 2022**

Pledge Level	Member Count	50th Anniversary Club
$100	1500	*1500 Club*
$500	1550	*1550 Club*
$1,000	1600	*1600 Club*
$5,000	1650	*1650 Club*
$10,000	1700	*1700 Club*
$50,000	1800	*1800 Club*
$100,000	1900	*1900 Club*
$500,000	**2000**	**Half-Century Club**
$1,000,000	**2258**	***Millionaires Club***
> $1,000,000	***"CEO Gauntlet"***	**President's Club**

**Commemorative Lapel Pin*
Design subject to change

Alcor is a non-profit, federally tax-exempt, 501(c)(3) corporation. Your donation may be tax-deductible. Please speak with a tax professional regarding your taxable income. Alcor's Federal Tax I.D. Number is 23-7154039.

Questions & Answers

Why is Alcor running a Donor Challenge instead of just asking for donations?

- Alcor's CEO, Patrick Harris, wants Donors to challenge him and his team to **earn** your donation.

Why is Alcor's Donor Challenge focused on membership growth instead of something like research?

- A lot of research, innovation, and development is required to support our Mission, all of which requires funding. Growth of membership is foundational to funding mission-critical objectives.

How will Alcor determine the Member Count at the end of each month?

- Alcor will count the number of *active, signed** membership agreements. If a member becomes a patient, they will be removed from the Member Count. (**including e-signatures*)

Do I need to be an Alcor member to enter the Donor Challenge?

- No, entry into the Donor Challenge is not limited to Alcor members. We've established criteria for entry, and if someone meets the criteria, they can participate, so long as they:
  - Want to enter the **Donor Challenge**, and
  - Choose a Pledge Level

So practically anyone can enter the Donor Challenge. May I share Patrick's letter, the Donor Challenge, and these Questions & Answers with others?

- Yes! We encourage you to share this with your family, friends, colleagues, acquaintances, and random people you meet at the grocery store.

How do I enter Alcor's Donor Challenge?

- Choose a pledge level of $100 or more and send an email to Donate@Alcor.org. Alcor will register your pledge and your **50th Anniversary Club Level.**

If I pledge at a certain level and that level is not reached, will I still be a part of the Club associated with my pledge level?

- Yes. If you pledge $1,000 and Alcor does not reach 1600 members next year, you will automatically be part of the **1600 Club**. Likewise, if you pledge at the Millionaire's Club level and we fall short, you will still be in the **Millionaires Club**.

What if I pledge $10,000 so I can be part of the 1700 Club, but I fall on hard economic times, and I can only donate $1,000?

- Unexpected things happen to everyone, and we will work with you. If you pledge at a higher level but can only donate at a lower level, you will be in the Club corresponding to your actual donation.

If I pledge $500,000 to be in the Half-Century Club and Alcor does not reach 2000 members, how much will my donation be next year?

- If you pledge $500,000 and we reach the milestone of 1500 members, Alcor will only ask you to donate at the Pledge Level we **earned**. (Example: You pledge $500,000, Member Count reaches 1500, we ask you to donate $100)

What is the "CEO Gauntlet" and the President's Club?

- If you pledge more than $1,000,000, you **"throw down the gauntlet" and directly challenge Alcor's CEO**. You choose a custom Pledge and Member Count greater than 2258, and Patrick will let you know if he accepts your challenge. If he picks up your "gauntlet," you will qualify for Alcor's 50th Anniversary President's Club**.**

The Millionaire's Club has a weird Member Count of 2258. Is that a typo?

- No, that's not a typo. In 1985, Alcor gained 27 members when its roster grew from 44 to 71, a growth rate of ~ **61.36%**. Patrick forecasts Member Count will reach 1399 by the end of FY2021. To surpass Alcor's highest historical growth rate, Member Count will need to increase by 859 people, capturing a growth rate of ~ **61.4%**. The 2258 Member Count represents the achievement of Alcor's most significant growth rate in its 50-year history.

What are Alcor's historical gains/losses in total members and growth rates?

- See the table below

Year	Member Count	Count Change	% Change	Year	Member Count	Count Change	% Change	Year	Member Count	Count Change	% Change
2021	*1399**	*68*	*5.11%*	2005	786	89	12.77%	1988	111	11	11.00%
2020	1331	44	3.42%	2004	697	36	5.45%	1987	100	15	17.65%
2019	1287	51	4.13%	2003	661	50	8.18%	1986	85	14	19.72%
2018	1236	**93**	8.14%	2002	611	56	10.09%	1985	71	27	**61.36%**
2017	1143	27	2.42%	2001	555	39	7.56%	1984	44	15	51.72%
2016	1116	62	5.88%	2000	516	41	8.63%	1983	29	1	3.57%
2015	1054	44	4.36%	1999	475	24	5.32%	1982	28	4	16.67%
2014	1010	39	4.02%	1998	451	21	4.88%	1981	24	(1)	-4.00%
2013	971	(9)	-0.92%	1997	430	29	7.23%	1980	25	2	8.70%
2012	980	23	2.40%	1996	401	34	9.26%	1979	23	4	21.05%
2011	957	25	2.68%	1995	367	13	3.67%	1978	19	4	26.67%
2010	932	24	2.64%	1994	354	(15)	-4.07%	1977	15	3	25.00%
2009	908	34	3.89%	1993	369	27	7.89%	1976	12	Unknown	Unknown
2008	874	42	5.05%	1992	342	70	25.74%	1975	Unknown	Unknown	Unknown
2007	832	11	1.34%	1991	272	84	44.68%	1974	Unknown	Unknown	Unknown
2006	821	35	4.45%	1990	188	43	29.66%	1973	Unknown	Unknown	Unknown
**Forecast, not actual*				1989	145	34	30.63%	1972	5	N/A	N/A

Wait a minute. In Alcor's 50-year history, there's never been more than an increase of 93 members?

- That's correct. Yearly Member Count increases topped 70, only three times in Alcor's 50-year history, and the current record is an increase of 93 members in 2018.

If Patrick is forecasting the Member Count to be 1399 for FY2021, then you know Alcor needs to break a record by increasing Member Count by 101 before the first $100 Pledge Level is reached, right?

- Yes, that's why we call it a **Donor** "**Challenge**," and we aim to **earn** every dollar you pledge.

If history is the best predictor of future performance, and Patrick sets growth targets so high, how will you achieve any of the Pledge Levels?

- We have new "top secret" strategic initiatives and changes we will reveal on Alcor's Birthday. Patrick is confident our strategies will lead to unprecedented growth. We're excited, and we want you to be excited, so we invite you to challenge Alcor, or "throw down the gauntlet" and challenge Patrick directly.

Will you let me know what these "top secret" strategies are before I pledge?

- No, they are top secret until Alcor's 50th Birthday on February 23, 2022.

What if I decide to wait until after the strategies are revealed?

- You can only enter the Donor Challenge until February 22, 2022, right before our strategies are announced. Of course, you're always welcome to donate to Alcor anytime, including after the close of the Donor Challenge.

Common sense suggests Alcor will need a marketing budget to achieve that level of growth. Did the Board approve any spending to hire an advertising firm?

- No, there is no budget to hire an advertising firm.

You understand that by waiting until February 23 to launch these "top secret" strategies, Alcor is losing almost two months in 2022 to reach new membership goals, right?

- Patrick will announce his strategies on Alcor's 50th Birthday, but he believes donors are at an unfair disadvantage by not knowing what we will launch. He is happy to take an almost two-month "handicap" to level the playing field.

If membership grows as much as Patrick thinks, Alcor will need additional people to support business operations. Has the Board approved additional headcount for 2022?

- No, there is no new headcount in the budget. While Alcor doesn't have any current plans to hire more people, that could change depending on how much membership grows next year and how many pledges we **earn**.

Besides the Commemorative Lapel Pin, are there other benefits to being part of a specific Club Level?

- While nothing is currently planned, there might be specific communications, involvement, or events for different Club level members in the future

Is the Donor Challenge tax-deductible?

- Alcor is a federally tax-exempt, 501(c)(3) corporation, and your donation may be tax-deductible. Any time you want to review Alcor's tax status, you can visit the IRS's website at https://apps.irs.gov/app/eos/ and enter our EIN 23-7154039. Donations may be tax-deductible if they are made before the close of the tax year. Alcor cannot give tax advice, so we encourage you to speak with a tax professional regarding your donation and taxable income.

If I have more questions about the Donor Challenge or am ready to make my pledge, who do I contact?

- Please send an email to Donate@Alcor.org, and a member of Alcor's team will get back to you as soon as possible.

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Commemorative Lapel Pin
Design subject to change

Alcor-50 Donor Challenge

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Getting Better
Part 3: Limits of *Limits to Growth*

By Max More, Ph.D.

Minister of Doom

You have probably heard of Thomas Malthus. He was the man responsible for economics being saddled with the label "the dismal science." His 1798 book, *An Essay on the Principle of Population*, made a case for the hopelessness of the battle against hunger and poverty. Based on his survey of history (pre-capitalist, pre-industrial history), Malthus concluded that when the supply of food increases, human population increases faster. Humans cannot exercise self-control and have no way of overcoming this supposedly iron logic. As he put it, "The perpetual tendency of the race of man to increase beyond the means of subsistence is one of the general laws of animated nature, which we can have no reason to expect to change."

In Malthus' simple model, food supplies grow arithmetically or linearly (1, 2, 3, 4, 5) while the number of people grows geometrically (1, 2, 4, 8, 16). Left to their own devices, human populations will explode in size. Two forces counter this tendency, which Malthus named "preventive" and "positive" checks. Preventive checks include delays in or avoidance of childbearing, moral restraint, and legislation. (China's now-abandoned one-child policy being a heavy-handed example of the latter.) Malthus doubted that preventive checks would do the job.

The more powerful positive checks include war, plague, and famine. If people failed to restrict their reproduction through preventive checks then nature would take over. War would erupt as everyone scrambled for scarce resources, plagues would grow from overcrowding, and people would die as food ran out. Malthus, a man active in the Church, said we should facilitate the positive checks.

> "To act consistently, therefore, we should facilitate, instead of foolishly and vainly endeavoring to impede, the operation of nature in producing this mortality, and if we dread the too frequent visitation of the horrid form of famine, we should sedulously encourage the other forms of destruction, which we compel nature to use." [Malthus, 1798]

It's not hard to see Malthus as a comic book villain. His surname begins with the Latin *mal-*, meaning evil, bad, or disease. It suggests maliciousness, malignancy, and malintent. While artistically fitting, his name actually derives from malthouse, a building in which grains are prepared and stored for use in brewing. At first sight, Malthus might also appear the villain for his explicit opposition to the voices of Enlightenment optimism and progress, such as Condorcet and Godwin. However, Godwin's utopia was resonant with the deadly French Revolution, seeing Heaven-on-Earth as coming from radical social change with private property abolished and equality imposed from above by people who are rational, benevolent, and self-sacrificing. The subtitle of his book's first edition makes this opposition clear: Population "as it affects the future improvement of Society, with remarks on the speculation of Mr. Godwin, Mr. Condorcet, and other writers." (Gunderman, 2021) Malthus understood better than those particular optimists the importance of acknowledging and harnessing self-interest for the benefit of all, rather than relying on the dangerous brew of centralized power and the assumption of self-sacrificing benevolence.

In the imaginary ledger of historical plus and minuses, on the plus side Malthus inspired Charles Darwin in the development of his theory of natural selection. Darwin (and Wallace) saw the work of evolution in the fossil record and comparative anatomy. But how did it get a grip? The Malthusian principle of population entered the picture. In Darwin's autobiography, he recalls reading Malthus in 1838:

> "It at once struck me that under these circumstances favorable variations would tend to be preserved, and unfavorable ones to be destroyed. The result of this would be the formation of new species. Here, then, I had at last got a theory by which to work."

You can think of what Malthus calls the "principle of population" as a "steady-state" theory. Applied to any population of organisms, this principle says the population is always at or near the limit of the food supply. All the food is always being eaten and there is no extra to feed more people. If Condorcet and Godwin were to achieve equality, "distress for want of food would be constantly pressing on all mankind." In other words, rather than some being relatively impoverished, all would be absolutely impoverished. Malthus changed his mind in later editions, diluting what he wrote about the principle of population until it amounted to nothing.

Although Malthus was correct in opposing Godwinian forms of optimism, his overall and enduring effect has been to instill a desperate, zero-sum mentality in Western culture. The principle of population acts as a prison within which we regard

other people as threats to what we have. It distracts us from understanding what we might create, contribute, and trade. It traps us within a pessimistic, enervating, and anti-humanist worldview. As Brendan O'Neill puts it:

> "one of the great political conflicts of the modern era was between those who thought mankind had no choice but to live according to nature's limits, and that he had to modify his behavior and his procreation choices accordingly, and those who believed that mankind might be liberated from these alleged limits through the application of his wisdom, his imagination, his technology and his labor to create a world in which everyone would live free from need. [O'Neill, 2021]

Today, for anyone with open eyes, it is obvious how wrong Malthus was. Global population has increased from around one billion when Malthus published his book to almost eight billion today. In the United States, population has multiplied by approximately a factor of 85 over the same time. And yet the percentage of people starving has fallen. For decades, the absolute number of people starving has fallen. Calories per person has been rising along with population size.

This should be impossible according to the Malthus population principle. Malthus did not foresee advances in agricultural technology, most starkly realized in the "green revolution." Unsurprisingly, Malthus did not expect the introduction of contraceptives and did not expect the self-restraint exercised by people who have chosen to limit births to improve their standard of living. People have responded to fewer infant deaths by having fewer children. Wealthier countries tend to have fewer births, not more.

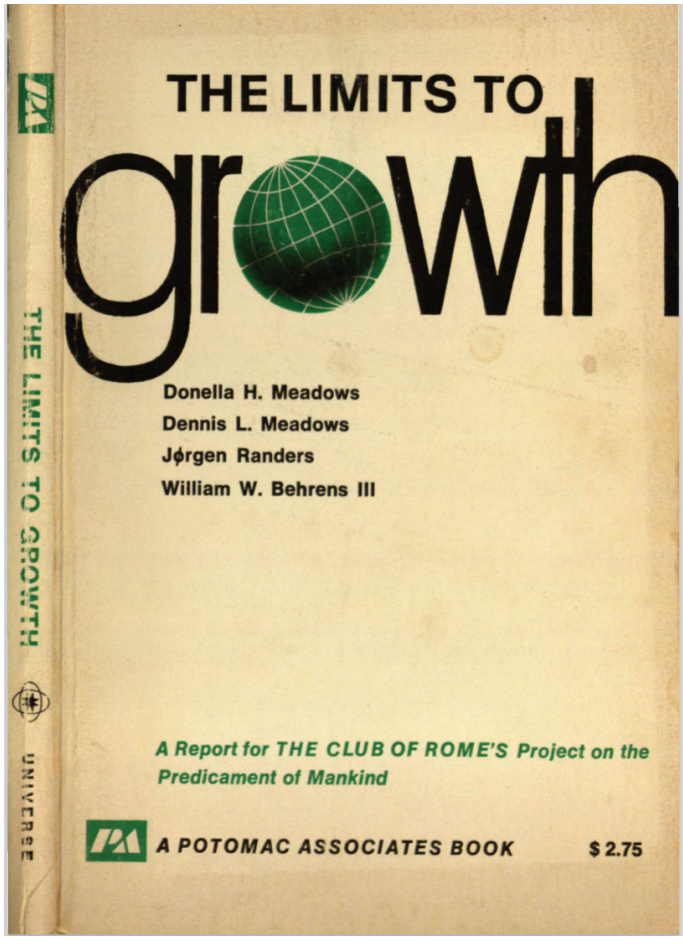
Malthus' limitationist view of human well-being was exceedingly simple. Later versions have at least given the appearance of greater sophistication, wrapping themselves in the metal cloak of the computer.

From System Dynamics to *Limits to Growth*, 1972

The method of 'system dynamics' was proposed in 1953 by John von Neumann. This enabled the complicated interaction of variables to be handled by a computer and the outcome determined. From the late 1950s to the late 1960s, system dynamics was restricted to corporate and managerial problems. Forrester became a professor at the new MIT School of Management in 1956. His work with managers at General Electric led to his 1961 book, *Industrial Dynamics*. An acquaintance with the former mayor of Boston led to conversations about how system dynamics might be used to tackle the problems of cities. The result of the Collins-Forrester collaboration was a book titled *Urban Dynamics.*

In 1970, Forrester was invited to a meeting of the portentously named Club of Rome, an organization devoted to solving what its members describe as the "predicament of mankind". Their worldview anticipated a global crisis due to the demands being placed on the earth's carrying capacity and its capacity for disposing of pollutants by the world's growing population. Of course, Forrester was convinced that system dynamics could help with the Club's mission. The second iteration of the resulting model, named WORLD2, was published in his 1973 book, *World Dynamics*. This model explored interrelationships between world population, industrial production, pollution, resources, and food.

Given the Club of Rome's remit, perhaps unsurprisingly the model showed a collapse of the world socioeconomic system sometime during the twenty-first century, if steps were not taken to lessen the demands on the earth's carrying capacity. In *World Dynamics*, Forrester wrote: "The Malthusian thesis has been true and at work at all times." Forrester called for a radical transformation of minds and societies, with wealth to be distributed (by force) equally.



The third version of the Malthusian model, WORLD3, was used by one of Forrester's graduate students, Dennis Meadows, and resulted in the infamous 1972 book, *Limits to Growth (Limits)*. World3 explored past and future relations among population,

capital, agricultural production, natural resources, and pollution. There was no mention of technological level, institutional factors, economics, policies, or innovation. The model consisted of 100 variables and 80 fixed parameters.

The report was launched with much fanfare at a widely reported conference in February 1972. The introductory blurb tells us:

> "A world where industrial production has sunk to zero. Where population has suffered a catastrophic decline. Where the air, sea, and land are polluted beyond redemption. Where civilization is a distant memory."

"This is the world that the computer forecasts. What is even more alarming, the collapse will not come gradually, but with awesome suddenness, with no way of stopping it." *Limits* project leader Meadows, told Time: "All growth projections end in collapse."

Or, as Ronald Bailey put it in his excellent critical study: "Billions of people will die horribly in a massive famine and/or epidemic bringing about the collapse of civilization sometime during the next century." [Bailey, 1993.] *Limits'* prophecy foresaw Four Horsemen of the New Age Apocalypse: depletion of nonrenewable resources, decline of food supplies, pollution, and overcrowding. There was no room for hope. If one limit didn't kill growth, another would. The message has been sustained since. In their 2004 update: In other words, "a few decades into the twenty-first century" (*Limits* 2004:170) things happen that can be described as a "collapse" or "vast human misery."

Context and reactions

The timing of the book's release was impeccable. By 1972, the sense of technological optimism had been largely crushed, economies were stagnating with rising unemployment and inflation, and the Vietnam War was a disastrous failure. The book sold millions of copies, boosted by the temporary success of the Arab oil embargo.

Rachel Carson had done much to set the new tone with her 1962 book *Silent Spring* which heightened fears about pollution (and caused massive death by leading to the banning of DDT) and launched the modern environmental movement. This was also just a few years after Paul Ehrlich's *The Population Bomb* (covered in my previous article), and two years after the deeply pessimistic first Earth Day in 1970.

As Bjorn Lomborg notes, "The genius of *The Limits to Growth* was to fuse these worries with fears of running out of stuff. We were doomed, because too many people would consume too much. Even if our ingenuity bought us some time, we would end up killing the planet and ourselves with pollution. The only hope was to stop economic growth itself, cut consumption, recycle, and force people to have fewer children, stabilizing society at a significantly poorer level." [Lomborg, 2013.]

The Club of Rome used the release of *Limits to Growth* as a public relations exercise, launching it with a press conference organized by public-relations firm Charles Kytle Associates and financed by the Xerox Corporation. The story of the hype, along with harsh criticism, appeared in *Science* a week after the book's release.

Interestingly, just four years after the publication of *Limits*, it was disavowed by its sponsors, the Club of Rome. They now said that the conclusions of that first report were not correct and that they purposely misled the public in order to "awaken" public concern. They got behind team growth. According to *Time*, the Club's strategy had been to jolt people out from the comfortable idea that growth could continue indefinitely. Having frightened everyone, the Club could now tell us the *true* truth in their elite attempt to transform the global economy. But the reversal was ignored.

Yet, although the about-face was not widely reported, criticism was plentiful. *Limits* sparked a thunderous denunciation from economists. Most of them either saw in it numerous technical errors or rejected its approach and assumptions. They also criticized it for disclosing so little of what the authors did, making close inspection impossible. John Maddox, then editor of *Nature*, called the book "sinister", and Economic Nobelist Gunnar Myrdal of Sweden dismissed it as "pretentious nonsense". One MIT professor said "What they're doing is providing simple-minded answers for simple-minded people who are scared to death. And that's a dangerous thing… This messianic impulse is what disturbs me."

In an April 2, 1972, article in the *New York Times*, Peter Passell and two co-authors described *Limits* as "an empty and misleading work ... best summarized ... as a rediscovery of the oldest maxim of computer science: Garbage In, Garbage Out". Passell found the study's computer model to be simplistic while the entire approach underestimated the role of technological progress in solving the problems of resource depletion, pollution, and food production. In his view, the entire endeavor was motivated by a hidden agenda: to halt growth in its tracks.

A team at Sussex University's Science Policy Research Unit reviewed the structure and assumptions of the models used and published their findings in *Models of Doom* [Cole, 1975]. They showed that the forecasts of the world's future are highly sensitive to a few unduly pessimistic key assumptions. They also found that the Malthusian bias of the Meadows' team's models failed to accurately reflect reality and that their methods, data, and predictions were faulty.

Also, shortly after the publication of *Limits*, mathematicians Vermeulen and De Jongh analyzed the world model. They found it to be "very sensitive to small parameter variations" with "dubious assumptions and approximations." "By changing three parameters by 10% each in 1975 the world population collapse

predicted by the model is averted." [Vermeulen, 1976] So, how did the model work and what did it say?

The guts of the model

The World3 model was built to start in the year 1900 using historically available data and then generate trend lines up to the year 2100 showing increases or decreases among population, industrial output per capita, food per capita, "nonrenewable" natural resources, and pollution based on varying assumptions. Trends from 1900 to 1970 were based on available data and projections were made for the following 130 years. The "standard run" of the model assumes "that there will be in the future no great changes in human values nor in the functioning of the global population-capital system as it has operated for the last one hundred years." [*Limits*, 123.]

Although the resource base in 1970 is about 95 percent of its 1900 value, "it declines dramatically thereafter, as population and industrial output continue to grow. The behavior mode of the system shown in figure 35 is clearly that of overshoot and collapse. In this run the collapse occurs because of nonrenewable resource depletion." Food, industrial output, and population grow exponentially until the shrinking resources force growth to slow. Population and pollution continue to increase for a time, but the former is ended by an increase in the death rate due to decreased food and medical services.

The authors say that the exact timing is not meaningful due to uncertainties and aggregation; it *is* significant

> "that growth is stopped well before the year 2100. We have tried in every doubtful case to make the most optimistic estimate of unknown quantities, and we have also ignored discontinuous events such as wars or epidemics, which might act to bring an end to growth even sooner than our model would indicate."

So, the real world will turn out worse than the model suggests! The next run doubles assumed resources (even though they think the original assumption was optimistic) but produces a similar outcome.

If you look at the graph on p. 124 (reproduced here), it clearly shows population growth going up at a constant or accelerating rate as of 2021, with pollution going up at an accelerating pace, and resources clearly plummeting. All of these are wrong. It shows food per capita going down, which is also wrong. In the discussion, the authors note that population growth rate after 1970 goes up – exactly the opposite of what happened in the real world between 1972 and the present. Okay, but that's only the standard run. What about the others?

I will spare you, dear reader, from detailing all the modifications to the standard run. The book looks at 12 scenarios. After the standard run comes a group of six "technological scenarios."

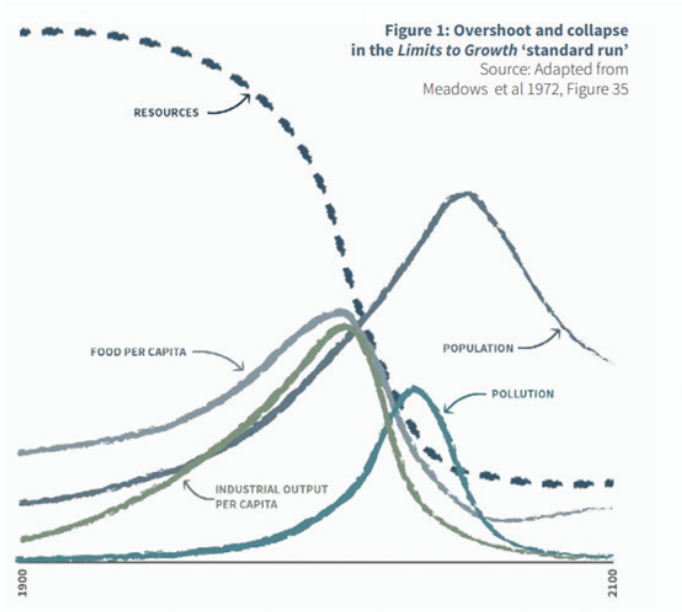


Figure 1: Overshoot and collapse in the *Limits to Growth* 'standard run'
Source: Adapted from Meadows et al 1972, Figure 35

These assume new advances in technology or that society would increase the amount of resources available (especially energy), increase agricultural productivity, reduce pollution, or limit population growth. The final set of five "stabilization" scenarios consider what the model says would happen if either population growth, or industrial output, were stabilized.

After considering the first two groups of model runs, the authors tell us that their world model: "has led us to one conclusion that appears to be justified under all the assumptions we have tested so far. **The basic behavior mode of the world system is exponential growth of population and capital, followed by collapse.**" The authors then go on to attack the green revolution for "increasing inequality."

To achieve a scenario that avoids collapse and remains stable through the 21st century, population must somehow be stabilized by "setting" the birth rate equal to that in 1975. The investment rate also must be "stabilized". Starting in 1975, resource consumption must be cut to a quarter of its 1970 value (which was much lower than today), essentially condemning the vast majority to poverty. The economic preferences of "society" are "shifted" from goods to services. Pollution per unit of production is cut by 75% from 1975 levels. To counter the "rather low value of food per capita," capital is "diverted" to food production at whatever cost, but this leads to rapid soil depletion. Resource depletion and pollution are also decreased by attempts to increase the average lifetime of industrial capital.

I've put terms such as "setting", "stabilized", and "shifted" in scare quotes to draw attention to these seemingly innocuous words. **The authors are saying that, to avoid collapse and achieve a future that's sustainable for a few decades (but ultimately doomed), nine policies must be enforced on**

everyone, throughout the world, over the decades without letup. All of these policies require coercion and centralized control.

To avoid collapse – at least in this century – the model tells us we will have to shrink the population drastically from today's level. We will have to reduce global life expectancy to just under 70 years. Global income per capita can never be allowed to rise above half the level in 1972 USA. Those who say the critics of *Limits* misrepresent it because not all runs quickly lead to collapse are being disingenuous. The models assert that we can only avoid collapse through the current century by keeping everyone poor and hungry.

Despite that, in the following century collapse will still happen, say the models. We can only trade off time against misery. Or, as the authors delicately put it, "The longer a society prefers to maintain the state of equilibrium, the lower the rates and levels must be." On the bright side, we can choose whether civilization collapses from excessive pollution, lack or resources, or lack of people. So, that's nice.

The fatal errors in *Limits*

Here's one resource that is not scarce: Good critiques of *Limits*. Elodie Vieille Blanchard (2010) identifies four major critiques made between 1973 and 1992. A study from The Science Policy Research Unit of Sussex University argued that the assumptions underlying the *Limits* model were excessively pessimistic. Eminent futurist Herman Kahn and the Hudson Institute argued that *Limits* underestimated technology's role in mitigating resource depletion. Scholars at the Bariloche Foundation in Argentina made a similar case but also argued that pollution is easier to control than assumed in *Limits*.

The Nobel Prize winning economist William Nordhaus argued that *Limits* failed to comprehend the role played by prices in regulating the use of resources. He also agreed with critics that *Limits* had undervalued the role of technology in solving problems of pollution and of potential resource scarcity. Impending scarcity leads to higher prices and provokes people to search for substitutes and to improve technologies used to exploit natural resources.

One of the best and most accessible critiques is in chapter 4, "The Depletion Myth" of Ronald Bailey's *Eco-Scam: The False Prophets of Ecological Apocalypse*. Bailey notes that, "Like all depletionists, Forrester assumed that natural resources are a fixed quantity." This echoes a point made, among others, by economist Julian Simon. Simon pointed out that "Dennis Meadows predictably went wrong by using the known-reserves concept." Meadows estimated that the global supply of aluminum would be exhausted in 49 years (i.e., in 2021!), despite aluminum being the most abundant metal in the Earth's crust.

Ronald Bailey

A related error was to make no allowance for technological progress in the standard run (and insufficient allowance in other simulations). Simon also pointed out that Meadows looked only at high-grade bauxite when lower grades are far more abundant. The affordability of aluminum has gotten better, not worse, in the decades since.

Bailey argues that no exhaustible resource is essential or irreplaceable. The price mechanism not only spurs investment in discovering new reserves of a resource, it also promotes conservation and substitution. A deeper point that the limitationists or depletionists fail to grasp is that what counts as a resource changes over time. The shipbuilding industry relied primarily on wood until the 1800s. Starting in the 1500s, people worried that wood would run out. Instead, boats were made of iron and steel, and then wood became plentiful again.

Resources never "run out." As Julian Simon argued in *The Ultimate Resource* [Simon, 1998], human ingenuity creates new resources as required from the raw materials of the universe. We will never run out of copper because its price will increase as it becomes scarcer, stimulating the discovery of more deposits, more recycling, new methods that use less of it, and better substitutes.

Bailey notes that

> "Forrester's model assumes that 'as crowding rises toward five times the present population, the death rate is taken to rise ever more steeply and to reach three times the present rate, for a crowding ratio of 5.' However, countries that are already well beyond

> Forrester's crowding ratio of 5 show no increase in their death rates."

On the contrary, their death rates continue to fall.

Pollution plays a major role in *Limits*. If we aren't stopped by the other limits, we will choke to death on our own wastes and emissions. The World3 model contradicts the observed facts. As population has grown in the USA and other developed countries, the most dangerous air pollutants have declined. Following the development curve, US water pollution worsened until 1960 but then improved. We see the same pattern around the world.

Bailey notes Forrester's strange assumption that as capital investment increases, pollution must also increase. Capital investment can reduce pollution as in the cases of wastewater treatment, sulfur-removing scrubbers on electricity generation lands, and improvements in mining and drilling.

Bailey asks: "How could Forrester, the Meadowses, and the Club of Rome be so far off? One answer is that the computer model was designed to confirm what its designers already believed." As others have shown, the assumptions of the model were tuned to produce the desired outputs. This and similar models share the false assumption of diminishing returns: Additional people who must work and live with the original fixed supply of land and capital implies less income for each person. As Simon, again, explains: This ignores "the contribution of additional people to technological advance through the creation of knowledge and through economies of scale." [Simon, 1998, 478]

Another issue with the model is that the authors stack the deck by letting some things grow exponentially and others not. In all models, population, capital, and pollution grow exponentially, but technologies for expanding resources and controlling pollution are allowed to grow, if at all, only in discrete increments that don't show any obvious exponential character.

As several critics including Peter Vajk have observed, the model "assumes that the Earth is a closed system, and that throughout this century and the next, the only material and energy resources available for human use will be those of the planet Earth." [Vajk, 1978] Using a framework paralleling that of *Limits*, Jeremy Rifkin's 1980 book, *Entropy: A New World View*, made the same mistake. You can't argue for limits by invoking the second law of Thermodynamics because the Earth is not a closed system.

Adrian Berry's boundary-stretching 1974 book, *The Next Ten Thousand Years*, poked holes in vital elements of the World3 model. Remarkably, pollution was undefined and represented by a single variable in every model. "How was this pollution measured? By the density of smog over Los Angeles? By the number of discarded beer cans found each year in a given district? By the surface area of marine oil slicks in latitude and longitude such-and-such?" [Berry, 1974] Resources, like pollution, are lumped together in a single undefined variable.

Since "resources" covers an enormous range of known and yet-unknown quantities, how can any sensible claim be made that resources would run out by a certain date? "A Club of Rome model written in 1900 would surely have predicted that civilization would collapse long before 1976." In 1900, no one knew of the use of uranium or nuclear energy. We knew nothing of plastics, stainless steel, the use of titanium, nor such techniques as laser welding and the uses of superconductivity.

The authors of *Limits* projected the exhaustion of aluminum, copper, gold, lead, mercury, molybdenum, natural gas, oil, silver, tin, tungsten, and zinc by 2013. In reality, commodity prices have generally fallen to about a third of their level 150 years ago. Bjorn Lomborg pointed out the 98% drop in consumption of mercury along with a 90% decline in price thanks to technological innovations. [Lomborg, 2013] Since 1946, new discoveries and new technologies have increased supplies of copper, aluminum, iron, and zinc more than consumption.

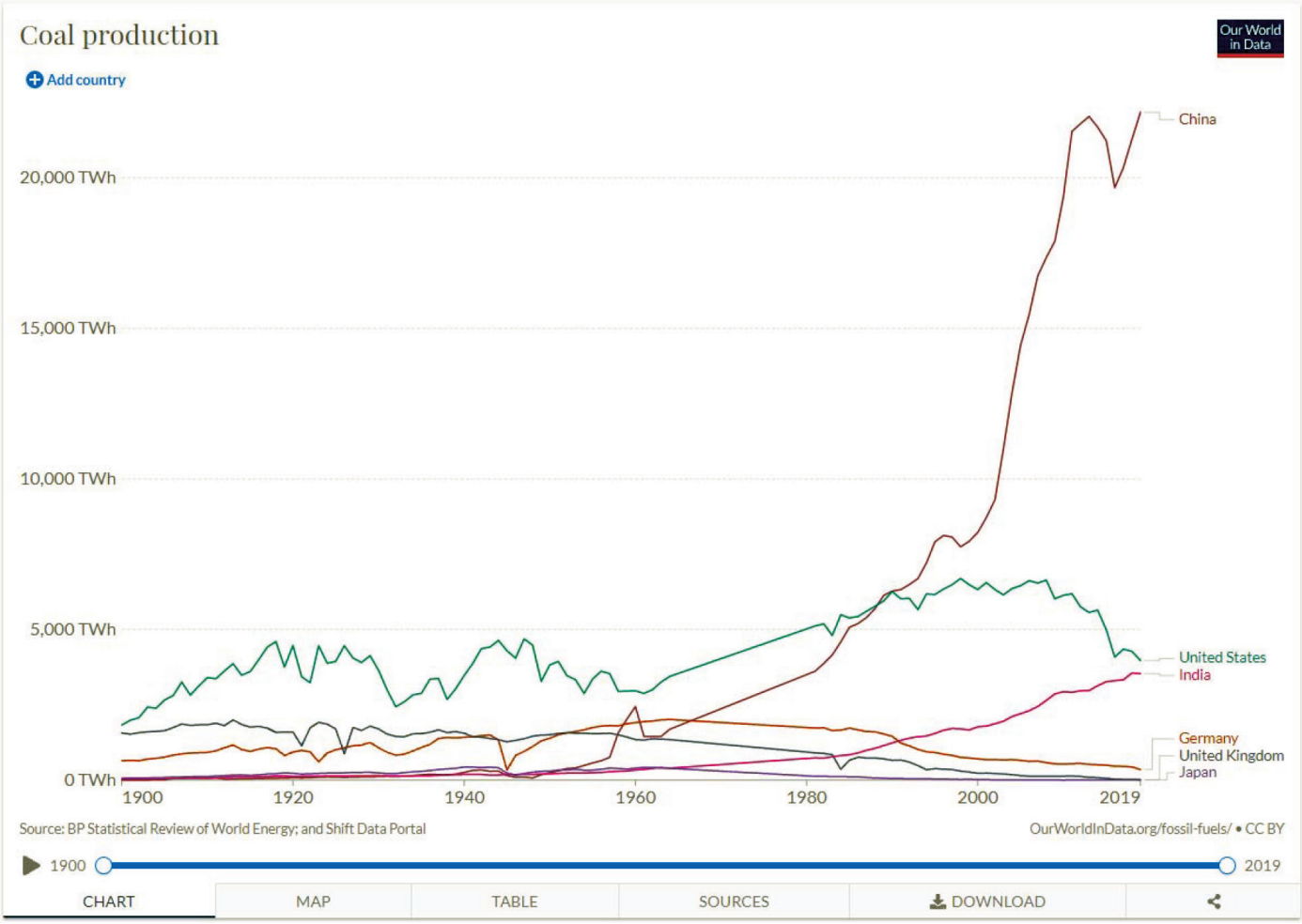
Rather than running out in the early 1990s, oil and natural gas reserves are larger than they were in 1970 despite increased consumption. Shale gas alone has vastly increased gas resources in the US. Canada has potentially record-breaking reserves. The only threat to resources comes from ill-advised energy policies enforced by governments. While *Limits* sees collapse ahead, even the far-from-cheery Intergovernmental Panel on Climate Change estimates that global GDP per capita will increase 14-fold over this century and 24-fold in the developing world.

All the trends are in a direction exactly contrary to that projected by *Limits*. That's true of population growth, food supply, malnourishment, and pollution. Despite the abject failure of *Limits* to reflect reality, the mindset it embodies is still shaping the thinking of both the elite and the public.

Failure to Learn

In the 1992 follow-up, *Beyond The Limits*, the authors maintain that *Limits* was right and only got the dates wrong. This would be like the authors of *Dow 36,000* saying that he *only* got the dates wrong since the Dow crossed the 36,000 line 20 years after he predicted that it would. That's unfair to Glassman and Hassett. They at least got the direction of the Dow right. *Limits* got the direction wrong for almost all measures. Suppose a weather forecaster asked not to be judged wrong because the snowstorm that they forecast for tomorrow was off by four months.

The thirty-year followup to *Limits to Growth*, published by the Club of Rome in 2004, and two subsequent modelling studies in 2008 and 2014 from the University of Melbourne concluded that the world is tracking on *Limits to Growth*'s 'standard run' projection. The work, led by Swedish and Icelandic teams, concluded that most of the resources they studied had either already reached peak production or will do so within the next 50 years. Coal production will peak in around 2015-20 and 'peak energy' around the same period.



How could they make these claims with a straight face? Historical and current data show that the model was wrong, and their forecasts are *already* wrong. The coal claim is readily dismissed, as shown in this graph.

In a stunning display of motivated reasoning, a 2020 report published by consulting firm KPMG used updated data to defend the methods and conclusions of *Limits*. [Herrington, 2020] Herrington (first name, "Gaya") claims that the BAU2 and CT scenarios best match the data since 1972. BAU is "business as usual 2." This is the same as the standard run but with a doubling of the natural resources. CT is not defined but is an updated version of *Limits*'s sixth scenario, "World model with 'unlimited' resources, pollution controls, and increased agricultural productivity.

This claims the BAU2 and CT scenarios best match the data. BAU2 still shows a collapse, but industrial output doesn't start falling until about 2035, although food peaks around 2025, and "pollution" continues to rise. The latter doesn't sound bad, but the model run found pollution skyrocketing, industrial output per capita, food per capita, and population crashing.

The 2020 update has all the problems of the 1972 version. The original *Limits* was grossly over simplistic. As we have seen, for example, it has a single factor called "pollution" that pretended to represent something meaningful. In the new version, pollution apparently means carbon dioxide plus plastic. This is not an improvement.

Herrington compounds the errors of *Limits* by arguing that things are actually "considerably worse than the Club of Rome's projections." As you might guess, this is because there is no wailing and crying in the 1972 report about climate change (or "climate crisis"), ocean acidification, and other panics of the day. Herrington has not learned from the last half century and is doubling down with error.

I have to say that I found the 2020 report and some of the other research for this article discouraging. Motivated cognition turns up frequently among those claiming that the thoroughly disproven and discredited *Limits* may have been wrong about the dates but was essentially correct. "Oops, the math was a bit off. Let's do use the same assumptions and do it again." This is the same kind of apocalyptic mindset seen in religious predictions

of the end of the world. Faith comes before theory, and theory shapes the evidence.

California preacher Harold Camping first predicted Judgment Day for September 6, 1994. When it didn't happen, he rescheduled the end of the world for September 29 and then to October 2. Not one to be discouraged, in 2005 Camping predicted the Second Coming of Christ for May 21, 2011 with millions dying daily until the final end on October 21, 2011. This was of a piece with other serial failed doomsayers, such as the Millerites. They even had a term for it: The Great Disappointment.

These endlessly repeated prophecies of doom are not merely amusing mistakes. They cause us to "obsess over misguided remedies for largely trivial problems, while often ignoring big problems and sensible remedies." [Lomborg, 2013] These dramatic scenarios pull our attention away from the real threats to life and wellbeing. Poverty immiserates and kills huge numbers while around 15 million people per year die of easily curable diseases. The solution to this suffering and death is economic growth. Yet the policies proposed to counter the imagined crisis scenarios destroy wealth and slow economic growth.

Limits to Growth came out in the same year that Alcor was founded. Champions of life want more of Alcor and less – much less – of *Limits*.

In part 4, I expect to look at claims of a recent trend toward "dematerialization" or doing more with less. I also want to examine the recurring idea of "turning points" and "precipices," along with the economics of demographic transitions. ■

References

Bailey, Ronald, *Eco-Scam: The False Prophets of Ecological Apocalypse*. St. Martin's Press, 1993.

Berry, Adrian, *The Next Ten Thousand Years*. Jonathan Cape, 1974.

Barnett, Harold J., and Chandler Morse, *Scarcity and Growth: The Economics of Natural Resource Availability*. Resource for the Future, and John Hopkins University Press, 1963.

Blanchard, Elodie Vieille, "Modelling the Future: An Overview of the 'Limits to Growth' Debate." *Centaurus* 52:91−116, 2010.

Cole, H.S.D., and Christopher Freeman, et al., *Models of Doom: A Critique of the Limits to Growth*. Universe Books, 1975.

Forrester, Jay, 1973. *World Dynamics*. Cambridge, Mass.: Wright-Allen Press.

Franke, Richard W., "The Limits to Growth Study: Some Thoughts about Its Relation to Sustainability." May 12, 2015, updated February, 8, 2020.

Gunderman, Richard. "Malthusian Misanthropy." AEIR, October 11, 2021

Herrington. Gaya, "Update to Limits to Growth: Comparing the World3 model with empirical data." KPMG, *Journal of Industrial Ecology*, 2020: 1-13

Jackson, Tim and Robin Webster, "Limits Revisited: a review of the limits to growth debate." Limits2growth.org, April 2016

Lomborg, Bjorn, "The Limits to Panic", Project Syndicate, Jun 17, 2013 https://www.project-syndicate.org/commentary/economic-growth-and-its-critics-by-bj-rn-lomborg

Malthus, Thomas, *An Essay on the Principle of Population as It Affects the Future Improvement of Society, with Remarks on the Speculations of Mr. Godwin, M. Condorcet, and Other Writers*. 1798

McAfee, Andrew, *More from Less: The surprising story of how we learned to prosper using fewer resources and what happens next*. Scribner, 2019.

Meadows, Donella H., Dennis L. Meadows, Jorgen Randers, William W. Behrens III, *The Limits to Growth: A Report for The Club of Rome's Project on the Predicament of Mankind*. Potomac Associates, 1972

Nordhaus, William D. "Climate change: The Ultimate Challenge for Economics" Prize Lecture, December 8, 2018 by William D. Nordhaus https://www.nobelprize.org/uploads/2018/10/nordhaus-lecture.pdf

O'Neill, Brendan, "Internalizing Malthus." Spiked Online, September 24, 2021. https://www.spiked-online.com/2021/09/24/internalising-malthus/

Pielke Jr., Roger, and Justin Ritchie. "How Climate Scenarios Lost Touch with Reality." *Issues in Science and Technology* 37, no. 4 (Summer 2021): 74–83.

Simon, Julian L. *The Ultimate Resource 2*. Princeton University Press; Revised ed. Edition, July 1, 1998.

"Origin of System Dynamics", System Dynamics Society. https://systemdynamics.org/origin-of-system-dynamics/

Vajk, Peter, *Doomsday Has Been Cancelled*. Peace Press, 1978.

Vermeulen, P.J., and D.C.J. de Jongh, "Parameter sensitivity of the 'Limits to Growth' world model." *Applied Mathematical Modelling*, Volume 1, Issue 1, June 1976, Pages 29-32.

Worrall, Eric, "Claim: 1972 Club of Rome End of World Prediction Still on Track, Thanks to Climate Change." Wattsupwiththat, July 26, 2021. https://wattsupwiththat.com/2021/07/26/guardian-2040-club-of-rome-end-of-world-prediction-on-track-thanks-to-climate-change/

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The Alcor Board of Directors is pleased to announce the formation of the **Alcor Longevity Circle of Distinguished Donors**. This new organization will honor those members and their foundations that have donated in excess of $100,000 over the past few years to support Alcor and its affiliated organizations. In addition to being recognized in Alcor publications and at conferences and other events, members will also be entitled to:

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- A unique, professionally designed and engraved memento of their membership.

These benefits are, of course, overshadowed by the immense gratitude members' and patients' families will always have for these especially generous individuals. New levels of membership (higher and lower levels of participation) may also be announced in the future. ■

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Peak Oil Hysteria

By Max More, Ph.D.

Life extensionists and people with cryonics arrangements are battered with endless supposed reasons to avoid the future. One of the ever-popular reasons is the claim that we are rapidly running out of resources, especially energy. And if not energy, definitely oil. The peak oil discussion illustrates some of the points made in my Getting Better series, including the abundance of scarcity panics, excessively pessimistic forecasts, and the failure to allow for technological advance and the effects of incentives in the market.

My point here is *not* to argue that we will never reach a peak in oil production. At some point we probably will, and it will not be a problem. If you keep predicting the same thing over and over again, after enough time you may hit the mark. Every year, some commentators make a close prediction of the stock market's performance for the year ahead. That doesn't prove their models were right or that they are smarter than everyone else. No one gets those predictions right consistently.

As I write this in mid-October 2021, oil prices have risen to levels not seen since 2014. Whenever oil enters one of its periods of higher prices, we start hearing a lot about "peak oil" and "the end of oil."

What exactly is "peak oil"? It can refer to the maximum level of consumption in a country or in the world. It can refer to the maximum level of consumption or production of oil per person. Mostly it refers to a level of oil production higher than any in the past and higher than any to come in the future.

Peak oil is sometimes used to mean or to imply two other things: The end of oil; and the end of fossil fuels. Pessimists may point to a supposed peak in oil production and take that to imply that we will run out of oil completely – and sooner rather than later. This does not follow. The production of a commodity can peak and then decline but never reach zero. In fact, that is typically the case. Like most commodities, certainly including oil, some reserves are relatively easy to exploit while others are increasingly difficult and expensive. As the price rises, the less accessible reserves will be tapped. At the same time, economic activity shifts away from the commodity – perhaps by reducing activities dependent on it, or by replacing it, or by recycling it, or by becoming more efficient.

Others take peak oil as a stand-in for the end of all fossil fuels. The demonization of fossil fuels comes out of an essentially religious belief in which human activity is evil and should be minimized, the Earth is all-good, and carbon resulting from human activity and carbon emissions are especially evil outcomes. (The devotees of this religion usually avoid the give-away word "evil" in favor of "greedy," "rapacious," or "destructive.") This religion even shares with Catholicism the idea of buying "indulgences" but, in this case, they are called "carbon offsets."

The only fossil fuel perhaps seen as worse than oil is coal. Just like oil, people have been declaring the end of coal for many decades – for even longer than oil. In 1865, Stanley Jevons predicted that England would run out of coal by 1900, and that England's factories would grind to a halt. Jevons was not stupid. Far from it. He was a brilliant man with major achievements in economics (including founding the "marginal revolution"), logic, and geometry. He stated his gloomy conclusion in *The Coal Question* (1865). Although he got that wrong, he also expressed the idea that is still known as the "Jevons paradox": increases in energy production efficiency lead to more, not less, consumption. This has usually turned out to be correct, at least until recently. I will return to this idea in a later piece in the Getting Better series.

Failed predictions of peak oil

The claim that we have reached peak oil production and that production will fall has been around for over 135 years. 1885 got this tradition off to a strong start. In that year, the US Geological Survey declared that there was "little or no chance" of oil being discovered in California. The Pennsylvania State Geologist asserted that "the amazing exhibition of oil was only a temporary and vanishing phenomenon – one which young men will live to see come to its natural end." Also in 1885, John Archbold, original partner of John D. Rockefeller in Standard Oil boasted: "I'll drink every gallon of oil found west of the Mississippi."

1919, *Oil and Gas News*: "In meeting the world's needs, however, the oil from the United States will continue to occupy a less and less dominant position, because within the next two to five years the oil fields of this country will reach their maximum production and from [then] on we will face an ever-increasing decline."

1937: The March 9, 1937 B*rooklyn Daily Eagle reported that* Capt. H. A. Stuart, director of the naval petroleum reserves, told the Senate Naval Affairs Committee: "We have been making estimates for the last 15 years. We always underestimate because of the possibility of discovering new oil fields. The best information is that the present [United States] supply will last only 15 years. That is a conservative estimate."

Pub.	Made by	Peak year/range	Pub.	Made by	Peak year/range
1972	Esso	About 2000	**1999**	Parker	2040
1972	United Nations	By 2000	**2000**	A. A. Bartlett	2004 or 2019
1974	Hubbert	1991–2000	**2000**	Duncan	2006
1976	UK Dep. of Energy	About 2000	**2000**	EIA	2021–2067; 2037 most likely
1977	Hubbert	1996	**2000**	EIA (WEO)	Beyond 2020
1977	Ehrlich, et al.	2000	**2001**	Deffeyes	2003–2008
1979	Shell	Plateau by 2004	**2001**	Goodstein	2007
1981	World Bank	Plateau around 2000	**2002**	Smith	2010–2016
1985	J. Bookout	2020	**2002**	Campbell	2010
1989	Campbell	1989	**2002**	Cavallo	2025–2028
1994	L. F. Ivanhoe	OPEC plateau 2000–2050	**2003**	Greene, et al.	2020–2050
1995	Petroconsultants	2005	**2003**	Laherrère	2010–2020
1997	Ivanhoe	2010	**2003**	Lynch	No visible peak
1997	J. D. Edwards	2020	**2003**	Shell	After 2025
1998	IEA	2014	**2003**	Simmons	2007–2009
1998	Campbell & Laherrère	2004	**2004**	Bakhitari	2006–2007
1999	Campbell	2010	**2004**	CERA	After 2020
1999	Peter Odell	2060	**2004**	PFC Energy	2015–2020

A selection of estimates of the year of peak world oil production, compiled by the United States Energy Information Administration

1939: The US Department of the Interior said that American oil supplies would last only another 13 years.

1941: US Department of the Interior: "American oil supplies will last only another 13 years."

1956: Hubbert: "M. King Hubbert of the Shell Development Co. predicted [one year ago] that peak oil production would be reached in the next 10 to 15 years and after that would gradually decline."

1977: US Department of Energy Organization Act: "As a nation, Americans have been reluctant to accept the prospect of physical shortages. We must recognize that world oil production will likely peak in the early 1990's, and from that point on will be on a declining curve. By the early part of the 21st century, we must face the prospect of running out of oil and natural gas."

1980, Dr. Hans Bethe, winner of the 1967 Nobel Prize in Physics, claimed that the world will reach peak oil production before the year 2000. Then production of oil worldwide will drop to zero over about 20 years.

1998: *Scientific American* stated: "Predicting when oil production will stop rising is relatively straightforward once one has a good estimate of how much oil there is left to produce." (They predicted the peak within ten years; that was 20 years ago.)

Many of these predictions are from May, 2018, and Novak, 2014.

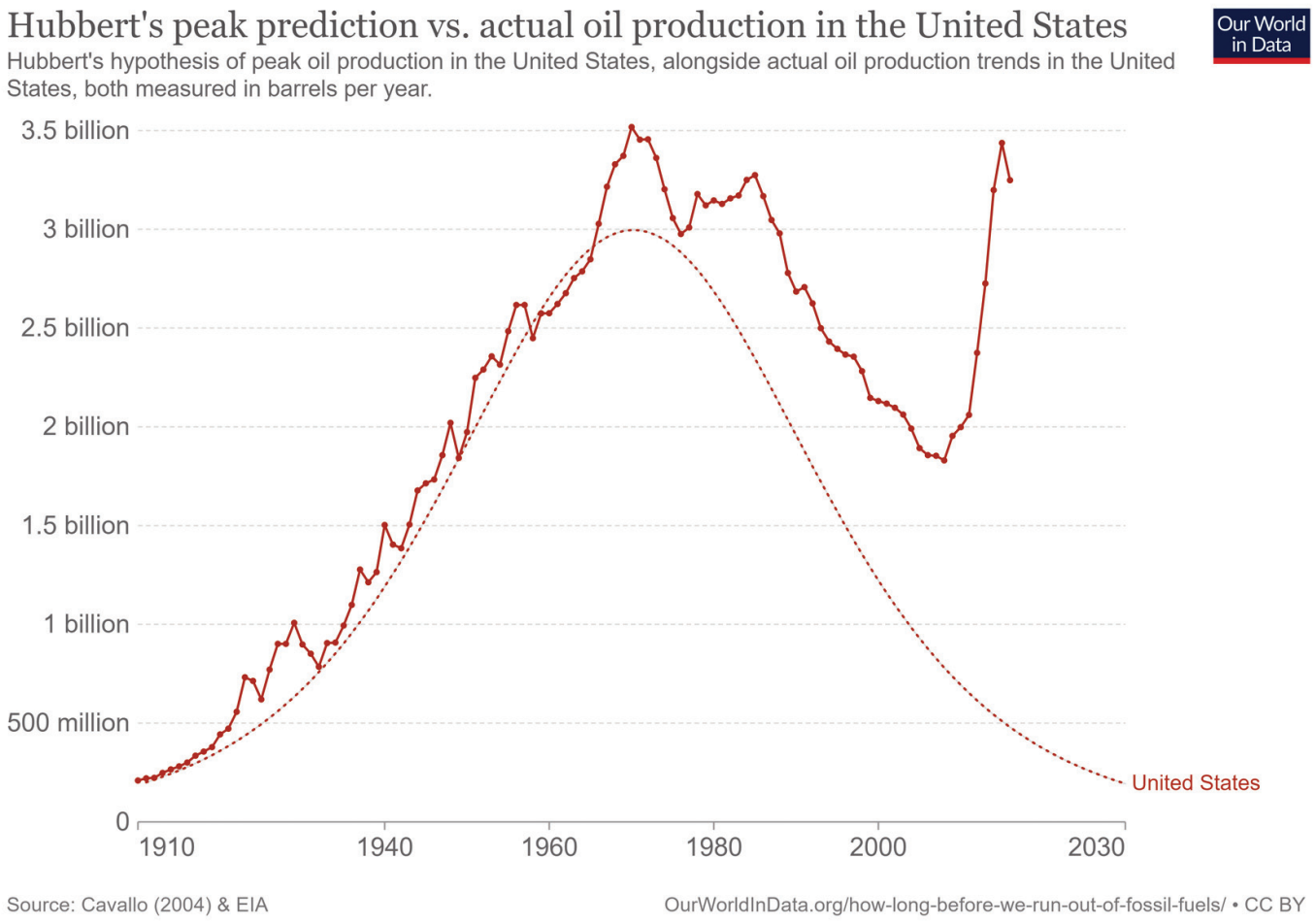
Note, in the above, the assumptions that a peak will be followed by "running out" and a "drop to zero."

Hubbert's Peak

Of the failed predictions above, by far the most discussed is the one by M. King Hubbert. Hubbert projected a bell curve for oil production in the United States. The peak of the curve was to be reached in 1970 at 3 billion barrels per year. He wasn't too far off with this peak estimate, at least for a few decades. The actual peak came 17% higher at 3.52 billion barrels per year.

Hubbert also projected future world oil production but didn't achieve even a temporary hit. He expected world production to peak at 12.5 billion barrels per year in the year 2000 or close. As of 2016, world production was 29.4 billion barrels per year.

In a 1989 interview shortly before his death, Hubbert acknowledged that his model was not only wrong but far from scientific. The only way his model came close was if restricted to the USA and to "conventional" oil production. His peak oil prediction assumed the total recoverable reserves in the US and our offshore, came to only 150-200 billion barrels. (The recent Department of Energy estimate is 400 billion barrels.) That



estimate was made before the shale boom beginning in 2006, such as the Bakken and Eagle Ford sources. These are conventional sources. But Hubbert also failed to allow for unconventional sources, and these are far larger than conventional.

The Bell curve that Hubbert used was the wrong function. The actual logistic curve has a long fat tail due to secondary and tertiary oil recovery. By limiting his projection to conventional oil, he missed all "heavy oil" such as the massive reserves in the Venezuelan Orinoco and the Canadian "tar" sands. His estimate also failed to factor in technological advancements such as fracked shale oil.

Universal agreement on the definition of "conventional oil" is lacking. "Conventional oil" has been defined as viscosity API>10, produced from a reservoir with >5% porosity and permeability >10 millidarcies. That excludes all the heavy oils and fracked oils. Others define it as any oil less dense than water, or as oil from higher permeability rocks. Yet others count ultra-deep-water production as unconventional because of the associated high costs. For purposes of usable energy, it doesn't matter what is conventional or unconventional. The definition game is merely a way of making a prediction come out correct.

Technology, ingenuity, and determination

Although the oil industry is often demonized today, its history illustrates the life-sustaining, energy-delivering effects of technology, ingenuity, and sheer determination.

The excessively pessimistic oil projections suffer from many of the same problems as other predictions of hard limits and "running out" of resources. They take currently proven reserves and assume that is all we have to work with. They may add up "economically feasible" reserves based on current exploration and extraction costs. More generously, they may estimate "total recoverable reserves." Or they may add up proven reserves. None of these are the likely actual total resources.

Oil discovery and production has always been highly dependent on technical and procedural innovations. Exploration technologies have developed from ancient "spring poles," to steam-powered percussion cable-tools, to modern rotary rigs with diamond bits that can drill miles deep into the earth. In 1802, drillers took 18 months to drill through rock to reach 58 feet using a spring pole. Today, the Z-44 Chayvo Well in the Russian Far East has a shaft 40,000 feet deep. This is the equivalent of

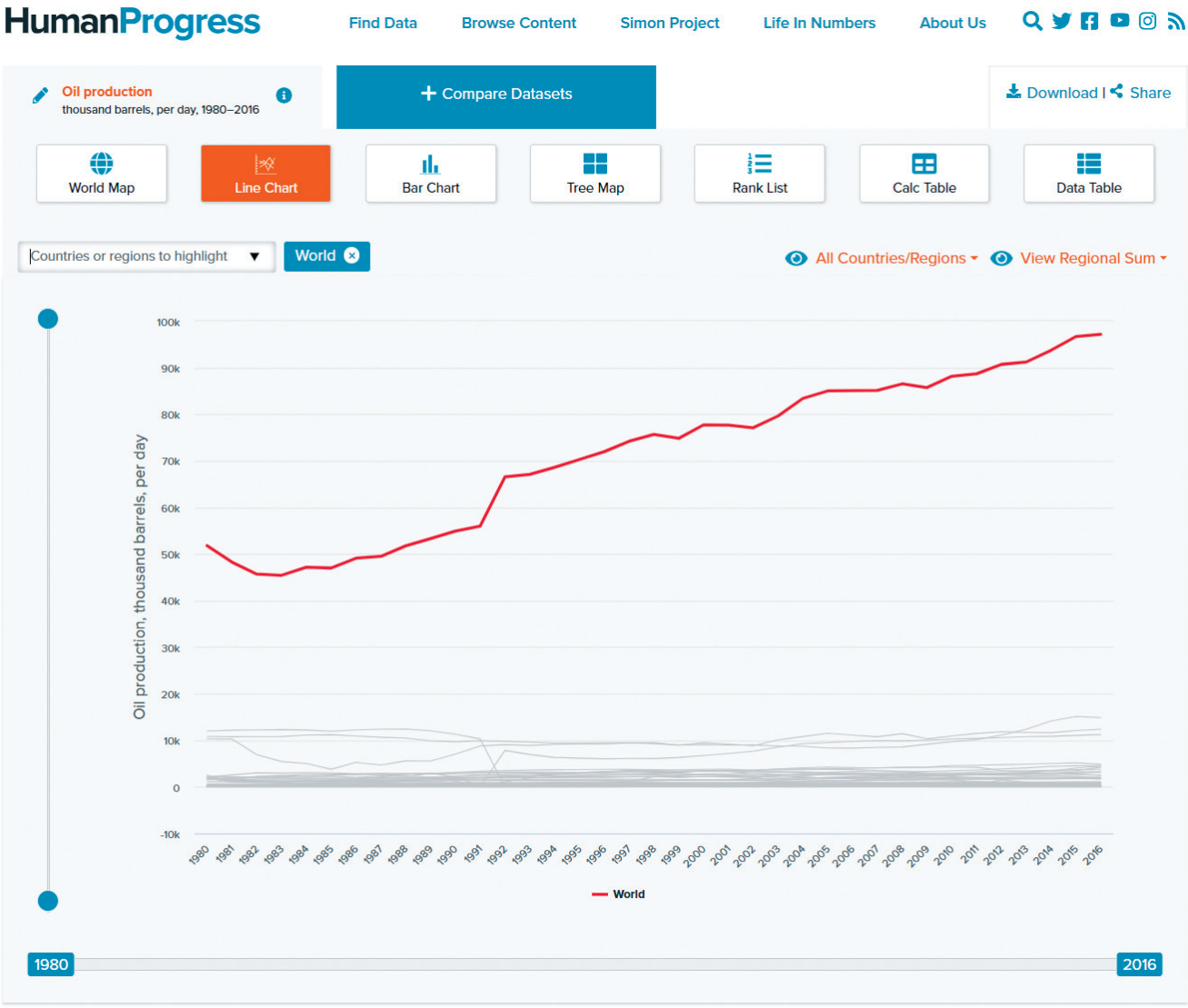
15 times the height of the world's tallest skyscraper, the Burj Khalifa in Dubai. [Desjardins, 2017]

Engineers and entrepreneurs brought us from spring poles to cable-tool drilling and the wooden derrick. They added steam power and smart mechanical engineering to the mix, as well as rotary drilling, the tri-cone bit, wireline logging, coring and rock core analysis, surface mapping, reflection seismic mapping, horizontal drilling, water flooding, and the slick water frack and microseismic monitoring. The history of the extraction of this resource stands as a stunning story of human achievement. For more historical detail, see the article by the aptly named Wells. [Wells & Wells, 2006; also, May 2021.]

Predicting the future of oil production is a risky business. Overall trends seem safer than short-term forecasts, but new discoveries can be of such a magnitude that they throw off the trajectory of a trend – and may completely derail it if the discovery is technical rather than geological. In 2016, the largest ever discovery of crude oil was made under parts of West Texas in the "Wolfcamp shale" formation. The US Geological Survey (USGS) estimated 20 billion barrels of accessible oil, as well as 16 trillion cubic feet of natural gas and 1.6 billion barrels of natural gas liquids.

"The fact that this is the largest assessment of continuous oil we have ever done just goes to show that, even in areas that have produced billions of barrels of oil, there is still the potential to find billions more." Those are the words of Walter Guidroz, program coordinator for the USGS Energy Resources Program. He attributed that potential to the introduction and refinement of hydraulic fracturing and horizontal drilling, and correctly noted that "Such advances can have significant effects on what resources are technically recoverable." [Collier, 2016]

Beware of estimates by government agencies of what the oil industry will find and produce. They typically underestimate drastically. For instance, the government originally forecast that Alaska's North Slope would yield 10 billion barrels. It had



produced 16 billion barrels by 2016 and already developed areas are expected to produce around 30 billion barrels. Many areas of Alaska have not been explored for oil, including the Arctic National Wildlife Refuge (ANWR).

The 2016 USGS estimate for undiscovered oil in the Bakken play of Montana and North Dakota is 25 times larger than the same agency's 1995 estimate. In 1987, the MMS (now the BOEM) undiscovered resource estimate for the Gulf of Mexico was 9 billion barrels. Today it is 45 billion barrels. [Middleton, 2016]

What are "reserves"?

The concept of "proven reserves" can be useful for corporate planning in the near-term. It's not an accurate way of understanding long-term availability of a commodity, and even less accurate in understanding the services we derive from a commodity. Proven reserves are defined as "the quantity of energy sources estimated with reasonable certainty, from the analysis of geologic and engineering data, to be recoverable from well-established or known reservoirs with the existing equipment and under the existing operating conditions."

Proven reserves are classified as having a 90% or greater likelihood of being present and economically viable for extraction in current conditions. Within the oil industry, proven reserves are also referred to as P1 or P90. Contrast this with "**probable reserves**" which are crude oil reserves calculated to be at least 50 percent likely to be recovered through drilling. Then there are possible reserves, defined with misleading precision as those that "refer to oil reserves for which the estimated likelihood of successful extraction is between 10% and 50%—assuming that existing equipment is used and the extraction is carried out under typical conditions." [Chen, 2021]

Beyond all of these are total recoverable resources. This depends on what is considered recoverable – something that changes over time, just like the amount of time after clinical death before someone can be revived. [See Sources of Services, from Simon, 1998, p.47]

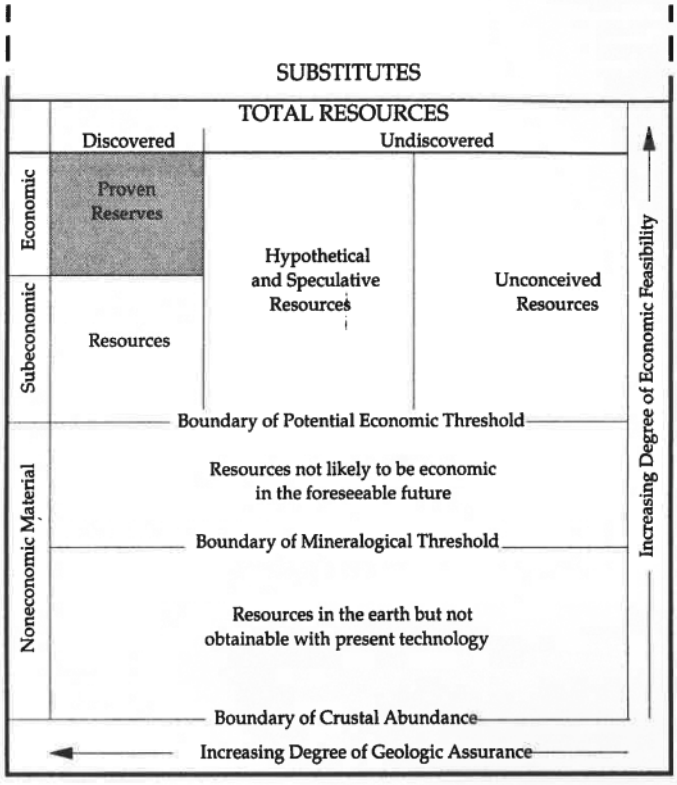
Here's a simple way to think about it. The total amount of oil in the Earth changes little year-by-year. But three more relevant measures of oil do change:

- How much oil we know about.
- How much of that oil we can technically extract.
- How much of that oil it is economical to extract.

[Book, 2021]

Economics of discovery

Technology can affect what is economically recoverable. It is equally true that economic factors can affect what is technically feasible.



In a market system where prices are allowed to signal, suppliers constantly seek to increase supplies so they can sell more. At the same time, they are reducing prices so they are not undersold. Direct and indirect users of commodities are trying to reduce their consumption so as to reduce costs. The higher the price of a commodity rises, the stronger the response from suppliers. This may mean more intensive usage of existing technologies, or the creation of new technologies and methods to locate, extract, and refine the resource. Higher prices also stimulate the search for substitutes.

As conventional oil becomes less available, its price will tend to rise. (Price increases may be restrained by economizing or by substituting.) The rising price signals to firms that they should look more intensively into alternatives. Conventional oil can be replaced with production of liquids from unconventional sources such as tight oil, oil sands, ultra-heavy oils, gas-to-liquid technologies, coal-to-liquid technologies, biofuel technologies, and shale oil.

Peak oil forecasts are made using technical-material forecasting rather than economic forecasting. Technical forecasts divide the 'known reserves' accessible by current methods by the current rate of use and derive the resulting 'years of consumption left'. Technical forecasts fail to allow for the large effect of changing prices on supply – the supply that is economically viable. [Simon, 1998: 27; 45.]

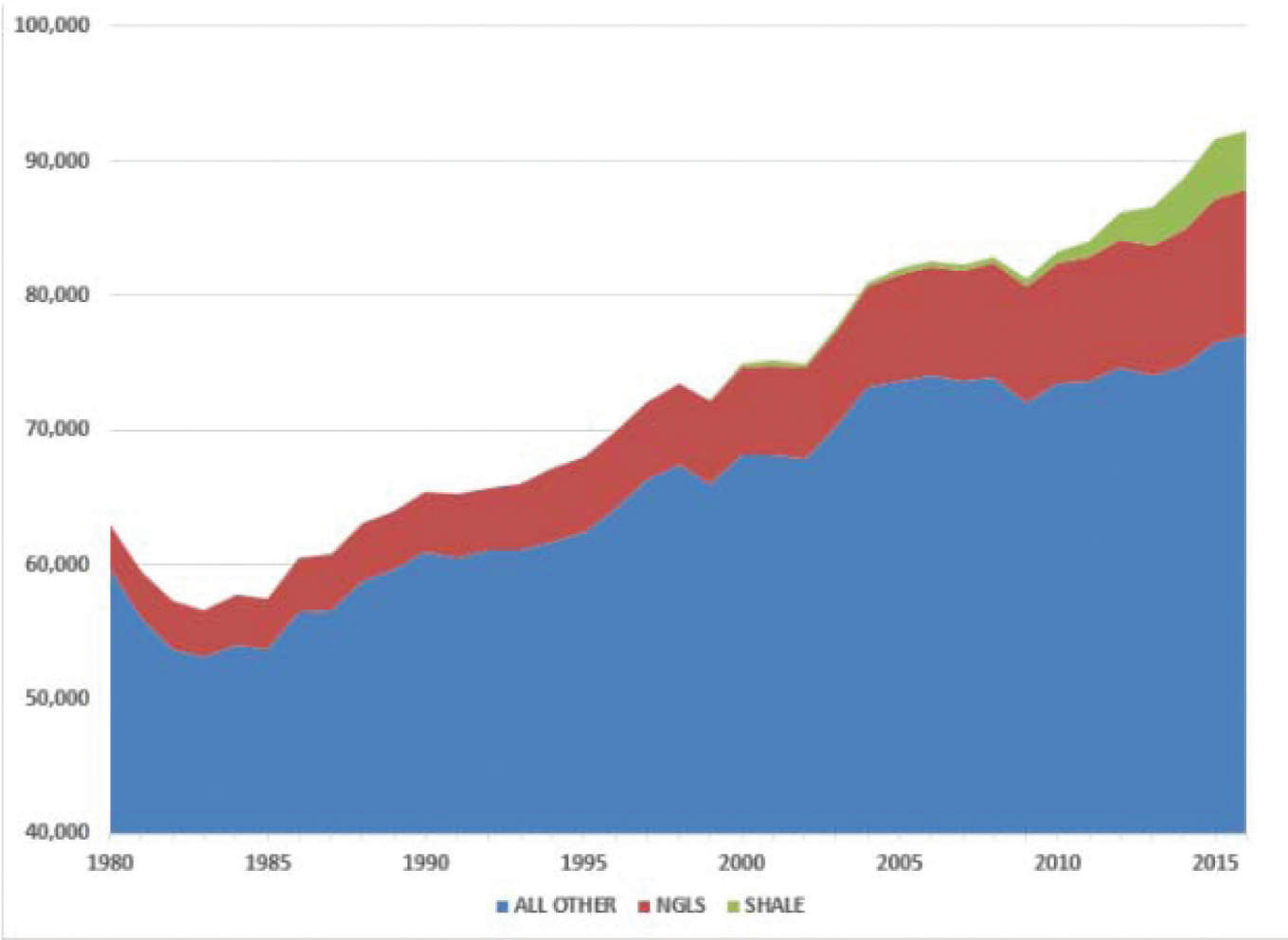
When forecasts are based on material principles bounded by supplies of the resource available at current prices and using existing technology, the result is predictable: a projection of rapidly dwindling reserves. In reality, the long-term trend is decreasing scarcity due to heightened incentives to discover new reserves and to invent superior methods of extraction. Contrary to what most people believe or expect, **the ratio of US reserves to US production also has generally increased**. Look at historical charts and you will find that reserves go up rather than down. Furthermore, they go up not just in total but as a ratio of rising consumption.

When prices rise, more companies enter the market and increase supply. Existing companies deploy more expensive discovery and extraction methods and develop new techniques. When prices fall, the less efficient companies either go out of business, merge, or shut down until better times. The remaining companies are forced to become more efficient. When prices go back up, the efficient companies will be highly profitable.

Rising consumption and rising reserves

If we are currently at or close to peak oil, you would expect reserves (even conservatively measured "proven reserves") to be falling. According to the latest BP Statistical Review of World Energy, proved U.S. reserves in 2000 were 30.4 billion barrels. In 2020, reserves had increased to 60.8 billion barrels. Globally, reserves increased from 1,300.1 to 1,732.4 billion barrels.

In 2000, we used 25.2 billion barrels of oil out of the proven reserves of the time. At that rate of consumption, a simple extrapolation would suggest that we had just under 52 years of proven oil left. In 2019, the closest pre-pandemic year, we used 31 billion barrels – a 23% increase over 2000. Based on proven reserves of 1,732.4 billion barrels, we now have 56 years of supply left. 7.7% more supply-years left while consuming 23% more! **We have used more oil over the last two decades and yet oil has become more plentiful**. [Book, 2021]



World Petroleum Supply THE AUTHOR; DATA FROM BP AND EIA.

Looking beyond "proven reserves" to technically recoverable oil equivalent (at prices seen recently), conservative estimates come to over eight trillion barrels. History suggests this is too low an estimate. We are already seeing vast new prospective areas being opened up by advancing deep-water drilling and production technology. This doesn't even count unconventional sources.

The peak oil contingent believed that the shift to unconventional oil sources such as shale and tar sands would be more costly, slower to come to market, and more environmentally damaging. This turned out to be backward. U.S. shale oil production ramped up with the fastest increase in a 3-year period ever – a startling and impressive outcome from the combination of price incentives and technological development.

In response to their predictions being falsified, peak oil advocates keep increasing their estimates of recoverable resources while shifting out the date of the peak. They also say that they are looking only at conventional sources. If we are interested in the services provided by a commodity rather than the material itself, this is not what matters. Even restricting the forecast and its evaluation to conventional sources, the peak claim is wrong. Much of the growth has been from natural gas liquids and shale, but conventional oil reserves have also expanded. You can see this in the graph from Lynch, 2018.

The material-minded peak oil advocates thought that economics didn't matter because "you have to find oil before you can produce it" and if it's there, it will be produced. Technology could not improve recovery because, in the words of Jean Laherrère, "Technology cannot change the geology of the reservoir, but technology (in particular horizontal drilling) can help to produce faster, but no more…" [Laherrère, 2012.]

Ultimately recoverable

We've seen that "proven reserves" isn't a very useful long-term measure. It's a far too restrictive and overly cautious concept. On the other hand, most people would say that the other extreme would be represented by total crustal abundance – the total amount of a material that exists in the Earth's crust. As resource economist Julian L. Simon put it: "Proven reserves are a ridiculously pessimistic floor for forecasting. At the other end – a ridiculously optimistic ceiling – is the total amount of a material that exists in the Earth's crust. The most economically relevant measure is that of 'ultimately recoverable resources.'"

What we consider "ultimately recoverable" depends both on how much of a commodity is physically present and on both the level of technology and relative prices. Simon noted that the US Geological Survey presently assumes that ultimately recoverable resources "is one hundredth of 1 percent of the amount in the top kilometer of the Earth's surface… Even this 'ultimately recoverable' estimate will surely be enlarged in the future when there are improvements in mining techniques or if prices rise." [Simon, 1998]

Former forecasts and subsequent diverging outcomes should teach us a little humility. Especially when confidence surrounds what can "never" happen. Looking at the giant fields in the Gulf of Mexico, operations that were not imagined a few decades ago, what might we find in the 85% of the US Outer Continental Shelf that has never been explored? We must also be cautious about confidently declaring that we can never extract more than, say 5% or 10% of oil in a reserve. In the mid-1990s, it was widely believed that the recovery factor in the Bakken formation would be no more than 1%. The USGS now assumes 10%.

No end to oil

We will never run out of oil. That's my prediction.

A material peak in the production of oil will happen. (Peak oil production *per capita* probably occurred in 1979, as advanced economies became more efficient.) As we've seen, *when* it will happen is far more uncertain than the peak oil advocates believe. It's also probably further away than they believe. And, much more certainly, production will not suddenly drop off a cliff once the peak arrives (and sticks). As it becomes harder to find, so long as governments allow markets to work, changing prices will incentivize new discoveries, new technologies, economizing, and substitution.

Eventually, we will probably reach a point where the diminishing returns of technology at prices people are willing to pay will not keep up with oil-related energy demand. The market will have generated alternatives to oil for the services it renders. Oil will never run out; we will use less and less of it because we no longer need it. This was true of the forests in England in the early Industrial Revolution. It will be true of the USA and the world in the future. Oil will become obsolete before it can run out. As Dr. Christof Rühl, chief economist of BP, wrote:

> Physical peak oil, which I have no reason to accept as a valid statement either on theoretical, scientific or ideological grounds, would be insensitive to prices. ... In fact, the whole hypothesis of peak oil – which is that there is a certain amount of oil in the ground, consumed at a certain rate, and then it's finished – does not react to anything ... Therefore there will never be a moment when the world runs out of oil because there will always be a price at which the last drop of oil can clear the market. And you can turn anything into oil if you are willing to pay the financial and environmental price. [BP, 2008]

Declining oil production can become a problem due to bad policy. We are seeing that in many Western countries right now, including the USA. In the US, the current administration has set about hindering fossil fuel production. This includes blocking

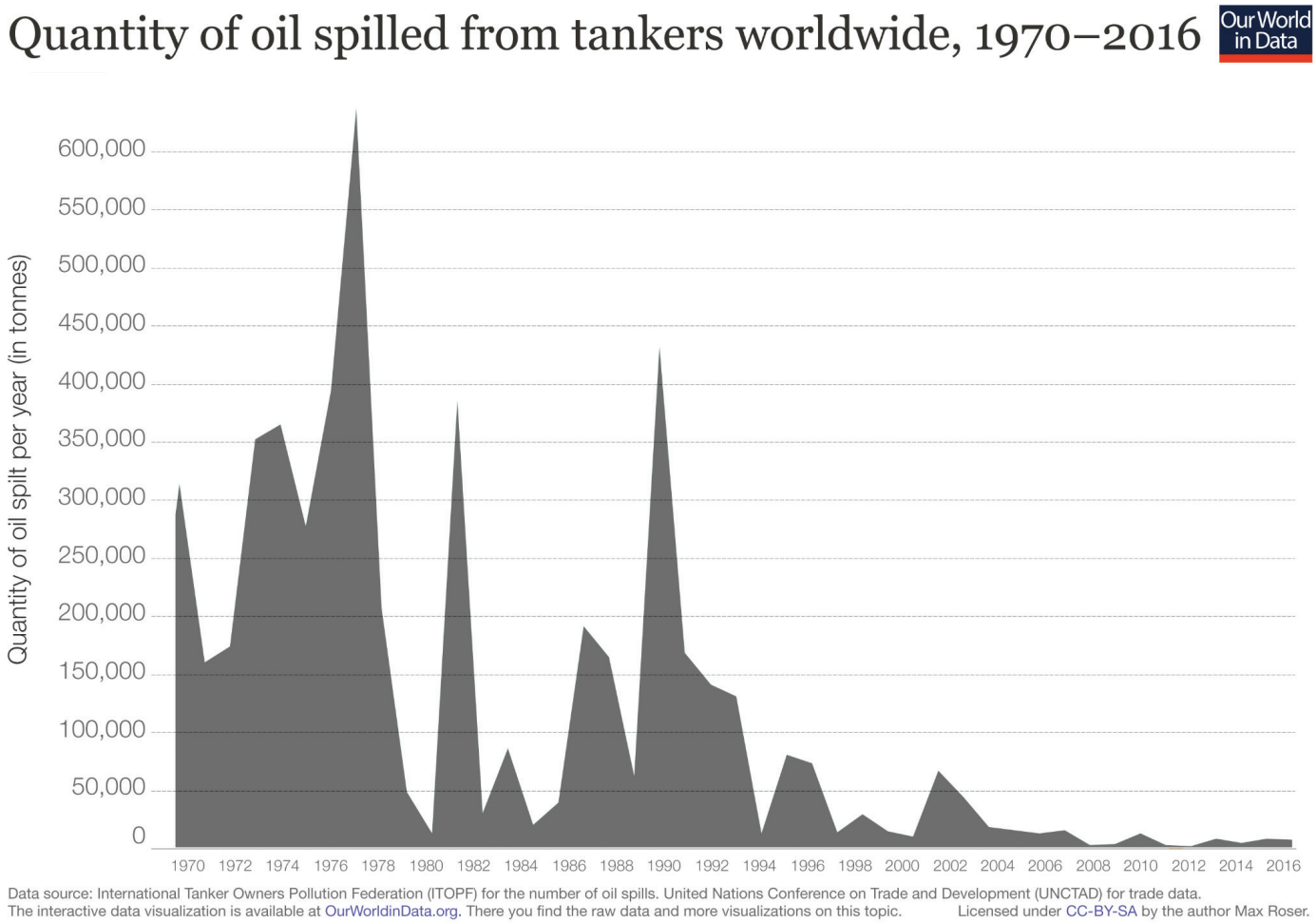
new pipeline construction, ending fracking and drilling on federal lands, and various other regulations to make production more difficult and expensive.

Policies that constrain "above ground" factors such as the availability of staff, expertise, technology, investment security, and funds can constrain supply. Avoiding such policies will allow oil to be exploited and to be moved away from without inflicting painful economic suffering – suffering which most strongly affects the poorest. Those trying to bring on peak oil sooner should understand that crude oils have provided human civilization with a stunning reserve of chemical energy. The energy density of oil is approximately 45 MJ/kg, nearly twice as much energy as coal for an equivalent mass. Crude oil has enabled billions of people to emerge from poverty. We will move away from oil but let's not demonize it in the meantime.

A final word goes to Indur Goklany from his excellent book. [Goklany, 2007: 100]: "Perhaps the end of oil will come about sometime in the future but whenever it comes, it will only be a footnote to history, just as the end of blubber is today."

Postscript: Peak oil spills

One area where we *are* far past peak oil is not one pessimists will mention: oil spills. Oil spills peaked decades ago and have been declining both in number and total amount of oil spilled. In the 1970s, the average was 24 oil spills per year. Since 2000, the average has been less than three. In the 15 years from 2000 to 2014, a total of 234,000 tonnes was spilled. That sounds bad. But it is far less than the *annual* amount spilled in the 1970s. In the period from 1970 to 2014, the quantity of oil spilled fell by 99%. ■



References

Book, Joakim, 2021. “In Defense of Cornucopianism.” HumanProgress, November 10, 2021 https://www.humanprogress.org/in-defense-of-cornucopianism/

BP, 2008. "BP: Preisschwankungen werden wahrscheinlich zunehmenen.” Interview (in English) mit Dr. Christoph Rühl, Mittwoch 1". Euractiv. October 2008.

Chen, James, 2021. “Proven Reserves.” Investopedia, May 24, 2021.

Collier, Kiah, 2016. “More recoverable oil in West Texas than previously thought.” Texas Tribune, November 15, 2016.

Desjardins, Jeff, 2017. “Visualizing the World’s Deepest Oil Well.” Visual Capitalist, March 20, 2017. https://www.visualcapitalist.com/visualizing-worlds-deepest-oil-well/

Goklany, Indur M. (2007). *The Improving State of the World*. Cato Institute, 2007.

Hubbert, M. King, 1956. “Nuclear Energy and the Fossil Fuels.” Presented before the Spring Meeting of the Southern District, American Petroleum Institute, Plaza Hotel, San Antonio, Texas, March 7–8–9, 1956.

Jevons, William Stanley, 1965: *The Coal Question; An Inquiry Concerning the Progress of the Nation, and the Probable Exhaustion of Our Coal Mines*. Macmillan & Co., 1965.

Laherrère, Jean, 2012. “Jean Maugeri part II.” Peakoil.com, October 16, 2012.

May, Andy, 2018. “The End of Oil and Gas.” Wattsupwiththat, July 7, 2018.

Novak, Matt, 2014. “We’ve Been Incorrectly Predicting Peak Oil For Over a Century.” *Gizmodo*, 12/11/14.

Simon, Julian L., 1998. *The Ultimate Resource 2*. Princeton University Press; Revised ed. Edition, July 1, 1998.

Wells, B.W., and K.L. Wells, 2006. “Making Hole – Drilling Technology.” American Oil & Gas Historical Society, September 1, 2006. https://aoghs.org/technology/oil-well-drilling-technology/

Let's Make Sure The Next Carl Sagan Is a Cryonicist

By Jason Harrow

The late, great physicist Carl Sagan really should have been a cryonicist. He was (of course) a first-rate scientific thinker. He had boundless intellectual curiosity. And he had a deep reverence and joy for life, and even a stated desire to extend it into the far future. Those are three traits that make for a perfect entrée into thinking like a cryonicist. And yet he still failed to appreciate that his life and consciousness could potentially be extended by cryonics. There's a lesson here: it takes more than just those three traits to take cryonics seriously. We in the cryonics community need to develop educational tools to make sure that the next Carl Sagan recognizes that cryonics is a better way to face death and the far future.

Sagan certainly had three key traits that many in the cryonics community share. First, many cryonicists are well-versed in science, medicine, or technology. It makes sense that many cryonicists have scientific or technical backgrounds, because the technology of cryonics, at least for now, seems cutting-edge, even futuristic. Sagan obviously meets this criterion: he was a professor of space science at Cornell, the author of hundreds of scientific papers, and the creator of the wonderful PBS television science series "Cosmos." Many of his famous quotes and aphorisms reflect this. "If you want to make an apple pie from scratch," he once said "you must first create the universe." Now there's a scientific worldview if I've ever seen it!

Second, Sagan had intellectual curiosity in spades. While he was a trained astrophysicist, he was also his era's preeminent popularizer of all types of science. He was the author of the acclaimed sci-fi novel *Contact* and others. He was a frequent guest on *The Tonight Show*. He even chaired the committee that selected the information on the famed "Voyager Golden Record," a record containing images and audio from our planet that is currently headed out into interstellar space on Voyager 1. In other words, like many cryonicists, he refused to stay in one intellectual lane.

Third, and perhaps most importantly, Sagan had a deep reverence for life and even expressed his desire for more of it—much more. In an essay in his final work, *Billions and Billions*, Sagan wrote not only of the "love and moral depth" of this world, which he called "exquisite," but also that he had "deep curiosities" about the far future. He wanted "to meet still unconceived grandchildren." And he wanted to witness "the exploration of many of the worlds in our Solar System and the search for life elsewhere" and "interstellar flight," among other things.

Yet, unfortunately, he failed to recognize that cryonics could provide him that hope to see the far future that he longed for. "If there were life after death," he noted wistfully, he might "satisfy most of these deep curiosities and longings." But he called this a "forlorn hope" because death was "nothing more than an endless dreamless sleep." He thus decided to look "death in the eye and to be grateful every day for the brief but magnificent opportunity that life provides."

As cryonicists recognize, though, this end need not be the case for everyone. Instead of looking at death with a "forlorn hope," cryonicists instead say that they will not go gentle into that good night, to quote Dylan Thomas. Instead, they will preserve the information in their remarkable brains and hope—not forlornly, I might add—that one day in the future they will awake from their dreamless sleep. It will be a dreamless sleep that will not be endless, as Sagan thought, but only temporary.

What puzzles me is how Sagan, who had so many of the key traits of other cryonicists, never publicly mentioned that cryonics was the only way to see his deep longings possibly fulfilled. Worse, we know from the small number of current members of cryonics organizations, that there must be many Carl Sagans out there. Perhaps not "billions and billions," to use Sagan's famous phrase, but certainly many more than a few thousand. These are the low-hanging fruit of the cryonics movement: those who have already done so much of the intellectual work to build the foundation necessary for cryonics without crossing the threshold.

It strikes me that we need a two-step plan to get those who think like Carl Sagan to become members of Alcor or other cryonics organizations. We must first find them, and that can't be too hard—there are only so many places that those with Sagan's three key qualities hang out, both online and off. And then we must create materials and tools that are designed to meet them where they are. These folks don't need to be told how much they might be missing in the far future: they already wish they could see interstellar travel or meet their great-great-great-grandkids. What they must come to understand is that there is some chance they can actually get there; that seeing the far future is not science-fiction but science *without* fiction, but just with a healthy dose of speculation and projection.

The original Carl Sagan is, sadly, a lost cause. He died in 1997, and will, by all accounts, be in an endless, dreamless sleep indefinitely. But there is no reason that the next Carl Sagan, and those who share his beliefs and values, should not become cryonicists. If they do not, we should consider that our failure, not theirs. ■

Jason Harrow is a constitutional lawyer and was recently elected to the Alcor Board of Directors.

Alcor Case Metrics 1967-2020

By Michael Benjamin and Aschwin de Wolf

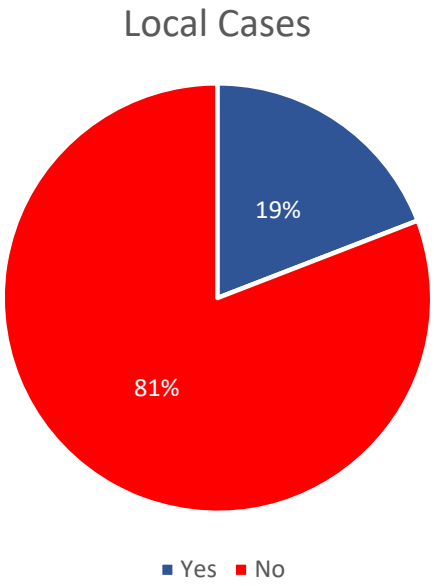
The Alcor Meta-Analysis Project has three distinct objectives: (1) To organize and enter all case data in a comprehensive database; (2) to visually present and publish the data in a format that allows the reader to see trends and patterns; and (3) to identify correlations between specific elements of a case and outcomes.

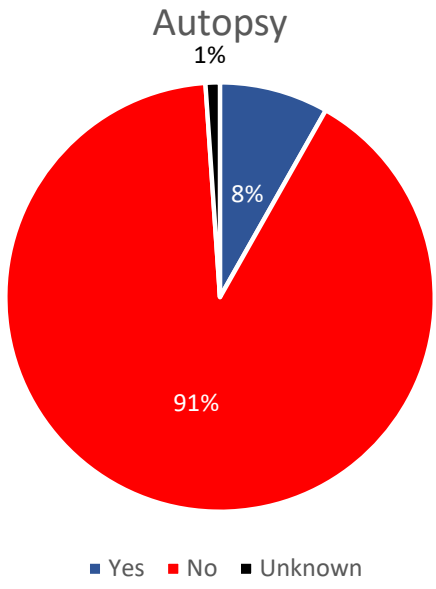
We present here a selection of case data of all Alcor cases for the years from 1967 to 2020. Alcor did not exist yet in 1967 but this year marks the cryopreservation of Dr. James Bedford, who is now in Alcor's care. Detailed case data for James Bedford were not available. Therefore, some metrics cannot be known (like the S-MIX). Generally speaking, CT scans were not performed until 2011.

At this stage in the meta-analysis project, we still confine ourselves to presenting factual data and calculated (or estimated) measures. After completing the compilation of all the data for all Alcor cases at the end of 2021, we will move to the next step of identifying trends and correlations.

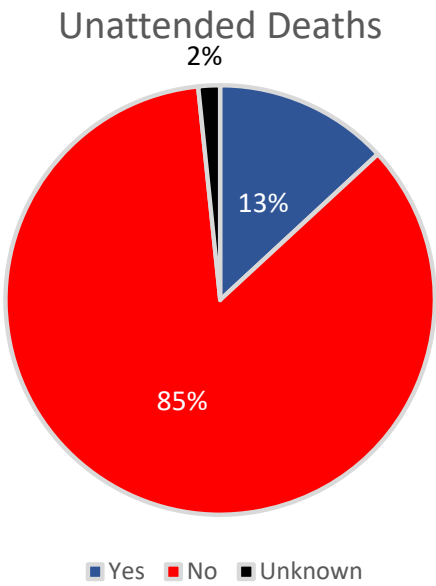
The magnitude of the project and sheer quantity of data makes it inevitable that some errors can be introduced in the reporting or interpretation of data. In some cases, detailed data is not available and rough estimates need to be made based on the case data that was available and extrapolation of what we know from other cases. We expect this project to increase in comprehensiveness, accuracy, and actionable information.

+ Note: The color "blue" represents a "good" outcome and the color "red" a sub-optimal outcome / situation.



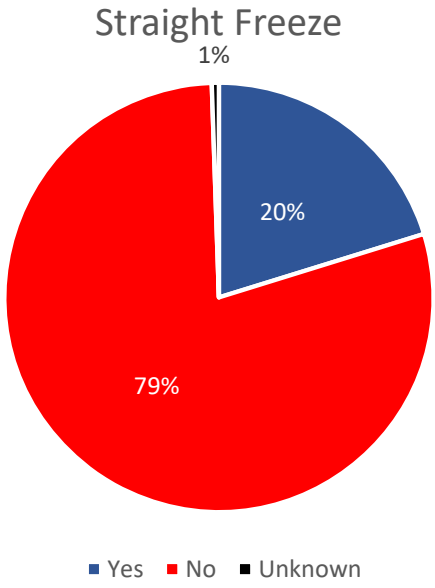


In some circumstances (like sudden death), an autopsy is ordered. Alcor typically objects to prevent an (invasive) autopsy but is not always successful. In future reports we will further distinguish between full (invasive) autopsies, limited autopsies, and virtual autopsies.

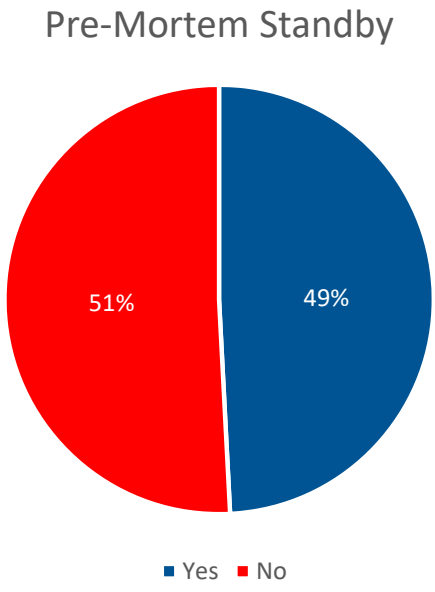


Unattended death cases are cases in which a patient experiences circulatory arrest without medical caregivers or family present.

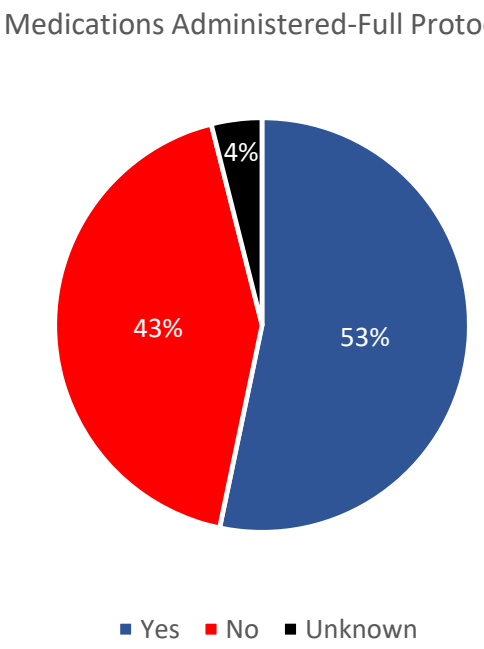
This often happens to older members who live alone.



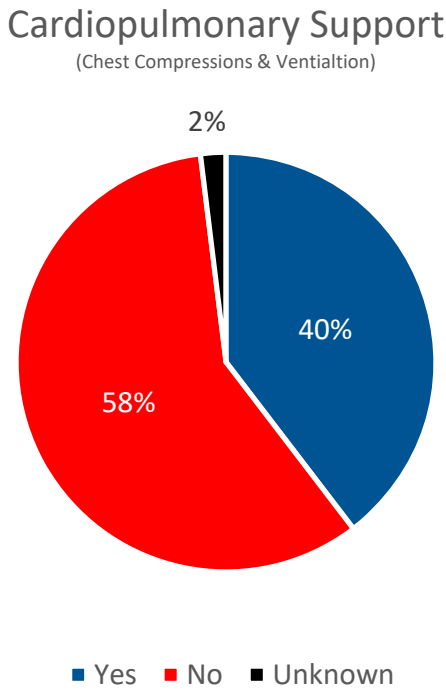
A straight freeze is a case in which a patient is frozen without any kind of cryoprotection to prevent freezing damage. Straight freezing usually happens in case of long ischemic delays, after autopsy, or when there is a delay in arranging for cryonics arrangements.



Pre-mortem standby refers to cases in which a (professional) standby team was deployed to the patient's location before pronouncement of legal death.

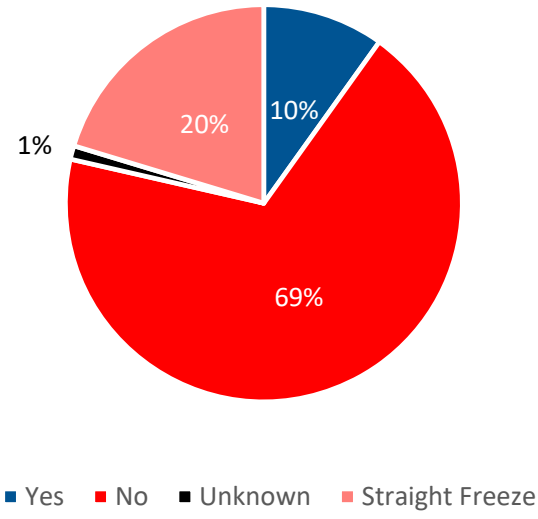


This chart refers to cases in which the complete stabilization medications protocol was administered. This is typically associated with pre-mortem standbys.

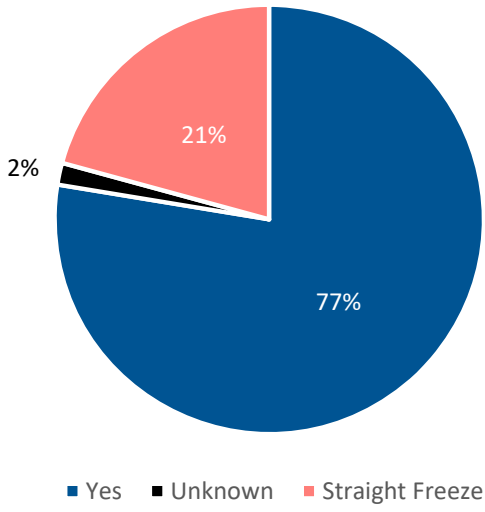


In the meta-analysis project cardiopulmonary support (CPS) cases are cases in which chest compressions PLUS ventilation is performed on the patient as part of stabilization procedures. Brief periods of chest compressions to circulate medications are not included in this category.

Field Cryoprotection

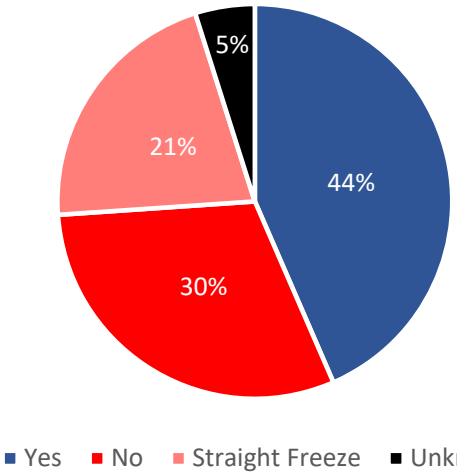


Cryoprotective Perfusion



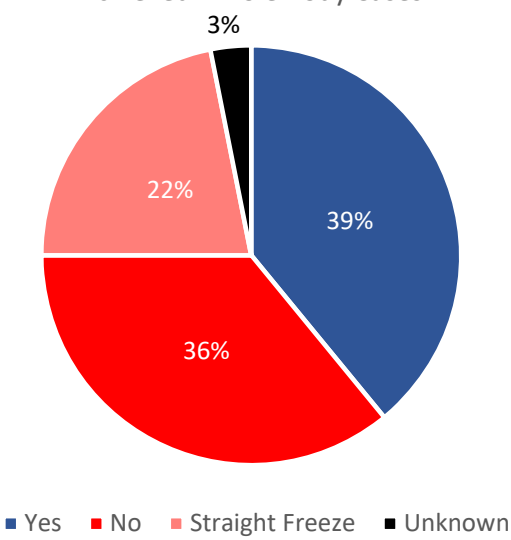
Cryoprotective perfusion cases are cases in which a cryoprotectant was delivered to the patient through perfusion of the blood vessels. As a general rule, when there is no cryoprotective perfusion, the case is a straight freeze.

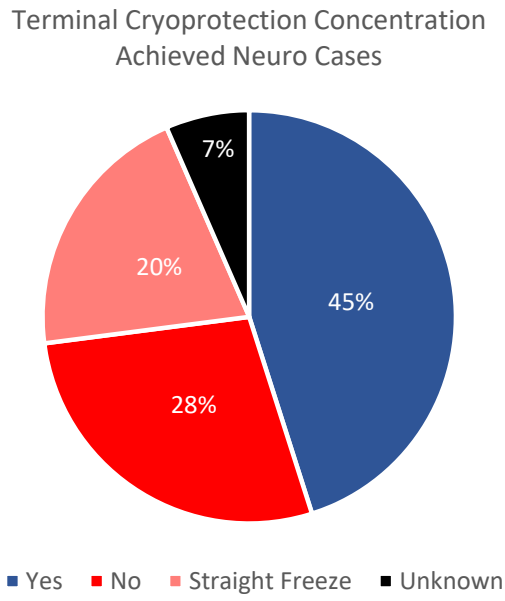
Terminal Cryoprotection Concentration Achieved

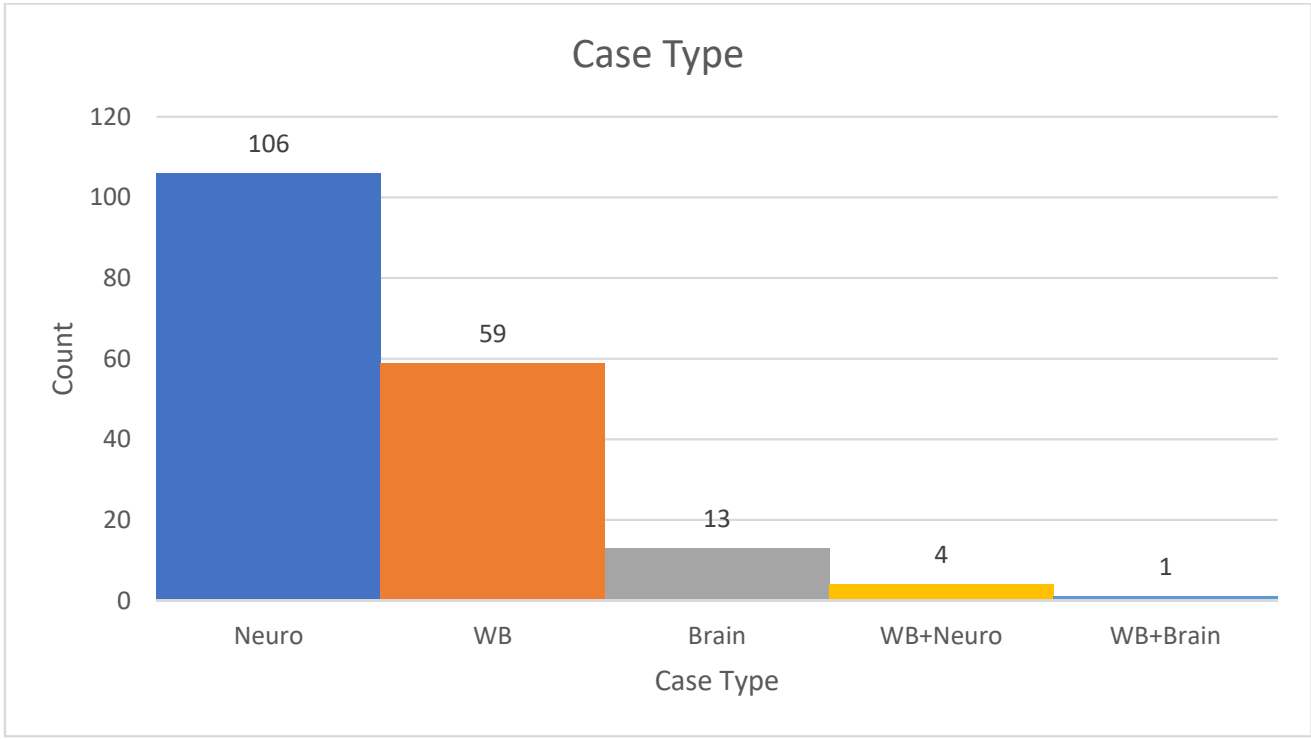


Cases in which the terminal cryoprotection concentration was achieved are cases in which the full concentration deemed necessary for vitrification to occur was obtained. In patients with prolonged ischemic exposure this target is not always achieved.

Terminal Cryoprotection Concentration Achieved Whole Body Cases




Terminal Cryoprotection Concentration
Achieved Neuro Cases
7%
20%
45%
28%
Yes
No
Straight Freeze
Unknown


Case Type
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100
80
60
40
20
0
Count
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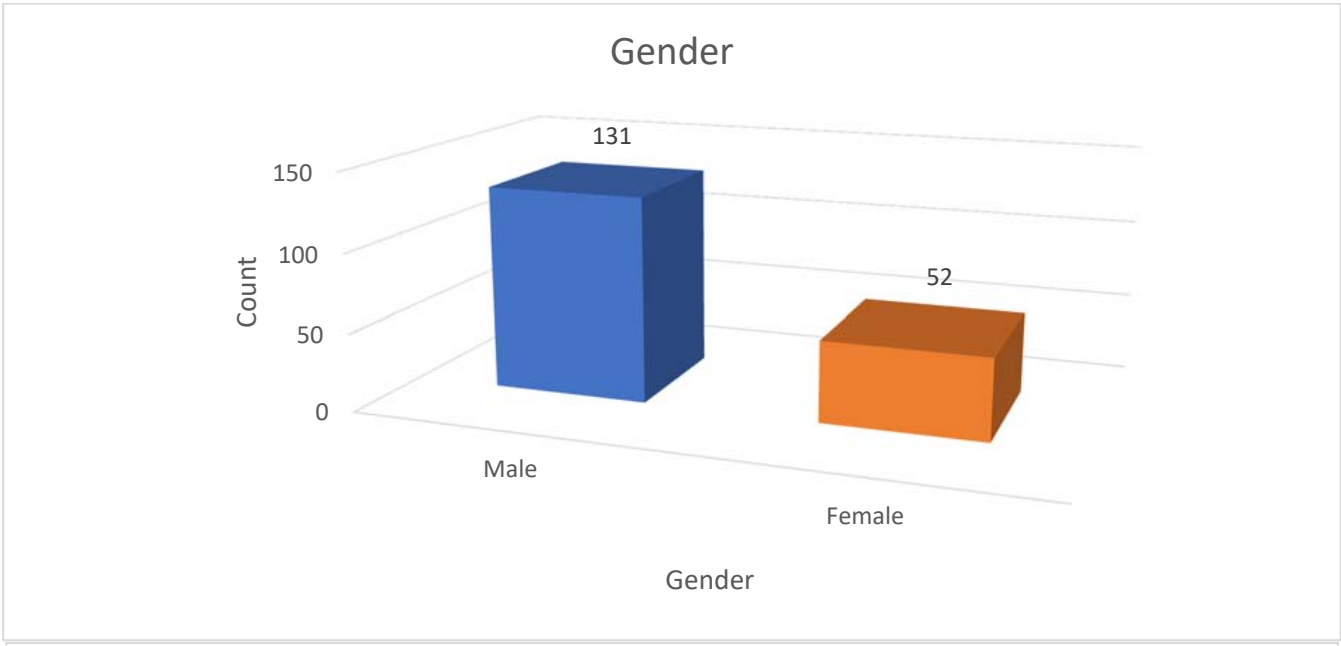
59
13
4
1
Neuro
WB
Brain
WB+Neuro
WB+Brain
Case Type


Gender
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52
150
100
50
0
Count
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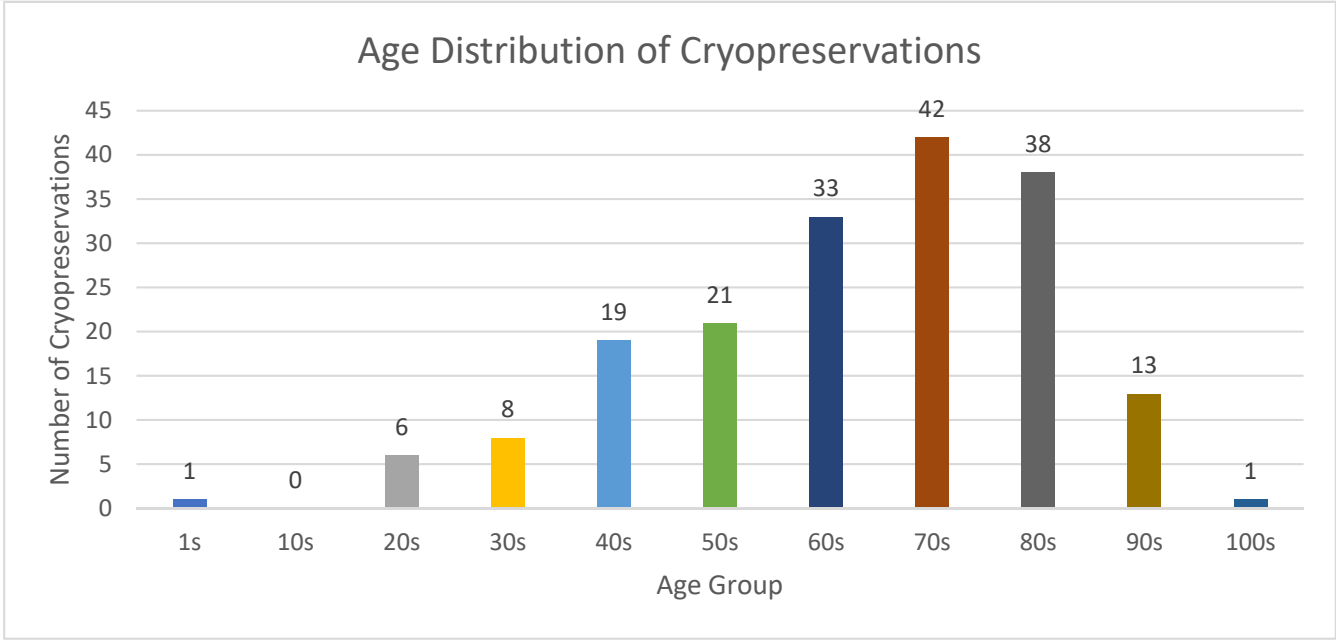
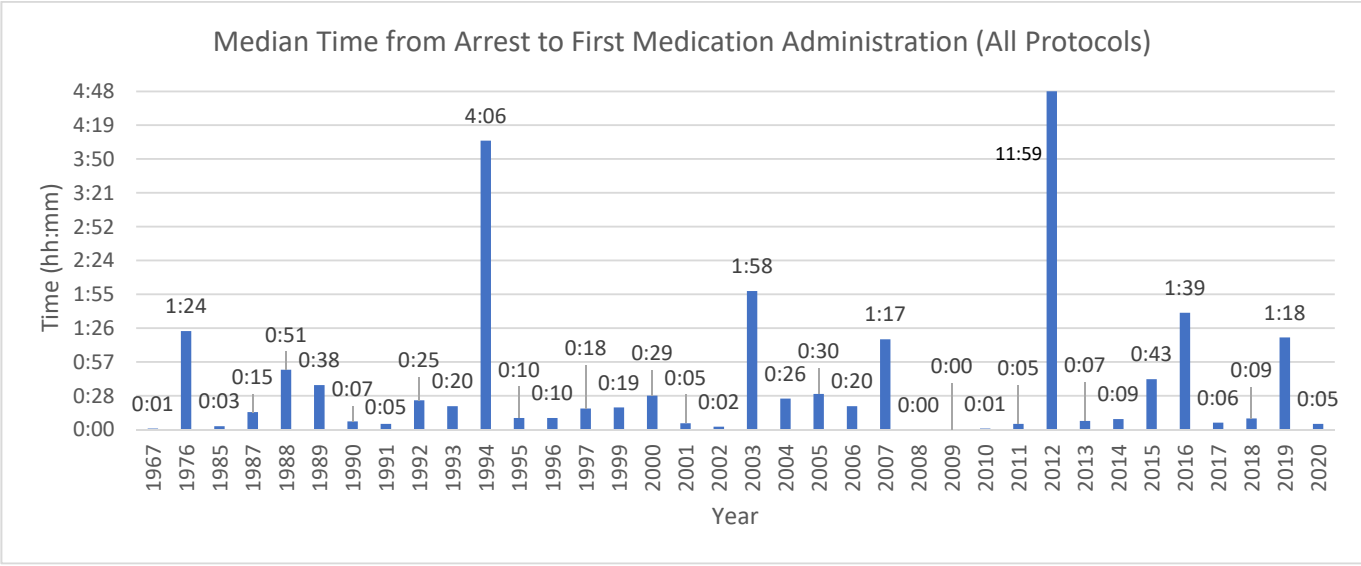
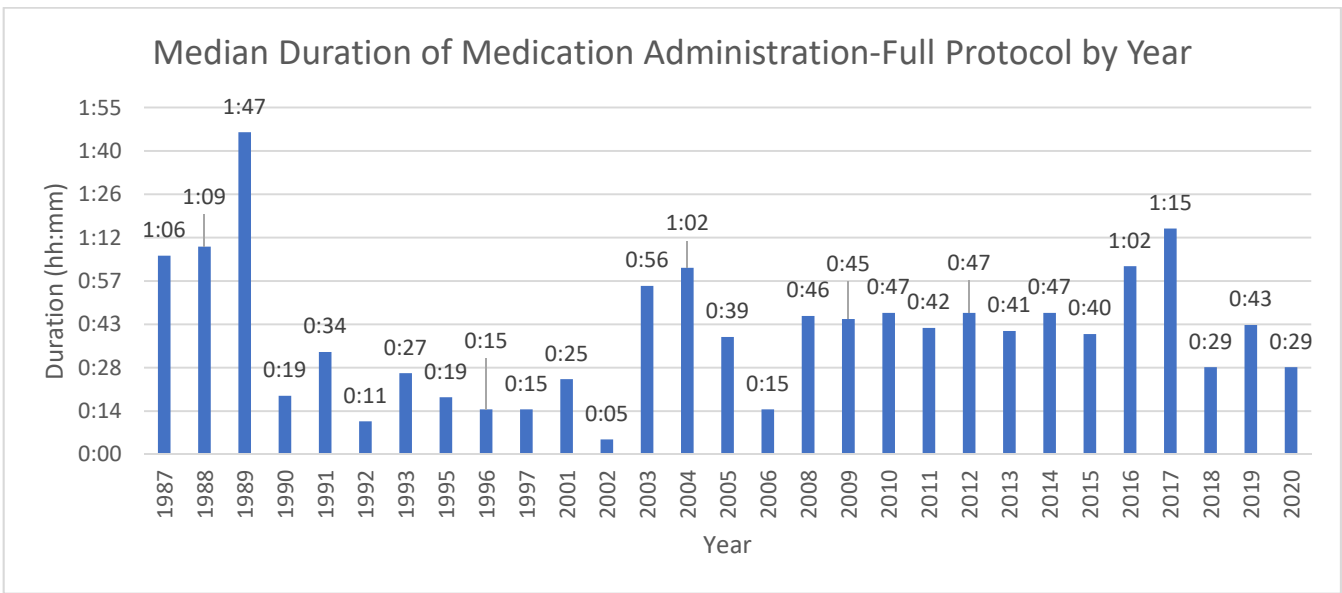
Female
Gender

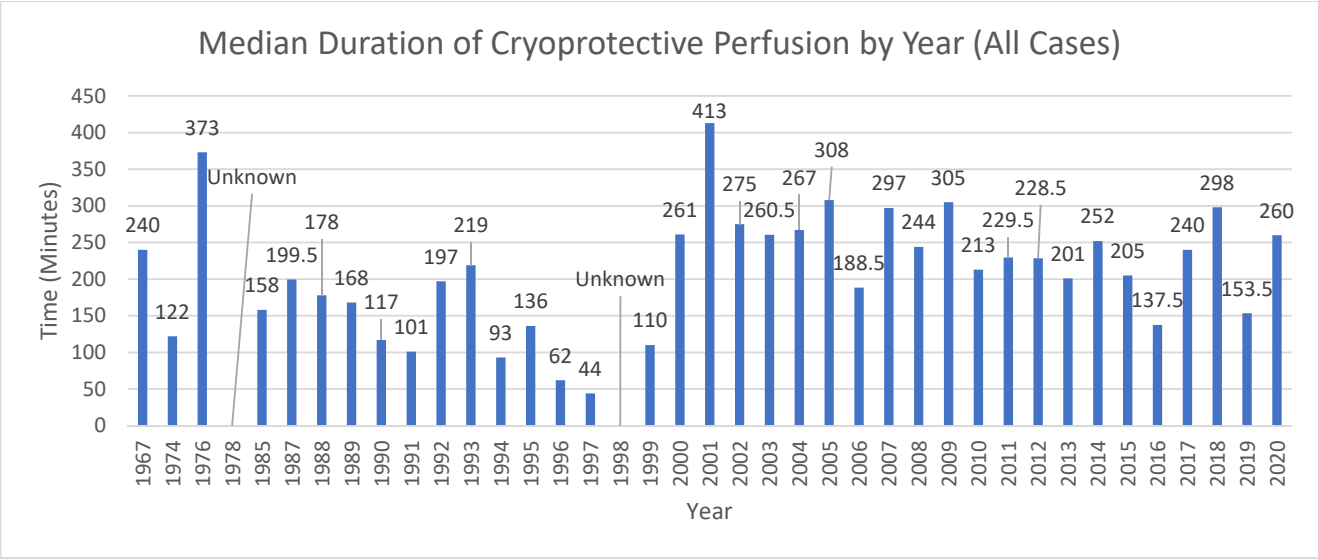

Age Distribution of Cryopreservations
Number of Cryopreservations
45
40
35
30
25
20
15
10
5
0
1
0
6
8
19
21
33
42
38
13
1
1s
10s
20s
30s
40s
50s
60s
70s
80s
90s
100s
Age Group



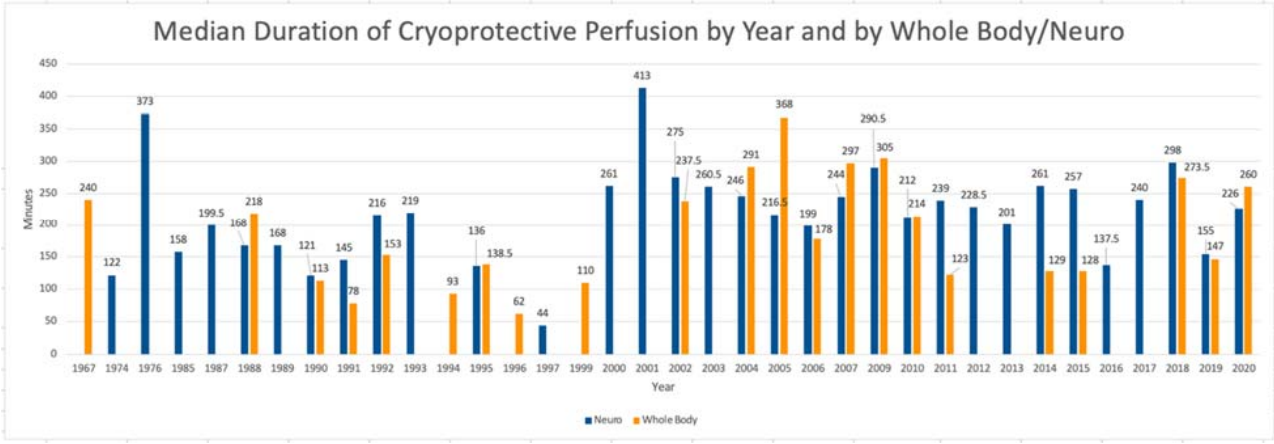
Time from arrest to first medication administration is the time between circulatory arrest and administration of the first medication. This can concern the full protocol, abbreviated protocol, or a single medication (like heparin). Notes: 1994 constitutes one single case, in which only Maalox could be administered post-mortem. In 2012 there were only 2 relevant cases, 23:58 and 00:01.

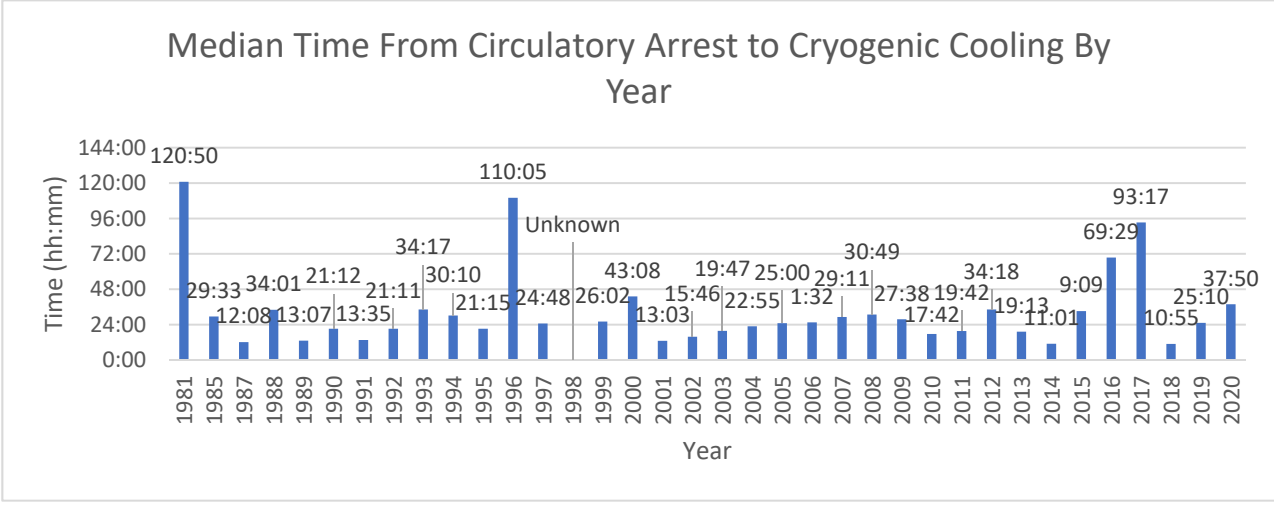


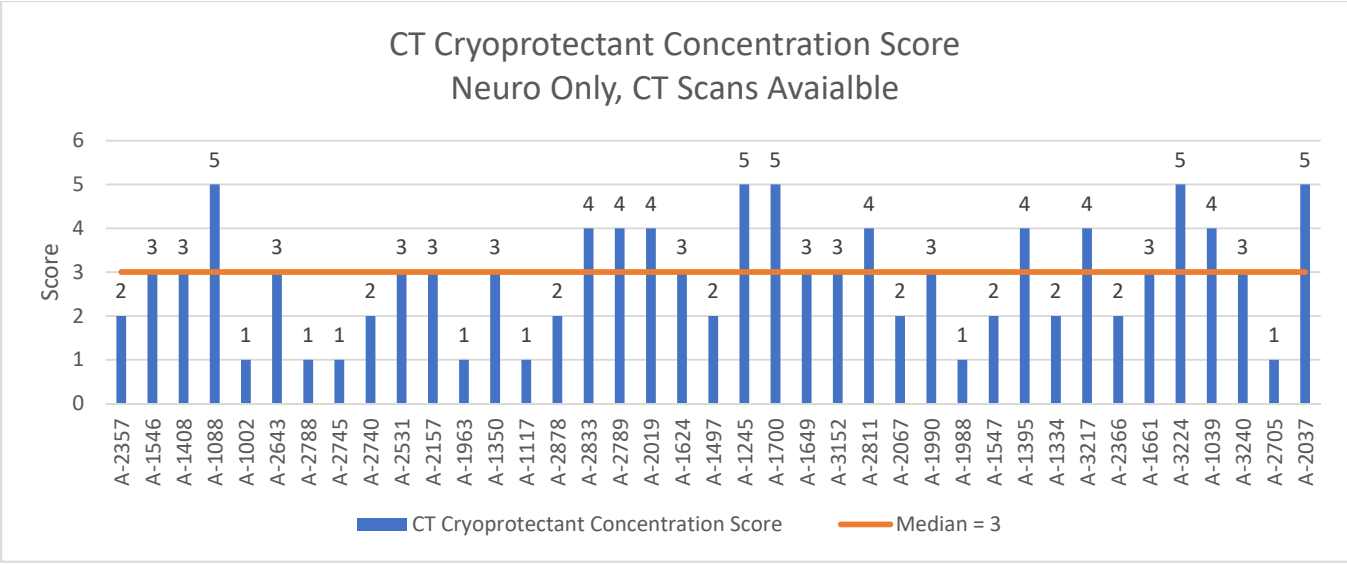
Duration of medication administration refers to the total time it took to administer all the stabilization medications in the full protocol.



Duration of cryoprotective perfusion defined as the total time from the start to the completion (or termination) of cryoprotective perfusion.

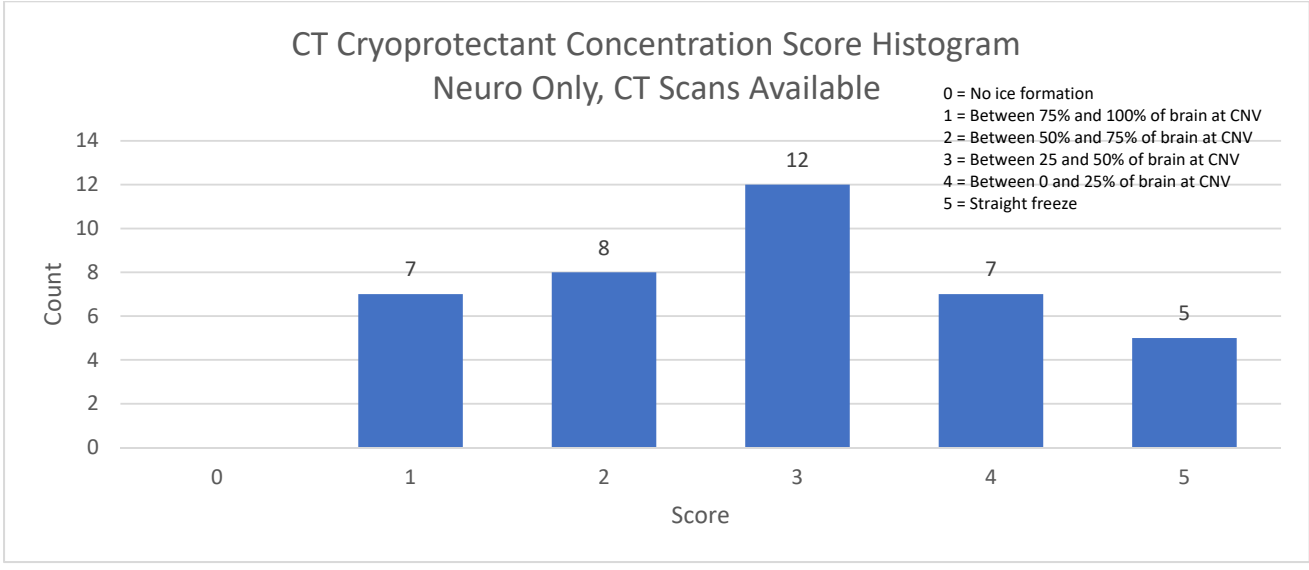




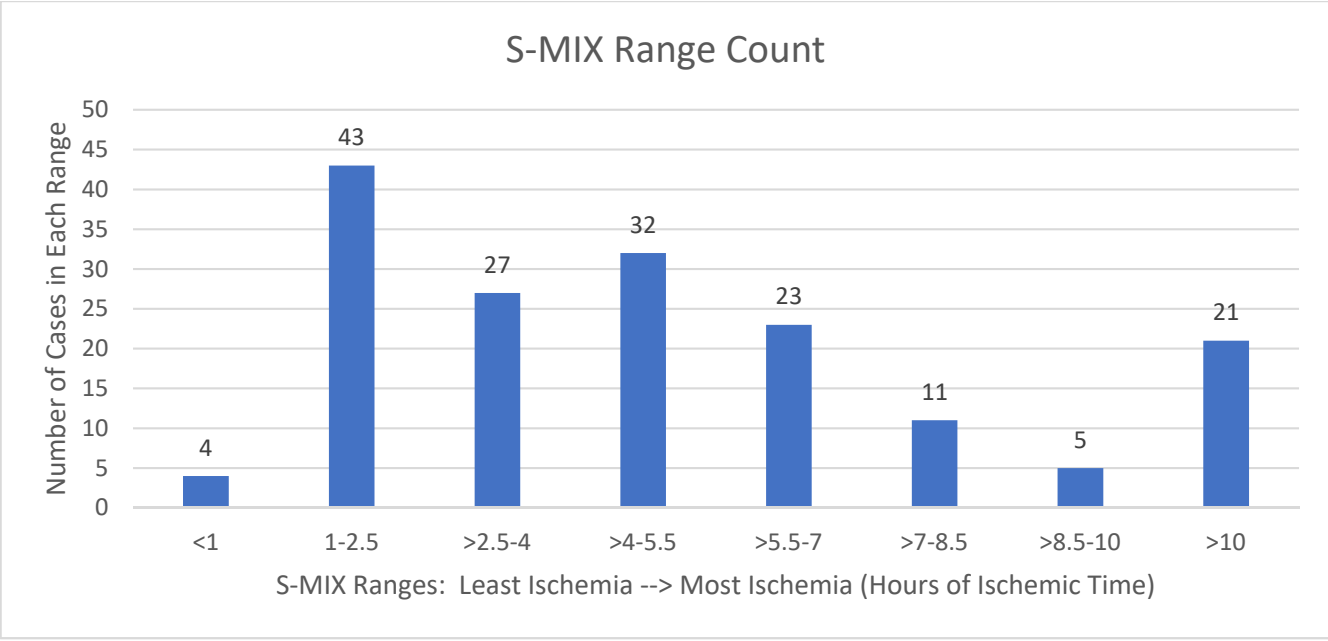


0 = CNV achieved in whole brain
1 = Between 75% and 100% of brain at CNV
2 = Between 50% and 75% of brain at CNV
3 = Between 25 and 50% of brain at CNV
4 = Between 0 and 25% of brain at CNV
5 = Straight freeze

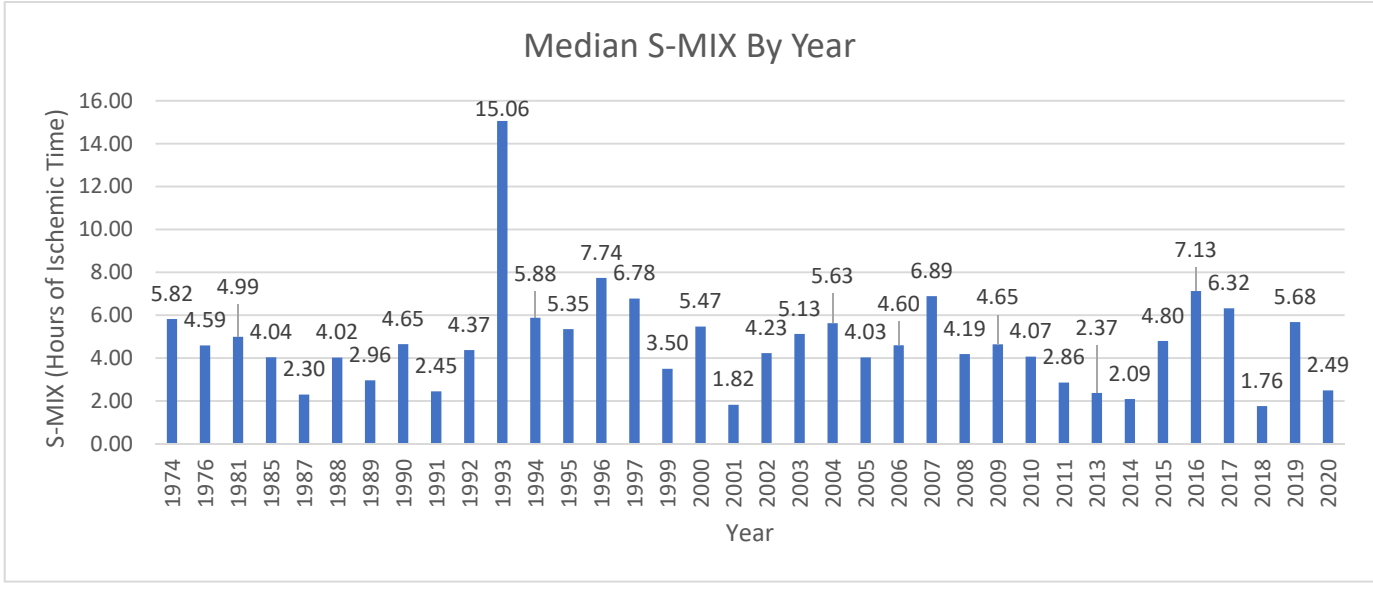
The CT cryoprotection concentration score is an estimation of the amount of brain area with concentrations of the cryoprotectant to inhibit ice formation.



The CT cryoprotection concentration score histogram shows the number of cases in each concentration score.



In the S-MIX histograms all cases are divided into 8 different categories by hour ranging from least ischemia to most ischemia.



S-MIX stands for Standardized Measure of Ischemic Exposure and calculates the total equivalent normothermic ischemic exposure of a patient. The higher the S-MIX, the higher the degree of ischemic exposure of a patient.

See: https://www.alcor.org/docs/measuring-ischemic-exposure.pdf

Note: Meaningful data collection on the 1967 case (James Bedford) is challenging. For example, Bedford was injected, not perfused with cryoprotectant (DMSO). Calculating the S-MIX was not possible for this case due to lack of data. ■

The Alcor Meta-Analysis Project in 2022

As currently scheduled, 2022 will be the final year of the Alcor meta-analysis project. After collecting, organizing, and presenting all relevant case data we will focus on three objectives for 2022:

1. Publish a monthly "deep dive" into a specific cryonics case topic.
2. Compile and organize data for our final meta-analysis report.
3. Identify areas for further research and review.

So far, we have identified the following "deep dive" topics for 2022:

1. Autopsy
2. Hospital / hospice logistics
3. SST deployment (local / remote / international)
4. Cardiopulmonary support (CPS)
5. Induction of hypothermia
6. Medication administration
7. Remote blood substitution
8. Cryoprotection / field cryoprotection
9. Refinement of the S-MIX (i.e., Standardized Measure of Ischemic Exposure)
10. S-MIX / CT scan correlation
11. Monitoring of SST and cryoprotection
12. Extraordinary cases

Our aim of these reports is bringing together the data we have collected, apply a logistical or clinical benchmark to understand how Alcor casework has evolved in a specific area, and identify topics for future research and improvement.

For example, for the autopsy report we will further break down autopsy cases into full autopsies, partial autopsies, virtual autopsies, examine the legal and logistical challenges in responding to a (pending) autopsy case, and review the handling and transport of an autopsied patient.

We aim to bring all these reviews together in a final report that will be published upon completion of the meta-analysis project. ■

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Schrödinger's Freezer and the Restoration of Lost Information: Some Consequences of an Interesting Variant of the Many Worlds Interpretation

By R. Michael Perry, Ph.D.

1. Introduction

We consider a variant of the Many-Worlds Interpretation of quantum mechanics (MWI), and how it provides for the restoration of information that in a single-world interpretation must remain irretrievably lost. In this as well as other versions of MWI an observer in one of the worlds (parallel branches of reality) can be identified as an ongoing process within that world, a time- and space-varying quantum system, which in turn is a component or subsystem of a surrounding system encompassing the entire world. [1, 2, 3, 4] Though deep mathematical results are not pursued here, we shall assume that systems and subsystems form a partially ordered set: Every system is uniquely a subsystem and a supersystem of itself, and a sub-subsystem of a particular system is also a subsystem of that system.

Our treatment invokes a hierarchy of "worlds" at different levels, starting at level 0, in which worlds at a successor level are equivalence classes of worlds at a given level. At level 0 are "threads" which in the course of events never split but only occupy smaller and smaller (in some sense) equivalence classes as events unfold in all their different, allowed varieties. At level 1 are worlds that conform to the explicitly "many worlds" versions of MWI, one world being modeled as a set (equivalence class) of threads or level-0 worlds. The MWI worlds will show how events progress as a function of time, captured in the splitting of equivalence classes of the level-0 worlds or threads. Worlds that have been the same up to a point in time (all in one equivalence class of threads) will split into separate branches (separate equivalence classes whose union is the original) as the different alternatives appear. These alternatives must be "alternatives at the quantum level" and not predictable in advance. An example would be whether a radioactive atom decays or not over a particular time interval – there a single world (equivalence class) would split into branches where the atom did and did not decay. Level-1 worlds are constantly splitting, and do not rejoin.

In an MWI (level-1) world at a particular time there will be a configuration expressing the "state of things" at that time, including any records of past events that may survive. (In a concrete example these "records" could include fossils or other traces of past events not put in place by any conscious observer, along with the usual sorts of records that were.) Not all such records are expected to survive (far from it), and many, many events will have gone unrecorded altogether, particularly the sort that occurred over short distances and times. It is possible that two MWI worlds would differ, at a particular time, only in those past events whose records have perished.

Level-2 worlds are obtained as equivalence classes of level-1 worlds that themselves, at a particular time, differ only in records of events that have perished, that is to say, are the same at that particular time, though possibly having different pasts whose differences are now lost to history. So, level-2 worlds are capable of both splitting and rejoining, where rejoining involves loss of information.

Finally, observers comprise level-3 worlds. Observers are seen as equivalence classes of "observer instantiations," in effect, level-2 worlds in their own right which in turn are situated in more extensive, enclosing level-2 worlds. (A given level-2 world will in general encompass much more than a single observer-instantiation). Two observer-instantiations are equivalent, even when in different, enclosing worlds, if they can be said to have duplicate consciousness. This will happen in particular when two observers are perfectly alike in different level-2 worlds in which something far from them and outside their experience is different, but also in other cases.

Overall, we obtain a Hierarchic Worlds Interpretation (HWI) which, as noted, is MWI with a hierarchy of "worlds" at different levels. The different hierarchies furnish a simple pathway to the main result aimed for: the possibility of restoring information otherwise lost to history and not likely to be recovered or deduced by any archaeological or other analytical process using surviving remains. It is proposed that, in a future time, such restored information might contribute to an "augmented archive" which would extend the level-2 archive, obtained by more usual analysis of surviving environmental evidence. This augmented archive might grow over time so that desired past information, possibly relating to observers who have perished, would accumulate.

Our different hierarchies of worlds have been defined by successive equivalence classes. Equivalence classes are mathematical constructs, not necessarily identifiable with "real" objects. They and other mathematical constructs may be useful

in appropriate instances for modeling features of reality. But philosophically we must be wary of boldly stating that this modeling "is" itself the reality that is being modeled. So, for the most part we are reticent here about any such claims yet will be bold enough in two instances to claim a basis in reality for properties exhibited in our theory. One is that alternate worlds with different historical outcomes really exist, on more-or-less equal footing. The other is that, as in earlier work [8], when it comes to observers or more properly, observer-instantiations in the different worlds, duplicate consciousness would be shared consciousness. In effect, one observer's existence could and normally will extend across multiple worlds.

This article is organized as follows: Section 2 briefly summarizes MWI in relation to the earlier, Copenhagen Interpretation. Section 3 compares MWI and HWI in greater detail. Section 4 briefly considers some matters on which HWI has a bearing, including quantum paradoxes, probabilities, and the Many Minds Interpretation. Section 5 offers a simple illustration, "Schrödinger's Freezer," of the restoration of lost information as rationalized by HWI, with emphasis on restoration to a level-2 world inhabited by observers, as a contribution to a growing archive of restored information. Section 6 considers in passing some matters not explored earlier: time development, entanglement, observers' "territory," multiple worlds as possible widely spaced regions in a single universe, and the like. Section 7 concludes. It should be emphasized that many additional details would be called for to fill out a robust theory of the sort proposed here. Doing so is beyond our scope, but it is hoped that the present article will at least provide some useful input.

2. Quantum Interpretations: Copenhagen versus Many Worlds [2, 3]

In quantum mechanics as it emerged in the first half of the 20th century, one is confronted with a "quantum system" for which a "quantum state" mathematically specifies the probabilities of outcomes of different measurements which could be made on the system. [5, 6] If the system can be considered isolated from its surroundings, as in the simpler cases, the quantum state becomes a "wave function." [7] Measurements in such cases can take the form of detection events, for example, whether a radioactive atom decays in a period of time, a photon goes through or is reflected by a half-silvered mirror, or a certain property is found, spin-up or spin-down of an electron, say.

In doing measurements such as these, a very odd circumstance was noted. In the classical (non-quantum) world, if you repeat a measurement with conditions the same the second time around, you should get the same result – measurements are deterministic. If you weigh a certain volume of a certain substance, say one cubic centimeter of aluminum, then weigh the same volume of the same substance later, you get the same result, about 2.7 grams. Other, more complicated procedures, such as running the same computer program twice over on the same machine, also yield the same results. Sometimes you encounter discrepancies, but those can in general be accounted for by slight variations in conditions between one trial and the next. (If this explanation doesn't hold up, you might suspect the influence of quantum effects.)

In quantum mechanics, however, the same measurement experiment done in, as far as we can tell, the same way, will in general produce markedly different results, with only the probabilities of the different alternatives remaining constant. For the simple detection event, the atom decays or not, the photon is sometimes transmitted and sometimes reflected, the spin of an electron measures up or down, and so on. In general, the act of measurement "collapses the wave function," giving a definite, 100% certainty to whatever has been observed, and 0% probability to any alternatives that might have been observed, but in this case were not. The same sort of occurrences follow from experiments with more than two outcomes, with associated probabilities. Otherwise, if no measurement is taken, the wave function does not collapse in this way but varies smoothly as a function of time and position in space.

The point of view arose that, to approach the quantum world where measurements are probabilistic not deterministic, it is necessary to also assume an enclosing, classical world where measurements not involving the (not too well defined) quantum level remain deterministic. The classical world was essential and could not be "done away with" in any simple way. This way of thinking became known as the Copenhagen Interpretation (CI). Meanwhile, it was clear that the quantum world could itself be extended up to macroscopic objects, and then would approximate the classical world to high accuracy. It seemed then that the extra assumption of a classical world was really unnecessary, and must be removable, but how best to do this?

In an effort to resolve the difficulty Hugh Everett III in 1957 zeroed in on the assumption that "the wave function collapses." That is really where the weirdness shows itself, for the collapse is acausal not deterministic – the outcome could not be predicted given the initial conditions. Instead, Everett proposed that, contrary to the claims of CI, the wave function never collapses. Instead, when a measurement is made, worlds split into alternatives in which each possible finding occurs. (If there is an observer, it means the observer must also split into copies each of which will observe the corresponding alternative. The observers in turn have no way to sense in any direct way that they have split and it does not seem to them that it happened.) So, for example, with the electron, the world would split into two alternatives in which the spin is alternately up or down.

Actually, Everett himself was resistant to the "worlds splitting" idea and favored "relative states" in which the wave function depended on the observer. [4] However, the relative states produce nearly non-interacting domains or splitting of reality into different "worlds," so that by now "many worlds" has

largely supplanted "relative states" as the term of reference for his theory. In terms of the hierarchy introduced above there appears to be a number of possibilities, with observers or type 3 worlds more in line with the relative states approach and type 1 worlds with "many worlds." This topic is not developed in detail here, though it is referred to in the next section where we consider further details of HWI in relation to MWI.

Before proceeding to the next section, it is worth noting that there is another major approach to dealing with the problem of randomness in measurement results, the "hidden variable" interpretation, which also exists in different varieties. [11] This like MWI regards the randomness as apparent not real, but assigns a different cause, simply a lack of knowledge about the system that is being measured. The electron, for instance, has hidden properties that if known would allow one to predict whether spin up or spin down would be observed. The properties that would allow such prediction can never be known, however. A more serious difficulty is that such theories generally require non-local interactions or faster-than-light signaling, contrary to relativity theory, and not a necessary feature of MWI. The possibility of using such a theory has not been explored here. The multiple-worlds cosmology we do assume will now be considered.

3. MWI and HWI

Some sort of multiple-worlds cosmology seems essential to our main task of restoring lost information [8, 9], and a variant of MWI is chosen though other choices might conceivably do service [10]. MWI in its more basic form (essentially, type 1 worlds only, that split apart and afterward are mostly non-interacting) has the desirable features of simplicity, widespread if not universal scientific support, and other useful properties, including being amenable to the elaboration to HWI that is developed here.

Before proceeding with details of the latter, it is worth considering versions of MWI more generically. According to [1], any MWI must be "[a] theory which yields the time evolution of the quantum state of the (single) Universe." The universe as a whole, then, is distinct from any "worlds" it may split into in the course of its evolution, and despite any of these subdivisions, can in another sense be regarded as being whole and undivided throughout the course of any changes that happen over time. Overall, MWI theories are not deficient in meeting this requirement and explaining all that is observed at the quantum level. The difficulty comes about from the second requirement, to provide "[a] prescription which sets up a correspondence between the quantum state of the Universe and our experiences." The difficulty here is that "our experiences" are difficult to quantify or rigorously define, so in fact different versions of MWI have sprung into being.

In particular there are "centered" theories that focus on the observer rather than a surrounding world (so, a type 3 world in HMI). In this case, "splitting" can occur for one observer while another remains intact. The price paid is that there is a different world for every observer, whereas with an "acentric" theory, a paradox can arise with the different perceptions of the observers, as we explore in the next section.

First, in regard to the HMI theory, some additional terminology will be useful. A type n world is denoted by Wn, n ranging from 0 to 3. Every Wn will have "instantiations" WnI of type n-1 (for $n > 0$) and be an equivalence class consisting of all those instantiations. It will follow that every WnI will be a Wn-1 but not necessarily conversely. Thus an observer (type 3 world) is denoted by W3, and an observer-instantiation W3I will be a component of a W2 and thus a W2 itself (though not necessarily is every W2 a W3I). Two W3Is are equivalent if and only if they have duplicate consciousness, thus are considered to have shared consciousness.

It was noted earlier that W3s are essentially centered worlds and W2s in turn acentric or observer-independent worlds. The W3s are "specialized" in the sense that a W3I, though classed as a type 2 world, is in fact but a small part of what we expect a W2 world to be. But in general, worlds of a given type form a partially ordered set, with some worlds proper lower bounds of others, that is to say, "subworlds," though as noted earlier, we are not going to pursue a mathematical treatment of the subject here. Here it suffices to note that for the most part, our focus is on "worlds" that are versions or images of the whole universe at a particular time, the exception being the case of the observer for which the "scope" is more restricted.

Overall it is expected that HMI will yield many of the same answers to questions of quantum interpretation as the standard MWI upon which it is based (one could confine attention mainly to W1s, as one possibility), except in two instances. The first is probabilities, which pose a special challenge for many-worlds theories with their determinism. Second, is the issue of restoring lost information, which has been the main motivator for constructing the HMI. The matters will now be considered along with others.

4. Quantum Paradoxes and Other Issues

We start with three quantum paradoxes:

1. *Schrödinger's cat.* The cat is placed in a closed chamber and hidden from view. Then, based on whether a radioactive atom decays or not (as detected by a Geiger counter) it breathes an air mixture that, with 50% probability, will either do nothing or put the cat to sleep. (In the original, "putting to sleep" implied euthanasia, here we beg a little clemency!) To the outside observer who is unable to ascertain the outcome, the cat is apparently in a superposition of states between "awake" and "asleep." For a macroscopic object like a cat, isn't this absurd? [12]

2. *Wigner's friend*. Wigner (a famous physicist whose student was Everett and possibly the original "friend") waits outside the closed door of a lab. The friend inside does a quantum measurement with 50% chance of going either way, say an electron is found to have spin up or spin down. Wigner does not know the result, so he apparently detects only a superposition of states, much as in Schrödinger's cat. However, this time there is a full-blown observer just like Wigner himself, who does see the result and can say whether it was one way or the other. So how can the other observer, Wigner, detect a superposition only? [13]

3. *Split identity*. Some worry over the idea that, under MWI, the worlds are splitting at a staggering rate: Every event in every distant galaxy or close by that "could have gone the other way" – an electron jumping into an orbital or not, a photon bouncing off something or being absorbed, and so on, causes our whole reality to split, and with it, observers. Science writer Philip Ball notes: "[O]ne of the most serious difficulties with the MWI is what it does to the notion of self. What can it mean to say that splittings generate copies of me? In what sense are those copies 'me'?" [14]

It is worth saying here that different interpretations of quantum mechanics have different ways of handling the above and other difficulties. No claim is being made that any of the above are uniquely resolvable through HWI, only that it is instructive to see how they could be resolved with HWI. The answer, it turns out, is "very simply," since an observer is, in effect, a centered world.

For Schrödinger's cat, until the observer, a W3, looks and sees what condition the cat is in, the observer's instantiations, W3Is, occupy parallel W2s in which, for some, the cat is "awake" and for others, "asleep." The W2s have split (along with the corresponding W1s) but not the W3s; the one W3 at this point can only note a superposition of possibilities. The case of Wigner's friend is similar, with the added complication that now there are two human-level observers. The friend sees one alternative or another in this case, and the friend's W3Is are split between different W2s where they are *not* equivalent. Wigner, however, is ignorant of his friend's findings so his W3Is *are* equivalent in the corresponding W2s, and he only sees a superposition. For the case of split identity, the very rapid splitting is occurring at the level of W1 and (likely in somewhat diminished form) W2, but definitely not at the observer level, W3. One's identity never splits unless it is forced to by differing states of consciousness that develop in the different branchings of the W3Is.

Probabilities are important in quantum mechanics, yet MWI is deterministic. Everything that happens is certain to happen. So how can we speak of probabilities? With the more standard versions of MWI that is a special challenge, generally resolved by noting that probabilities are properties that manifest themselves over time, so an observer who repeatedly does an experiment, say it is detecting "spin up" or "spin down," will find the expected frequencies of both alternatives, whether under MWI or its variant HWI, or another of the usual interpretations. [15, 16] HWI has additional possibilities, however, in view of the hierarchical structuring, including a very straightforward one based on going to the level of threads (W0s). The threads could be elements of a measure space, so that bundles of them (W1) would have different "weights" which could reproduce whatever probabilities might be needed. (Here we are allowing our threads to be "as numerous as necessary" to conform to the requirements of a measure space, going somewhat beyond the suggestions in [1] – this does not appear to pose any serious problem, though the individual "threads" may seem disturbingly "unreal" to some. But the response would be that a mathematical model is useful apart from whether its various features can or should all be considered "real.")

We have seen how HWI builds on MWI to pay special attention to the role of the observer in whatever happens. Another theory that accomplishes this is the Many Minds Interpretation (MMI, introduced in 1970 by H. Dieter Zeh [17]), in which the branches of reality do not split but the splitting is carried out at the level of the observer. Specifically, each observer is equipped with a nonphysical entity, the "mind," which determines what is perceived. When a measurement is made, the superposition of states remains intact, but a split occurs in the mind of the observer. One mind sees things one way, the other sees it the other way. (Or in the case of multiple possibilities, enough minds are generated by splitting to observe each of the alternatives in turn. Once split, the minds lead an independent existence, not interacting with the other minds.) Once a mind has split, it can split further to accommodate additional measurements and maintain a record of past history.

It is clear that this is a very different theory from HWI, where in turn it is imagined that worlds do split, and observers along with them, but the splitting of observers lags behind that of the worlds, due to the special circumstances associated with the imagined shared consciousness. Another point not to overlook is that the minds in MMI are nonphysical in nature – they aren't material or even, it seems, sets of material objects or otherwise modelable in a simple way in terms of the material world. Doubts, then, are raised about their existence that seem more fundamental than what can be raised about observers under the requirements of shared consciousness. We could at this point, in defense of MMI, take the route suggested for HWI itself, that details of a mathematical model need not all be "real" for the model to be useful. And so MMI could prove useful, yet it is clearly a different theory from HMW.

5. Schrödinger's Freezer

We now focus on the problem of restoring a lost historical archive, in which it is assumed that the missing information is truly lost and cannot be restored by archaeological means or other analysis of what remains, even using any advanced future

technology that may be developed. Initially we imagine that the archive existed, and (to simplify matters) the observer had access to it but did not, in fact, examine the archive and thus had no knowledge of its contents before the loss occurred.

A simple example of such a scenario is "Schrödinger's freezer," a variation of "Schrödinger's cat." A pitcher of water is placed in the freezer, the door is closed, and the water at time t_1 is frozen. An observer on the outside cannot see what is inside. If they could examine the pitcher and its contents, they would see an intricate pattern of ice crystals, a substantial quantity of information. (Granted, this may not be terribly interesting information, but is useful as an illustration.) As the water freezes, we have a quantum-random process of ice crystal formation: no two successive freezings are likely to reproduce the same pattern. Consequently, under MWI and HMW the worlds split so that each branch has one of the possible ice patterns. For HMW the splitting occurs at the level of W2 not just W1, since the ice remains intact at this point and could be observed, though we are assuming no observation takes place. So, since the observer-copies in the parallel branches did not see any of the ice, all are still identical, and each is only aware of a superposition of possibilities – there is no splitting at the level of W3. The ice with its intricate structure then plays the role of the archive that is initially present and accessible but is unexamined. The observer, a W3, is not split. But the associated W2 did split into myriad versions, each containing one of the frozen patterns.

Imagine now that a power failure causes the freezer's contents to warm up and the ice melts back to water. So the information in the ice is now lost at the W2 level. It is only at the W1 level (and lower) that the information is not lost because worlds at this level are prevented from rejoining through the usual (macroscopic) destructive processes. (And threads never join or split anyway.) When power is finally restored, things cool down again and the water refreezes, this being at time t_2. From a single-world perspective (CI, for example), after the refreezing, "the archive is back" only (with very high probability) it is a different archive, no relation to what was lost. What was lost is still lost; we have not recovered it. But from the perspective of HWI we conclude something quite different.

First, back up to the time of the first freezing, t_1. The ice is there; the (W2) worlds have split. Every possible configuration of ice is present in one of the parallel branches. Each is accompanied by a copy of the observer. But all copies of the observer are essentially alike; their consciousness is shared. So the one observer does not see any one configuration but only a superposition of all the possible configurations. Next, the ice melts, then refreezes. The observer-copies have not changed in any essential respects. Again their consciousness is shared. The observer, then, is a unity that again sees a superposition of all the possible configurations, just as before. So, *there is no essential change from the first freezing*, and in effect, *we have reversed the information loss*.

Pitcher of water before and after placement in "Schrödinger's Freezer." The ice on the right has intricate structural information not present in the liquid, which could be extracted in principle by detailed, microscopic analysis, but would be lost on melting. On refreezing after melting, an interpretation such as CI says it would be a new pattern, the old being irretrievably lost. With MWI the situation is different; with the added rationale of HWI, the "same" pattern would have been restored exactly, in all its varieties, across the parallel branches of reality, both at the level of the observer (W3) and the "predecessor" world level (W2). The observer, who has been undivided up to this point (assuming the ice was not studied), would now split, again and again, as more and more specific details of the ice in each branch were detected and remembered. The restoration also would apply at the level of the surrounding world (W2), in effect to an associated world-community.

In this case, from the standpoint of the observer, a W3, there is actually no information loss. The single observer does not look in the freezer before melting occurs and does not split. But at the level of the surrounding world (W2), a split occurred as the ice initially froze and a rejoining occurs as it melts. When the ice is refrozen the W2 worlds that have joined now split again. When the W2 worlds are joined it is meaningless to talk of "which one" had which version of the ice, thus when the versions are reassigned by refreezing, the loss is made good to all the now redivided W2 worlds, collectively. The observer may now examine the ice, which will for the first time start a splitting at the observer level.

To motivate this notion of recovery of information, we imagine that the lost information does indeed have interest. Instead of a pitcher of ice, it could be a historical record, which could take many forms. One possibility is the remains of a lost loved one, whose physical body, if it survived intact, would have information necessary to characterize their identity. (Efforts to preserve the body at cryogenic temperature may have been made, as one possibility, but were not fully successful.) In that case we imagine the observer has partial information and wants to fill it out to obtain a complete record. (A "complete record" would make it possible to reinstantiate the lost individual in living form, assuming advanced technology needed to repair the body or create a replica, in effect, raising the dead.)

The "observer" in turn might just as well be the whole W2 world, right from the start. If we can invoke a quantum-random process we can fill in the missing information so that all possible fill-ins occur to the different, initially identical W2Is across the parallel branches of reality. Here the difference with a single observer is that at the W2 level, the information once existed but has been lost; this, however, is not a serious impediment. For the freezer example, a simple refreezing served as the quantum-random process for recreating the lost archive. Something more involved would likely be necessary in the cases of real interest, but some appropriate protocol should arguably be feasible, or at least would not violate any known physics. Additional restorations of similar cases could also occur, with care taken to maintain the consistency of the whole. In this way a "blockchain of life" might form, at a distant future date, in which past individuals could again enjoy a living presence in a mutually consistent setting.

6. Some Additional Issues

We note in passing some issues that seem important and, in appropriate cases, worthy of further investigation; no doubt there are more.

We may imagine that, throughout reality as a whole, at the W2 level, duplicates of our consciousness might occur, in the essentially noninteracting branches provided by MWI, where there should be entanglement between different instantiations that maintain the duplication until a split occurs through knowledge of a measurement. Another possibility is that a single, unsplit branch of the wave function, supposed to be of infinite extent, might contain, in all, an infinite collection of duplicate observer-instantiations, but at very great distances from each other. This is explored in the book Our *Mathematical Universe* by Max Tegmark [10] where, for example, it is estimated that an exact, consciousness-sharing copy of a person like yourself will be expected to occur, very roughly, 10^(10^29) meters from here. For practical purposes, this might be considered just a different, non-interacting world.

One interesting property, though, seems implied by our approach and is worth mentioning here: consciousness is supervenient on the worlds in which it is instantiated, wherever they may be, so it is impossible that two distinct observers could have exactly the same "territory" consisting of all the W2 worlds in which they are instantiated. Here we have modeled the observer as a set of objects. Sets have subsets and supersets. In general, the more knowledge an observer has the smaller (not larger) is their territory. An observer who sees a superposition of possible outcomes has two or more parallel branches in their territory whereas a similar observer who notes only one of the possible outcomes not the rest will have correspondingly fewer branches in theirs. Going in the other direction, by having a larger territory (a superset) with suitable other provisions, we obtain a "subobserver" who will share some of the consciousness of the original observer, but not all. As an extreme, a subobserver might have "empty" consciousness, which, however, would be very widely shared. In general, the observers, subobservers and superobservers will comprise a partially ordered set, to go with a similar structuring in the subvening parallel worlds.

The issue could be raised of how HWI handles the issues of entanglement and non-locality, the answer being, the same as MWI, which is formulated to accommodate entanglement, with no sacrifice of locality. HWI is, of course, deterministic, in keeping with MWI.

Another topic worthy of attention is time modeling and time development. The observer does, after all, extend over a time interval and may acquire information or lose it. We have to ask what constitutes an "observer," especially in the face of loss of information. What would it mean for an observer to persist over a time interval? How would loss of information be managed, or what would be the allowable limits to ensure that a well-defined observer still persisted?

Something more should be said, echoing earlier remarks, about the distinction between modeling, mathematically, and "that which is modeled." In general, there will be many models for one natural phenomenon, and one wishes to choose the best possible under appropriate criteria. If, for example, we take the position that the observer is really the important thing and the surrounding world is of lesser significance, it could profoundly affect the model we choose as appropriate, even when the different choices in important ways are mathematically equivalent.

7. Summary

We started with an interpretation of quantum mechanics, MWI (in its main variants) which seemed useful for developing a further interpretation, adding special provisions to consider the case of observers. Specifically, we assumed that, across the largely non-interacting parallel branches of reality provided by MWI, duplicate consciousness in observer-copies would be shared consciousness. To allow additional desirable properties we assumed a hierarchic structure to the worlds, from lowest to highest: W0, W1, W2, W3, with successor orders defined as equivalence classes of their predecessors. Observers, at the W3 level, have instantiations at the W2 level which are united (made equivalent) by shared consciousness, which is assumed to be duplicate consciousness.

An equivalence class of observer instantiations (W3Is) at the W2 level comprises an observer, a W3. The W2 level is observer-independent but in turn has instantiations at the preceding, W1 level. At the W2 level, information can be lost (as also at the W3 level), and the loss is modeled through equivalence classes of W2Is. The W1 level, in turn, corresponds to MWI worlds in a strongly "many worlds" version in which whole worlds split every time a quantum measurement is made, or a "random"

event occurs. Finally, there is the ultimate underlying level, W0, consisting of "threads" which never split or join, whose bundles (equivalence classes) make up the W1 worlds. Overall, we obtained a new variant of MWI we called hierarchic many worlds (HWI).

It is worth saying here that HWI has additional complexity beyond MWI, and that the simplicity of MWI was one of its principal "drawing cards." [1]. On the other hand, HWI provides for something not addressed by MWI, that constitutes our underlying motive for formulating it. This motive in turn was that it is sometimes important to be able to recover lost, past information, something that would ordinarily be forever inaccessible, if we assume that the information has truly been obliterated. A simple example was noted in the case of "Schrödinger's Freezer" in which the information in ice crystals is obliterated through melting. The assumptions made about the observer provide that restoration of the lost information can occur in such a way that many restorations are accomplished at once, covering all the possible versions of the lost information that would have occurred across the parallel branches of reality. Such restorations could be important in a future setting, where, among other things, we may be interested in reviving observers themselves who otherwise would be lost. ■

References

1. https://plato.stanford.edu/entries/qm-manyworlds/, accessed 18 Oct. 2021.
2. https://en.wikipedia.org/wiki/Interpretations_of_quantum_mechanics, accessed 18 Oct. 2021.
3. https://en.wikipedia.org/wiki/Quantum_mechanics, accessed 21 Oct. 2021.
4. https://plato.stanford.edu/entries/qm-everett/, accessed 1 Nov. 2021.
5. https://en.wikipedia.org/wiki/Quantum_state, accessed 24 Oct. 2021.
6. https://en.wikipedia.org/wiki/Probability_amplitude, accessed 31 Oct. 2021.
7. https://en.wikipedia.org/wiki/Wave_function, accessed 1 Nov. 2021.
8. R. Michael Perry, "Contrastive Underdetermination Resolution, with application to Cryonics Revival and Other Possibilities for Life after Clinical Death," *Cryonics* 1Q 2019 27-36.
9. R. Michael Perry, "Restoration without Rediscovery: Authentic De Novo Recreation of Lost Information in a Multiple-Worlds Setting," *Cryonics* 1Q 2021, 10-18.
10. Max Tegmark, *Our Mathematical Universe: My Quest for the Ultimate Nature of Reality*, New York: Knopf, 2014.
11. https://en.wikipedia.org/wiki/Hidden-variable_theory, accessed 31Oct. 2021.
12. https://en.wikipedia.org/wiki/Schr%C3%B6dinger%27s_cat, accessed 19 Oct. 2021.
13. https://en.wikipedia.org/wiki/Wigner%27s_friend, accessed 18 Oct. 2021.
14. Philip Ball, *Beyond Weird: Why Everything You Thought You Knew about Quantum Mechanics Is Different*, Chicago: University of Chicago Press, 2018, 296.
15. https://www.quantamagazine.org/where-quantum-probability-comes-from-20190909/, accessed 17 Oct. 2021.
16. Sean Carroll, *Something Deeply Hidden: Quantum Worlds and the Emergence of Spacetime*, New York: Penguin Random House, 2019, Ch. 7, "Order and Randomness," 129-150.
17. https://en.wikipedia.org/wiki/Many-minds_interpretation, accessed 18 Oct. 2021.

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Fight Aging!

Reports From the Front Line in the Fight Against Aging

Reported by Reason

Fight Aging! exists to help ensure that initiatives with a good shot at greatly extending healthy human longevity become well known, supported, and accepted throughout the world. To this end, Fight Aging! publishes material intended to publicize, educate, and raise awareness of progress in longevity science, as well as the potential offered by future research. These are activities that form a vital step on the road towards far healthier, far longer lives for all.

There is No One Universal Pro-Longevity Gut Microbiome

June, 2021

Evidence suggests that the gut microbiome is influential on long-term health and late life mortality, to perhaps a similar degree as exercise. The various populations of microbial life found in the gut change with age; microbes producing beneficial metabolites are lost, while microbes that provoke chronic inflammation or other issues increase in number. Experiments in short-lived species have shown that transplanting a youthful microbiome into an older individual results in improved health and extended life span. In principle, similar effects could be achieved by some sort of intensive oral probiotic treatment, but that has not yet been demonstrated in animal studies. Researchers have also shown that guiding the immune system to more aggressively attack problem gut microbes can improve the microbiome and its influence on health.

In this open access paper, researchers propose that regional differences in diet mean that there is unlikely to be one optimal gut microbiome to promote longevity. This seems a reasonable prediction, given the degree to which human diet does vary around the world, and the way in which diet interacts with the gut microbiome. It still seems likely that there are universally beneficial changes that one can make to any aged microbiome, in humans or other species, such as enabling the immune system to better remove problem microbes. Early approaches to therapies are likely to involve such universal, narrow improvements; personalized medicine is a more challenging problem.

Regional Diets Targeting Gut Microbial Dynamics to Support Prolonged Healthspan

Centenarians, who have escaped or survived lethal diseases earlier in life, may be considered a spontaneous model of healthy ageing. The gut microbial composition of centenarians has consistently been reported to differ in phylogenetic composition from that of younger people. Interestingly, within centenarian populations, species have been reported to display regional characteristics, further supporting that environmental and/or lifestyle factors including the diet, shape microbial composition.

For example, in an Italian cohort, the centenarian microbiome was found to be dominated by the same two microbial families as in the other age groups (<75 years old) of the population, namely Veillonellaceae and Ruminococcaceae (Firmicutes phylum), but was specifically enriched in the genera Akkermansia, Bifidobacterium, and Christensenella. In contrast, the Chinese Hainan Centenarian Cohort was dominated by Bacteroides (Bacteroidetes phylum) and Escherichia (Proteobacteria phylum). Long-term elderly care residents in the Irish ELDERMET Cohort also had a gut microbiome dominated by Bacteroidetes. Importantly, although the aggregate faecal microbiome in ELDERMET was dominated by Bacteroidetes, the residents showed extraordinary inter-individual variation with 3-92% Bacteroidetes and 7-94% Firmicutes, hinting at a long-term effect of their dietary habits.

The results of the Italian study are also in contrast to those of another Chinese Centenarian Cohort from the Guangxi region, who harboured significantly higher abundance of the genera Escherichia and Roseburia, and reduced abundance of Akkermansia, Lactobacillus, Faecalibacterium, Parabacteroides, Butyricimonas, Coprococcus, Megamonas, Mitsuokella, and Sutterella. A Korean centenarian study found trends similar to both Italian and Guangxi Chinese centenarians, with higher abundance of Akkermansia and Christensenella, and Escherichia, respectively. They also displayed increased abundance of Clostridium and Collinsella, and reduced abundance of Faecalibacterium and Prevotella compared to the general population.

At present, we do not have a good understanding to explain these geographical variations in the centenarian gut microbial

composition or to unequivocally answer if there are certain microbial species globally associated with longevity. In the reviewed studies, some microbial genera associated with healthy elderly populations include Roseburia, Escherichia, Akkermansia, Christensenella, Bifidobacterium, and Clostridium, but they are all highly variable across populations. Based on these cross-sectional observations, it seems unlikely that a universal pro-longevity gut microbiome exists. Rather, the optimal microbiome for healthspan appears to be conditional on the microbial functionality acting on regional- and ethnicity-specific trends driven by cultural food context.

Details on the Failed Phase 3 Trial of the resTORbio mTORC1 Inhibitor

June, 2021

The short version of the story regarding the failure of resTORbio's phase 3 trial of an mTORC1 inhibitor targeting immune function and influenza infection in old people is that the FDA forced a last minute change of the phase 3 endpoint from the phase 2 endpoint of a reduction in clinically confirmed infections to a more nebulous outcome of whether or not people reported feeling better. Which is far from the worst offense that FDA staff have committed in the course of hindering the adoption of new medical technologies, but it is illustrative of the obstacle that regulators pose. We can all speculate as to what was going on under the hood here, and which influences led to this outcome.

To my eyes, the field of mTOR based therapies remains something of a sideshow when it comes to human aging and longevity. The same is true of many of the metabolic manipulation approaches based on upregulation of stress response mechanisms. These mechanisms are known to produce sizable effects in short-lived species, but not in long-lived species such as our own. Thus here, mTORC1 inhibition does not produce a startling and large effect on infection rate and immune function, nor should we expect it to, but it is cheap and it does produce some effect. mTORC1 inhibition replicates a thin slice of the beneficial calorie restriction response, and we know what calorie restriction can achieve in humans; this sort of approach isn't the path to very large gains.

We did a phase 2b and a phase 3 double-blind, randomised, placebo-controlled trial in adults aged at least 65 years enrolled in New Zealand, Australia, and the USA at 54 sites. In the phase 2b trial, patients were aged 65-85 years, with asthma, type 2 diabetes, chronic obstructive pulmonary disease (COPD), congestive heart failure, were current smokers, or had an emergency room or hospitalisation for a respiratory tract infection (RTI) within the past 12 months. In the phase 3 trial, patients were aged at least 65 years, did not have COPD, and were not current smokers.

In the phase 2b trial, patients were randomly assigned to using a validated automated randomisation system to oral RTB101 5 mg, RTB101 10 mg once daily, or placebo in part 1 and RTB101 10 mg once daily, RTB101 10 mg twice daily, RTB101 10 mg plus everolimus once daily, or matching placebo in part 2. In the phase 3 trial, patients were randomly assigned to RTB101 10mg once daily or matching placebo. The phase 2b primary outcome was the incidence of laboratory-confirmed RTIs during 16 weeks of winter cold and influenza season and the phase 3 primary outcome was the incidence of clinically symptomatic respiratory illness defined as symptoms consistent with an RTI, irrespective of whether an infection was laboratory-confirmed.

The purpose of our trials was to investigate whether targeting ageing biology with mTOR inhibitors could improve immune function and decrease the incidence of RTIs in older adults at doses that were well tolerated. The mTOR inhibitor RTB101 10 mg once daily for 16 weeks was well tolerated in adults aged at least 65 years, increased expression of IFN-stimulated antiviral genes in peripheral blood, and decreased the incidence of laboratory-confirmed RTIs (the phase 2b primary endpoint), but not the incidence of clinically symptomatic respiratory illness defined as respiratory symptoms consistent with an RTI irrespective of whether an infection was laboratory confirmed (the phase 3 primary endpoint).

Several possible explanations exist for the divergent results of the phase 2b and phase 3 trials, including the change in primary endpoint and changes in the way respiratory symptoms were collected between the two trials. In the phase 2b trial, respiratory illness symptoms were collected during twice weekly telephone calls with patients and the primary endpoint required predefined symptomatic criteria to be met as well as laboratory confirmation of an infection. In the phase 3 trial, respiratory illness symptoms were collected in eDiaries that patients filled out each evening and the primary endpoint was based on symptoms alone without requiring laboratory confirmation of an infection. Multiple investigators in the phase 3 trial anecdotally noted that patients reported in their nightly eDiary respiratory illness symptoms such as cough or headache that were part of the prespecified diagnostic criteria for a clinically symptomatic respiratory illness even when the patient and the investigator did not think that the patient had an RTI.

Despite the negative phase 3 results, important lessons were learned from this clinical development programme that is the largest to date targeting ageing biology in humans. First, the results show that it is possible to target mechanisms underlying ageing biology safely with therapies such as mTOR inhibitors in older adults. Second, the results suggest that therapies that target ageing biology in older adults might ameliorate at least some aspects of ageing organ system dysfunction (such as deficient IFN-induced antiviral responses). Further refinement of clinical endpoints and more precise identification of responder patient populations will be important in future trials of therapies that

intervene in ageing biology to improve immune function in older adults.

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A Systems Biology Approach to Manipulating the Biochemistry of Senescent Cells

June, 2021

Cells become senescent in response to reaching the Hayflick limit on replication, or to potentially cancerous mutations, or a toxic environment and consequent cell damage, or signaling from other senescent cells. Senescence is nominally an irreversible state. Replication halts and the cell begins secreting pro-inflammatory signals to attract the attention of the immune system. Senescent cells are normally removed via programmed cell death or the actions of cytotoxic immune cells. With age the rate of creation increases and the rate of removal falls, however, leading to a growing number of senescent cells throughout the body. The signaling of that growing number of senescent cells in aged tissues causes chronic inflammation and disrupts tissue maintenance, leading to age-related disease.

What to do about this? Much of the focus of the research community is on senolytic approaches that force senescent cells into apoptosis and self-destruction, or that provoke the immune system into more efficient clearance of senescent cells. These therapies have achieved impressive results in mice, reversing age-related disease and many measures of aging. Some researchers are interested in the reversal of senescence, however: reprogramming cells in ways that overcome the regulatory processes that normally ensure continuation of the senescent state.

Is reversal of senescence a good idea? It seems likely that at least some senescent cells are senescent for a good reason. That they are damaged, and in some cases that damage is potentially cancerous. Reversing senescence may well produce short term gains that are similar to those of senolytic therapies, since in either case the harmful signaling produced by senescent cells is removed. But a significantly raised risk of cancer may be the cost of that approach.

Systems biology for reverse aging

Although partial reprogramming proved that senescent cells can be reverted, early termination of this reprogramming process is known to cause epigenetic dysregulation, resulting in dedifferentiated dysplastic cells such as renal cancer. Therefore, a novel therapeutic strategy without such critical limitations is highly needed. Cellular senescence is caused by complex interactions among biomolecules that govern cell cycle, DNA damage response, energy metabolism, and cytokine secretion. Recent studies showed that cellular senescence, previously considered as an irreversible biological phenomenon, can be reversed, but due to the nature of such complex interactions governing cellular senescence, the mechanism by which cellular senescence can be reversed has not been revealed.

Researchers reconstructed an ensemble of 5000 Boolean network models that can represent senescence, quiescence, and proliferation phenotypes by integrating information from the literature, network databases and phosphoprotein array data of dermal fibroblasts. In their models, cellular senescence is induced by simultaneous activation of DNA damage signal (doxorubicin) and growth signal (IGF-1 plus serum). They identified 3-phosphoinositide-dependent protein kinase 1 (PDK1) as the optimal protein target that can safely revert senescence to quiescence while avoiding uncontrolled proliferation, through extensive computer simulation analysis of the ensemble model. PDK1 forms a positive feedback structure along with AKT, IKBKB, and PTEN, that simultaneously control both nuclear factor κB, which controls cytokine secretion, and mTOR, which regulates cell growth.

In order to validate the simulation results, researchers conducted in vitro experiments and confirmed that when PDK1 was inhibited, various markers of cellular senescence are returned to normal and proliferation potential is restored. From wound healing assays and 3D reconstructed skin tissue experiments, they also reaffirmed that the reverted cells are able to respond appropriately to external stimuli. In particular, by observing dermal fibroblast within dermis along with keratinocyte within epidermis, 3D reconstructed skin tissue experiments verified that PDK1 inhibition promotes epidermal renewal and restores skin thickness, resulting in reversal of age-related skin degeneration.

Arguing for Metformin's Effects on Life Expectancy to be Due to Suppression of Excessive Inflammation

June, 2021

Researchers have been arguing for some years now that metformin improves life span via suppression of excessive inflammation. Metformin, it has to be said, has terrible, unreliable, very mixed animal data when it comes to slowing aging. Plus that one human study in diabetic patients in which life expectancy was very modestly increased. So it seems to me that progress in understanding what is going on under the hood is largely of academic interest at this point in time. The effect size is just not large enough to be a medical focus. If suppression of inflammation and extended healthy lives are the goals on the table, then senolytic therapies to clear out senescent cells and their inflammatory signaling look much more promising.

Metformin is a widely prescribed blood sugar-lowering drug. It is often used as an early therapy (in combination with diet and lifestyle changes) for type 2 diabetes. Metformin works by lowering glucose production in the liver, reducing blood glucose levels that, in turn, improve the body's response to insulin. But scientists have also noted that metformin possesses anti-inflammatory properties, though the basis for this activity was not known. Researchers have now identified the molecular mechanism for the anti-inflammatory activity of metformin and, in mouse studies, found that metformin prevents pulmonary or lung inflammation in animals infected with SARS-CoV-2, the virus that causes COVID-19.

But while clinical studies suggested metformin's anti-inflammatory activity, rather than lowering of blood glucose, could be responsible for reduced COVID-19 severity and mortality, none of the studies offered an explanation or prompted large, randomized clinical trials needed for obtaining conclusive answers.

IL-1β, along with IL-6, are small proteins called cytokines that cause inflammation as an early immune response. Their amounts are often highly elevated in persons infected by SARS-CoV-2, creating "cytokine storms" in which the body starts attacking its own cells and tissues. They are signs of an acute immune response gone awry. Production of IL-1β depends on a large protein complex called the inflammasome.

Researchers confirmed that metformin inhibited inflammasome activation and prevented SARS-CoV-2-induced pulmonary inflammation in mice. Cell culture studies using macrophages revealed the underlying mechanism by which metformin exerts its anti-inflammatory activity: reduced production of ATP by mitochondria. ATP is the molecule that mitochondria use to store chemical energy for cells. It is essential to all cellular processes, but blunted ATP production in liver cells is responsible for the glucose lowering effect of metformin.

Lower amounts of ATP in macrophages led to inhibition of mitochondrial DNA synthesis, a critical step in NLRP3 inflammasome activation. Subsequent research found that clearing away damaged mitochondria reduced NLRP3 inflammasome activity and reduced inflammation. "These experiments strongly suggest that improved delivery of metformin into lung macrophages can provide new treatments for severe COVID-19. The findings suggest metformin may have therapeutic potential for treating a variety of neurodegenerative and cardiovascular diseases in which NLRP3 inflammasome activation is a factor. Inhibition of inflammasome activation may also account for the poorly explained anti-aging effect of metformin."

Link: https://www.eurekalert.org/pub_releases/2021-06/uoc--cdd060821.php

The GrimAge Epigenetic Clock Reflects Mortality Risk Differences Between Twins

June, 2021

Epigenetic clocks are correlations identified between physiological age and algorithmic combinations of DNA methylation status at various CpG sites on the genome. Cells constantly change their epigenetic marks, such as DNA methylation, in response to circumstances. Some of those circumstances involve characteristic damage and responses to damage that occur with age, and that are broadly similar between individuals in later life. The clocks thus reflect, to some degree, biological rather than chronological age, the progression of processes of damage rather than time.

It is entirely unclear, and will remain so for some time, as to what exactly is measured by these clocks, however. Which processes of aging drive these epigenetic changes? Without knowing the answer to that question, it is hard to use the clocks to test the efficacy of a potential rejuvenation therapy. Perhaps a clock entirely fails to consider the specific form of damage repaired in a study. There is no practical way to find out other than to run a lot of studies with a lot of different clocks and different potential rejuvenation therapies. Early clocks have interesting and potentially problematic blind spots: the Horvath clock is insensitive to fitness, for example, as demonstrated in twin studies with fit and unfit twin pairs. This is known, and improvements were made. The study noted here demonstrates that the later GrimAge clock is a clear improvement, as it does identify differences in mortality risk between genetically identical twins.

Novel measures of biological aging known as "epigenetic clocks" have been used to assess biological aging process and mortality risk. The major advantage of epigenetic clocks is that they can be utilized to estimate the progress of aging over the life course. Horvath's algorithm was the first widely used epigenetic clock. It was trained against chronological age, and therefore it has been argued that Horvath's DNAmAge estimates may exclude CpGs whose methylation patterns may reflect a deviation of biological age from chronological age. DNAm GrimAge was subsequently developed to predict mortality. It is a combination of DNAm-based surrogate biomarkers for health-related plasma proteins and smoking pack-years as well as sex and chronological age. It is associated with the key "hallmarks of aging," such as mitochondrial dysfunction and cellular senescence.

So far, multiple studies with varying study designs and outcomes have found epigenetic age acceleration - an older DNAm age estimated by epigenetic clocks compared to chronological age - to be associated with increased mortality risk. It has been

suggested that epigenetic age predicts all-cause mortality above and beyond chronological age and traditional risk factors.

We examined the association of epigenetic age acceleration, defined by Horvath's DNAmAge and DNAm GrimAge, with all-cause mortality within a population-based cohort of 413 Finnish twin sisters. The female participants are twin pairs who share sex, age, and all (monozygotic pairs) or half (dizygotic pairs) of their genetic polymorphisms and most of the intrauterine and childhood environment. This allows us to distinguish the effect of lifestyle and genetic factors on the association of epigenetic aging and mortality.

Our results suggest that DNAm GrimAge outperforms Horvath's DNAmAge in mortality risk prediction. We performed pairwise analysis in which risk for survival as a function of an epigenetic age acceleration was conducted to minimize potential pleiotropic genetic and familial influences on the association between epigenetic aging and mortality. Our genetically controlled analysis suggests that faster epigenetic aging is associated with a higher risk of mortality irrespective of genetic influences. Further, the results indicate that smoking plays an important role in the association between epigenetic aging and mortality. In conclusion, the findings suggest that DNAm GrimAge is a strong predictor of mortality independent of genetic influences.

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Immune Aging Clock Identifies CXCL9 as a Target to Suppress Age-Related Inflammation

July, 2021

Researchers are increasingly making use of machine learning approaches in order to produce measures of biological age, known as clocks, derived from weighted combinations of biological data: epigenetic status, protein levels, transcript levels, and so forth. In most such clocks, it is unclear as to how the underlying processes of aging act to produce the identified epigenetic marks or differences in protein levels. Researchers here build a protein-based clock that is restricted to immune system signaling molecules that are found in blood samples. Working backwards from the proteins identified as being important to the clock, they note one that can be suppressed to potentially reverse some of the inflammatory aspects of age-related immune dysfunction.

Researchers have created an inflammatory clock of aging (iAge) which measures inflammatory load and predicts multi-morbidity, frailty, immune health, cardiovascular aging and is also associated with exceptional longevity in centenarians. The study identified the soluble chemokine CXCL9 as the strongest contributor to iAge. It is a small immune protein that is usually called into action to attract lymphocytes to the site of an infection. "But in this case we showed that CXCL9 upregulates multiple genes implicated in inflammation and is involved in cellular senescence, vascular aging, and adverse cardiac remodeling. Silencing CXCL9 reversed loss of function in aging endothelial cells in both humans and mice."

Results from the initial analysis, which also included information from comprehensive clinical health assessments of 902 individuals, were validated in an independent cohort of centenarians and all-cause mortality in the Framingham Heart Study. According to the researchers, when it comes to health and longevity, the "age" of one's immune system most certainly trumps the chronological information that can be derived from a driver's license. "On average, centenarians have an immune age that is 40 years younger than what is considered 'normal' and we have one outlier, a super-healthy 105 year-old man who has the immune system of a 25 year old."

Study results involving cardiac health were also validated in a separate group of 97 extremely healthy adults (age 25 - 90 years of age). Researchers found a correlation between CXCL9 and results from pulse wave velocity testing, a measure of vascular stiffness. "These people are all healthy according to all available lab tests and clinical assessments, but by using iAge we were able to predict who is likely to suffer from left ventricular hypertrophy (an enlargement and thickening of the walls of the heart's main pumping chamber) and vascular dysfunction."

Link: https://www.buckinstitute.org/news/first-actionable-clock-that-predicts-immunological-health-and-chronic-diseases-of-aging/

It is Plausible that Continual Removal of Senescent Cells Would Impair Regeneration and Limit Benefits to Life Span

July, 2021

The accumulation of senescent cells with advancing age is harmful. Selectively destroying those cells, even as few as a third of them, and even just once in later life, produces significant benefits to health and life span in mice. Cells become senescent in response to molecular damage, or to the signaling of nearby senescent cells, or on reaching the Hayflick limit on cell replication, or in response to tissue injury. In youth, senescent cells are rapidly cleared by the immune system and programmed cell death, but in later life the balance of creation and destruction is tipped towards an ever-increasing number of such cells.

Senescent cells serve useful functions prior to running awry in old age. They help to coordinate regeneration and suppress the

incidence of cancer. They secrete signals that attract the attention of the immune system, spur growth, and provoke the short-term inflammation needed to resolve issues of damage in the body. Thus we might suspect that a blanket and continual removal of senescent cells could be harmful in some ways. In fact, mice do live longer when all senescent cells are continually removed, but that may only mean that the beneficial outcomes outweigh the negative outcomes, rather than there being no meaningful negative outcomes.

The present consensus is that periodic removal of senescent cells, which does produce rejuvenation and extend life span in mice, likely has no meaningful downside. It would clear out the problem of lingering cells during short treatments, while at all other times allowing for the temporary formation of new senescent cells as needed, such as in response to injury. This consensus may or may not reflect reality, we shall see as ever more data accumulates. In this open access paper, researchers hypothesize on the question of why senolytic treatments to clear senescent cells extend median life span to a greater degree than they extend maximum life span in mice. Does that outcome result from harmful effects that arise in later life to counterbalance the benefits?

This seems a question that is hard to answer, involving the need for a much greater understanding of the relative contributions of different mechanisms of aging at different ages. It is quite possible that any one given mechanism of aging, such as cellular senescence, is more or less influential on mortality in middle age versus extreme old age. That may not require any great difference in the details of cellular senescence in an aging body, but rather arise because another mechanism becomes more important in late life, for reasons that have little to do with cellular senescence, outweighing gains due to a reduced burden of senescent cells. Without intervening in these other mechanisms, it is challenging to say anything about their importance. We only know that senescent cell clearance is exciting as a basis for rejuvenation because it was successfully attempted. Prior to that point, there was no good way to assign a relative importance to the role of cellular senescence in degenerative aging.

Senolytics and the compression of late-life mortality

Whilst work continues to explore the possible therapeutic benefits of senolysis, we recently suggested that it is important to ask what evolutionary forces might have been behind the emergence of cellular senescence. Entry into the senescent state appears to be regulated, presenting questions about why such a response should have evolved. It seems a priori unlikely that a purely negative action would be favoured by natural selection. In terms of potential benefits, cellular senescence is often regarded as an anti-cancer mechanism, since it limits the division potential of cells. However, many studies have shown that senescent cells often also have carcinogenic properties. Furthermore, other studies have shown that cellular senescence is beneficially involved in wound healing, development, and tissue repair.

We recently brought these findings and ideas together and concluded that evolutionary logic strongly supports the idea that the latter positive contributions are the main reason for the evolution of cellular senescence. We further suggested that, since the immune system appears to play a role in clearing senescent cells once they have performed their temporary functions, the observed age-related accumulations of senescent cells might arise simply because the immune system had to strike a balance between false negatives (overlooking some senescent cells) and false positives (destroying healthy body cells).

The importance of understanding the role of senescent cells is further indicated by recent senolysis studies in mice, where it was found that treatment with senolytics resulted in a substantial increase in mean and median survival times. However, in each of the studies there was much less increase in the maximum survival time. Such an outcome is only possible if, following senolytic treatments, the deaths that are postponed to produce the increased mean / median lifespans become concentrated in the interval prior to the relatively unaltered maximum lifespan. Such a phenomenon constitutes a 'compression of mortality', which needs to be explained

We developed computer simulations of three possible mechanistic scenarios in order to gain a better understanding of possible modes of action of senolytic treatments. Scenario A, which supposes simply that senescent cells are all-important in ageing, was shown to be incompatible with experimental findings. Scenario B, which allows for other forms of damage to be involved and which also allows for senescent cells to drive these other forms of damage to some degree, was also found not to explain the data, although it does generate some interesting behaviours. In contrast, Scenario C proved to have the potential to explain the experimental findings. Scenario C includes the idea that the immune system plays an important role in removing senescent cells and related damage, but that this 'repair capacity' of the immune system is also negatively affected by senolytic drugs. In the case of a single senolytic treatment the repair capacity can recover, but if the treatment is given continuously (as in all the experimental studies), the repair capacity is chronically reduced. This leads to an accelerated accumulation of damage, causing a faster increase of mortality.

https://www.biorxiv.org/content/10.1101/2021.04.24.441236v1

Send email to Reason at Fight Aging!: **reason@fightaging.org**

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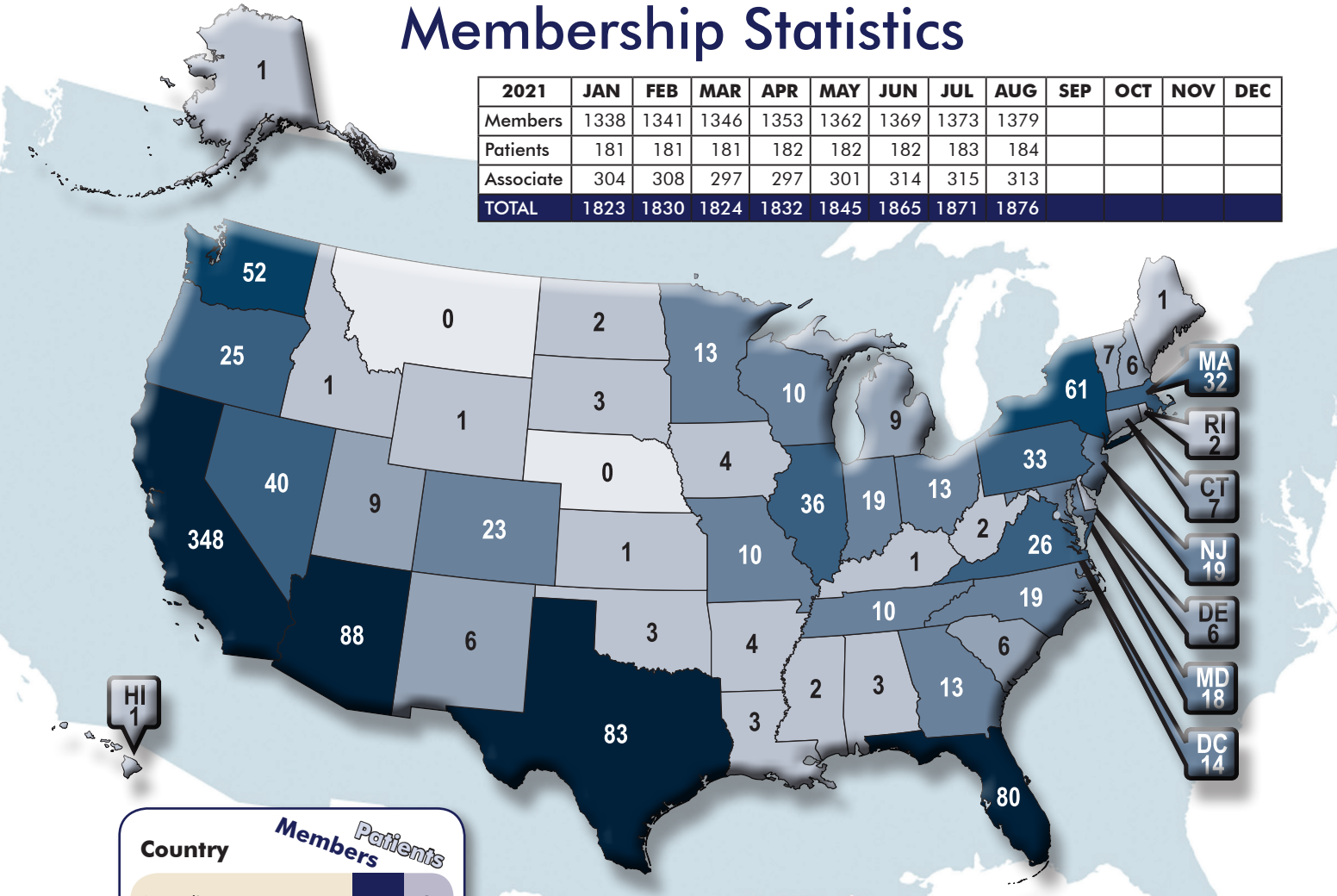
Membership Statistics

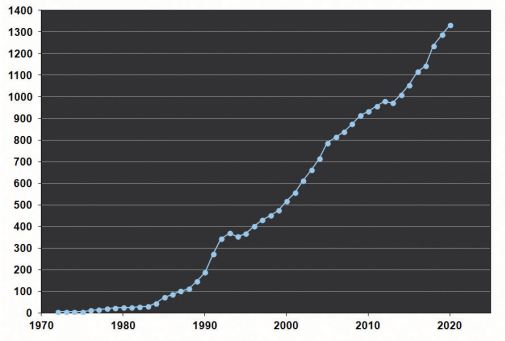
2021	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Members	1338	1341	1346	1353	1362	1369	1373	1379				
Patients	181	181	181	182	182	182	183	184				
Associate	304	308	297	297	301	314	315	313				
TOTAL	1823	1830	1824	1832	1845	1865	1871	1876				



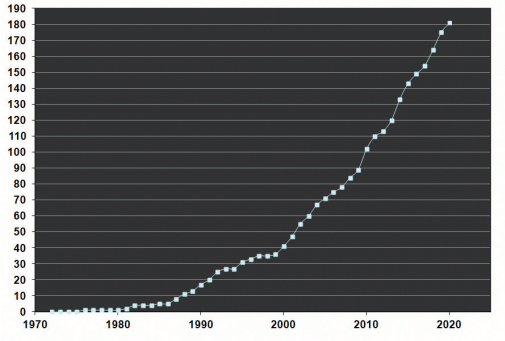
International Members & Patients

Country	Members	Patients
Australia	11	3
Austria	1	0
Belgium	1	0
Brazil	1	0
Bulgaria	1	0
Canada	76	4
China	2	1
Finland	2	0
France	3	1
Germany	19	0
Hong Kong	2	0
Hungary	1	0
Israel	1	1
Italy	1	0
Japan	6	0
Luxembourg	1	0
Mexico	5	0
Monaco	1	0
Netherlands	1	0
New Zealand	1	0
Norway	2	0
Portugal	4	1
Puerto Rico	3	0
Slovenia	1	0
Spain	5	1
Sweden	1	0
Switzerland	2	0
Taiwan	1	0
Thailand	3	1
United Kingdom	43	3
Virgin Islands	1	0
TOTAL	203	16

- 0 Members
- 1–4 Members
- 5–9 Members
- 10–24 Members
- 25–49 Members
- 50–74 Members
- 75+ Members



Number of Alcor members



Number of Alcor patients

Revival Update

Scientific Developments Supporting Revival Technologies

Reported by R. Michael Perry, Ph.D.

Revealing Enzyme Functional Architecture via High-Throughput Microfluidic Enzyme Kinetics

C J Markin, D A Mokhtari, F Sunden, M J Appel, E Akiva, S A Longwell, C Sabatti, D Herschlag, P M Fordyce

Science 23 Jul 2021; 373(6553):eabf8761, https://pubmed.ncbi.nlm.nih.gov/34437092/, accessed 13 Nov 2021.

Abstract

Systematic and extensive investigation of enzymes is needed to understand their extraordinary efficiency and meet current challenges in medicine and engineering. We present HT-MEK (High-Throughput Microfluidic Enzyme Kinetics), a microfluidic platform for high-throughput expression, purification, and characterization of more than 1500 enzyme variants per experiment. For 1036 mutants of the alkaline phosphatase PafA (phosphate-irrepressible alkaline phosphatase of Flavobacterium), we performed more than 670,000 reactions and determined more than 5000 kinetic and physical constants for multiple substrates and inhibitors. We uncovered extensive kinetic partitioning to a misfolded state and isolated catalytic effects, revealing spatially contiguous regions of residues linked to particular aspects of function. Regions included active-site proximal residues but extended to the enzyme surface, providing a map of underlying architecture not possible to derive from existing approaches. HT-MEK has applications that range from understanding molecular mechanisms to medicine, engineering, and design.

From: Stanford Researchers Develop Tool to Drastically Speed Up the Study of Enzymes

Ker Than, *Stanford News*, 22 Jul 2021, https://news.stanford.edu/2021/07/22/new-tool-drastically-speeds-study-enzymes/, accessed 14 Nov 2021.

"A chemical reaction that would take longer than the lifetime of the universe to happen on its own can occur in seconds with the aid of enzymes," said Polly Fordyce, an assistant professor of bioengineering and of genetics at Stanford University.

While much is now known about enzymes, including their structures and the chemical groups they use to facilitate reactions, the details surrounding how their forms connect to their functions, and how they pull off their biochemical wizardry with such extraordinary speed and specificity are still not well understood.

A new technique, developed by Fordyce and her colleagues at Stanford and detailed this week in the journal Science, could help change that. Dubbed HT-MEK – short for High-Throughput Microfluidic Enzyme Kinetics – the technique can compress years of work into just a few weeks by enabling thousands of enzyme experiments to be performed simultaneously. "Limits in our ability to do enough experiments have prevented us from truly dissecting and understanding enzymes," said study co-leader Dan Herschlag, a professor of biochemistry at Stanford's School of Medicine.

By allowing scientists to deeply probe beyond the small "active site" of an enzyme where substrate binding occurs, HT-MEK could reveal clues about how even the most distant parts of enzymes work together to achieve their remarkable reactivity.

"It's like we're now taking a flashlight and instead of just shining it on the active site we're shining it over the entire enzyme," Fordyce said. "When we did this, we saw a lot of things we didn't expect."

The technology behind HT-MEK was developed and refined over six years through a partnership between the labs of Fordyce and Herschlag. "This is an amazing case of engineering and enzymology coming together to – we hope – revolutionize a field," Herschlag said. "This project went beyond your typical collaboration – it was a group of people working jointly to solve a very difficult problem – and continues with the methodologies in place to try to answer difficult questions."

HT-MEK combines two existing technologies to rapidly speed up enzyme analysis. The first is microfluidics, which involves molding polymer chips to create microscopic channels for the precise manipulation of fluids. The second is cell-free protein synthesis, a technology that takes only those crucial pieces of biological machinery required for protein production and combines them into a soupy extract that can be used to create enzymes synthetically, without requiring living cells to serve as incubators. "We've automated it so that we can use printers to deposit microscopic spots of synthetic DNA coding for the enzyme that we want onto a slide and then align nanoliter-sized

chambers filled with the protein starter mix over the spots," Fordyce explained.

Because each tiny chamber contains only a thousandth of a millionth of a liter of material, the scientists can engineer thousands of variants of an enzyme in a single device and study them in parallel. By tweaking the DNA instructions in each chamber, they can modify the chains of amino acid molecules that comprise the enzyme. In this way, it's possible to systematically study how different modifications to an enzyme affects its folding, catalytic ability and ability to bind small molecules and other proteins.

When the team applied their technique to a well-studied enzyme called PafA, they found that mutations well beyond the active site affected its ability to catalyze chemical reactions – indeed, most of the amino acids, or "residues," making up the enzyme had effects.

The scientists also discovered that a surprising number of mutations caused PafA to misfold into an alternate state that was unable to perform catalysis. "Biochemists have known for decades that misfolding can occur but it's been extremely difficult to identify these cases and even more difficult to quantitatively estimate the amount of this misfolded stuff," said study co-first author Craig Markin, a research scientist with joint appointments in the Fordyce and Herschlag labs.

"This is one enzyme out of thousands and thousands," Herschlag emphasized. "We expect there to be more discoveries and more surprises."

Neuroprosthesis for Decoding Speech in a Paralyzed Person with Anarthria

David A. Moses, PhD; Sean L. Metzger, MS; Jessie R. Liu, BS; Gopala K. Anumanchipalli, PhD; Joseph G. Makin, PhD; Pengfei F. Sun, PhD; Josh Chartier, PhD; Maximilian E. Dougherty, BA; Patricia M. Liu, MA; Gary M. Abrams, MD; Adelyn Tu-Chan, DO; Karunesh Ganguly, MD, PhD; and Edward F. Chang, MD,
15 Jul 2021, N Engl J Med 2021; 385:217-227

https://www.nejm.org/doi/full/10.1056/NEJMoa2027540, accessed 14 Nov 2021.

Abstract

Background: Technology to restore the ability to communicate in paralyzed persons who cannot speak has the potential to improve autonomy and quality of life. An approach that decodes words and sentences directly from the cerebral cortical activity of such patients may represent an advancement over existing methods for assisted communication.

Methods: We implanted a subdural, high-density, multielectrode array over the area of the sensorimotor cortex that controls speech in a person with anarthria (the loss of the ability to articulate speech) and spastic quadriparesis caused by a brain-stem stroke. Over the course of 48 sessions, we recorded 22 hours of cortical activity while the participant attempted to say individual words from a vocabulary set of 50 words. We used deep-learning algorithms to create computational models for the detection and classification of words from patterns in the recorded cortical activity. We applied these computational models, as well as a natural-language model that yielded next-word probabilities given the preceding words in a sequence, to decode full sentences as the participant attempted to say them.

Results: We decoded sentences from the participant's cortical activity in real time at a median rate of 15.2 words per minute, with a median word error rate of 25.6%. In post hoc analyses, we detected 98% of the attempts by the participant to produce individual words, and we classified words with 47.1% accuracy using cortical signals that were stable throughout the 81-week study period.

Conclusions: In a person with anarthria and spastic quadriparesis caused by a brain-stem stroke, words and sentences were decoded directly from cortical activity during attempted speech with the use of deep-learning models and a natural-language model.

From: "Neuroprosthesis" Restores Words to Man with Paralysis

Robin Marks, U*CSF News*, 14 Jul 2021, https://www.ucsf.edu/news/2021/07/420946/neuroprosthesis-restores-words-man-paralysis, accessed 14 Nov 2021.

Researchers at UC San Francisco have successfully developed a "speech neuroprosthesis" that has enabled a man with severe paralysis to communicate in sentences, translating signals from his brain to the vocal tract directly into words that appear as text on a screen. The achievement, which was developed in collaboration with the first participant of a clinical research trial, builds on more than a decade of effort by UCSF neurosurgeon Edward Chang, MD, to develop a technology that allows people with paralysis to communicate even if they are unable to speak on their own. The study appears July 15 in the *New England Journal of Medicine*.

"To our knowledge, this is the first successful demonstration of direct decoding of full words from the brain activity of someone who is paralyzed and cannot speak," said Chang, senior author on the study. "It shows strong promise to restore communication by tapping into the brain's natural speech machinery."

To investigate the potential of this technology in patients with paralysis, Chang partnered with colleague Karunesh Ganguly, MD, PhD, an associate professor of neurology, to launch a study

known as "BRAVO" (Brain-Computer Interface Restoration of Arm and Voice). The first participant in the trial is a man in his late 30s who suffered a devastating brainstem stroke more than 15 years ago that severely damaged the connection between his brain and his vocal tract and limbs. Since his injury, he has had extremely limited head, neck, and limb movements, and communicates by using a pointer attached to a baseball cap to poke letters on a screen.

The participant, who asked to be referred to as BRAVO1, worked with the researchers to create a 50-word vocabulary that Chang's team could recognize from brain activity using advanced computer algorithms. The vocabulary – which includes words such as "water," "family," and "good" – was sufficient to create hundreds of sentences expressing concepts applicable to BRAVO1's daily life.

For the study, Chang surgically implanted a high-density electrode array over BRAVO1's speech motor cortex. After the participant's full recovery, his team recorded 22 hours of neural activity in this brain region over 48 sessions and several months. In each session, BRAVO1 attempted to say each of the 50 vocabulary words many times while the electrodes recorded brain signals from his speech cortex.

To translate the patterns of recorded neural activity into specific intended words, the other two lead authors of the study, Sean Metzger, MS and Jessie Liu, BS, both of the UCSF-UC Berkeley Joint PhD Program in Bioengineering, used custom neural network models, which are forms of artificial intelligence. When the participant attempted to speak, these networks distinguished subtle patterns in brain activity to detect speech attempts and identify which words he was trying to say.

To test their approach, the team first presented BRAVO1 with short sentences constructed from the 50 vocabulary words and asked him to try saying them several times. As he made his attempts, the words were decoded from his brain activity, one by one, on a screen.

Then the team switched to prompting him with questions such as "How are you today?" and "Would you like some water?" As before, BRAVO1's attempted speech appeared on the screen. "I am very good," and "No, I am not thirsty."

The team found that the system was able to decode words from brain activity at rates of up to 18 words per minute with up to 93 percent accuracy (75 percent median). Contributing to the success was a language model Moses applied that implemented an "auto-correct" function, similar to what is used by consumer texting and speech recognition software.

Polymorphic Tandem DNA Repeats Activate the Human Telomerase Reverse Transcriptase Gene

Tao Xu, De Cheng, Yuanjun Zhao, Jinglong Zhang, Xiaolu Zhu, Fan Zhang, Gang Chen, Yang Wang, Xiufeng Yan, Gavin P. Robertson, Shobhan Gaddameedhi, Philip Lazarus, Shuwen Wang, and Jiyue Zhu

PNAS 29 Jun 2021, 118 (26) e2019043118; https://doi.org/10.1073/pnas.2019043118, accessed 15 Nov 2021.

Abstract

Multiple independent sequence variants of the hTERT locus have been associated with telomere length and cancer risks in genome-wide association studies. Here, we identified an intronic variable number tandem repeat, VNTR2-1, as an enhancer-like element, which activated hTERT transcription in a cell in a chromatin-dependent manner. VNTR2-1, consisting of 42-bp repeats with an array of enhancer boxes, cooperated with the proximal promoter in the regulation of hTERT transcription by basic helix–loop–helix transcription factors and maintained hTERT expression during embryonic stem-cell differentiation. Genomic deletion of VNTR2-1 in MelJuSo melanoma cells markedly reduced hTERT transcription, leading to telomere shortening, cellular senescence, and impairment of xenograft tumor growth. Interestingly, VNTR2-1 lengths varied widely in human populations; hTERT alleles with shorter VNTR2-1 were underrepresented in African American centenarians, indicating its role in human aging. Therefore, this polymorphic element is likely a missing link in the telomerase regulatory network and a molecular basis for genetic diversities of telomere homeostasis and age-related disease susceptibilities.

From: Research Identifies Potential Role of 'Junk DNA' Sequence in Aging, Cancer

Judith Van Dongen, Office of Research, WSU Health Sciences Spokane, WA, 23 Jul 2021, https://pharmacy.wsu.edu/2021/07/23/research-identifies-potential-role-of-junk-dna-sequence-in-aging-cancer/, accessed 15 Nov 2021.

We don't often think about ourselves this way, but our bodies are made up of trillions of living cells. We age as our cells age, which happens when those cells eventually stop replicating and dividing. Scientists have long known that our genes influence how our cells age and how long we live, but how that works exactly remains unclear. Findings from a new study led by researchers at Washington State University have solved a small piece of that puzzle, bringing scientists one step closer to solving the mystery of aging.

A research team headed by Jiyue Zhu, a professor in the College of Pharmacy and Pharmaceutical Sciences, recently identified a

DNA region known as VNTR2-1 that appears to drive the activity of the telomerase gene, which has been shown to prevent aging in certain types of cells. The study was published in the journal *Proceedings of the National Academy of Sciences* (*PNAS*).

The telomerase gene controls the activity of the telomerase enzyme, which helps produce telomeres, the caps at the end of each strand of DNA that protect the chromosomes within our cells. In normal cells, the length of telomeres gets a little bit shorter every time cells duplicate their DNA before they divide. When telomeres get too short, cells can no longer reproduce, causing them to age and die. However, in certain cell types – including reproductive cells and cancer cells – the activity of the telomerase gene ensures that telomeres are reset to the same length when DNA is copied. This is essentially what restarts the aging clock in new offspring but is also the reason why cancer cells can continue to multiply and form tumors.

Knowing how the telomerase gene is regulated and activated and why it is only active in certain types of cells could someday be the key to understanding how we age, as well as how to stop the spread of cancer. That is why Zhu has focused the past 20 years of his career as a scientist solely on the study of this gene.

Zhu said that his team's latest finding that VNTR2-1 helps to drive the activity of the telomerase gene is especially notable because of the type of DNA sequence it represents.

"Almost 50 percent of our genome consists of repetitive DNA that does not code for protein," Zhu said. "These DNA sequences tend to be considered as 'junk DNA' or dark matters in our genome, and they are difficult to study. Our study describes that one of those units actually has a function in that it enhances the activity of the telomerase gene."

Their finding is based on a series of experiments that found that deleting the DNA sequence from cancer cells – both in a human cell line and in mice – caused telomeres to shorten, cells to age, and tumors to stop growing. Subsequently, they conducted a study that looked at the length of the sequence in DNA samples taken from Caucasian and African American centenarians and control participants in the Georgia Centenarian Study, a study that followed a group of people aged 100 or above between 1988 and 2008. The researchers found that the length of the sequence ranged from as short as 53 repeats – or copies – of the DNA to as long as 160 repeats.

"It varies a lot, and our study actually shows that the telomerase gene is more active in people with a longer sequence," Zhu said.

Since very short sequences were found only in African Americans participants, they looked more closely at that group and found that there were relatively few centenarians with a short VNTR2-1 sequence as compared to control participants. However, Zhu said it was worth noting that having a shorter sequence does not necessarily mean your lifespan will be shorter, because it means the telomerase gene is less active and your telomere length may be shorter, which could make you less likely to develop cancer.

NHE6 Depletion Corrects ApoE4-Mediated Synaptic Impairments and Reduces Amyloid Plaque Load

Theresa Pohlkamp, Xunde Xian, Connie H Wong, Murat S Durakoglugil, Gordon Chandler Werthmann, Takaomi C Saido, Bret M Evers, Charles L White III, Jade Connor, Robert E Hammer, Joachim Herz

eLife 2021;10:e72034, 7 Oct 2021, https://elifesciences.org/articles/72034, accessed 15 Nov 2021.

Abstract

Apolipoprotein E4 (ApoE4) is the most important and prevalent risk factor for late-onset Alzheimer's disease (AD). The isoelectric point of ApoE4 matches the pH of the early endosome (EE), causing its delayed dissociation from ApoE receptors and hence impaired endolysosomal trafficking, disruption of synaptic homeostasis, and reduced amyloid clearance. We have shown that enhancing endosomal acidification by inhibiting the EE-specific sodium-hydrogen exchanger 6 (NHE6) restores vesicular trafficking and normalizes synaptic homeostasis. Remarkably and unexpectedly, loss of NHE6 (encoded by the gene Slc9a6) in mice effectively suppressed amyloid deposition even in the absence of ApoE4, suggesting that accelerated acidification of EEs caused by the absence of NHE6 occludes the effect of ApoE on amyloid plaque formation. NHE6 suppression or inhibition may thus be a universal, ApoE-independent approach to prevent amyloid buildup in the brain. These findings suggest a novel therapeutic approach for the prevention of AD by which partial NHE6 inhibition reverses the ApoE4-induced endolysosomal trafficking defect and reduces plaque load.

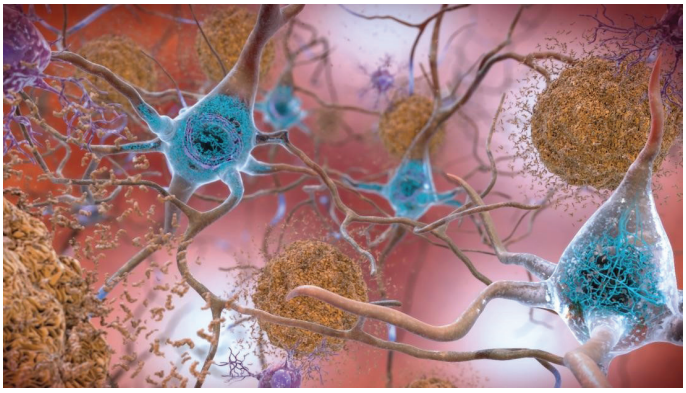
From: UTSW Scientists Eliminate Key Alzheimer's Feature in Animal Model

Unattributed, UT Southwestern Medical Center, 28 Oct 2021, https://www.utsouthwestern.edu/newsroom/articles/year-2021/alzheimers-feature.html, accessed 15 Nov 2021.

A study by UT Southwestern researchers finds that changing the biochemistry of parts of brain cells abolished the formation of amyloid beta plaques in a mouse model of Alzheimer's disease. The finding, published in *eLife*, might eventually lead to treatments that prevent the memory-robbing condition in humans.

"We envision that drugs that act on the same protein we inhibited in these mice could someday play a similar role in Alzheimer's disease as statins do in heart disease, helping to prevent the

condition from ever developing," said Joachim Herz, M.D., Professor of Molecular Genetics, Neurology, and Neuroscience at UTSW. Dr. Herz led the study, and graduate student Connie Wong was a co-lead author.



Amyloid beta plaques and tau in the brain
Credit: National Institute on Aging, National Institutes of Health

Nearly 6 million Americans have Alzheimer's disease, with the vast majority developing a late-onset form that arises after age 65. Alzheimer's disease is characterized by brain cells plagued by extracellular plaques made of a protein called amyloid beta and intracellular tangles made of an abnormal form of a protein called tau. Although the causes of the disease are not well defined, scientists have long known that the most significant genetic risk factor for late-onset Alzheimer's is apolipoprotein E4 (ApoE4), one of three variants of a protein involved in fat metabolism in mammals. In humans, having the ApoE4 variant reduces the average age of Alzheimer's onset by several years compared with having the most common variant, ApoE3, while rarer ApoE2 appears to have a protective effect against this disease.

From left: Joachim Herz, M.D., Connie Wong

The three versions of ApoE are very similar structurally, Ms. Wong explained: Compared with ApoE2, ApoE3 contains one amino acid substitution, resulting in that protein having a more positive charge. The ApoE4 variant contains two amino acid substitutions, resulting in the highest positive charge of the three forms of ApoE protein. The mechanism by which these differences affect late-onset Alzheimer's risk has been unknown.

In their new study, Dr. Herz, Ms. Wong, and their colleagues homed in on early endosomes, organelles responsible for sorting proteins, recycling them for reuse, or transporting them through the cell interior to cellular garbage dumps called lysosomes. Previous research had shown that early endosomes are enlarged in people and animals with ApoE4, compared with those who carried the other two ApoE variants.

Using genetically modified mice that model Alzheimer's disease and produce the human forms of ApoE4 and amyloid beta, the researchers showed that the positive charges on ApoE4 caused this protein to clump inside early endosomes because the charge of ApoE4 matches that of the environment inside endosomes. This clumping prevents these organelles from continuing their journey through the cell to transport, recycle, or help dispose of other proteins, including amyloid beta.

However, when the researchers used a genetic technique to turn off a gene called *NHE6* in brain cells, they found that the negative effects of ApoE4 were eliminated, and the protein was transported through the cell without impediment. *NHE6* produces a protein that acts as a pH regulator for endosomes, exchanging acidic protons for sodium ions. When the researchers shut off the *NHE6* gene, removing its protein from the cell, the early endosomes quickly became more acidic and that biochemical change seemed to prevent amyloid beta aggregation.

"Inhibiting *NHE6* produced the same protective effect as having ApoE2, an effect we hope can eventually be replicated using pharmaceuticals," Ms. Wong said.

Bioactive Scaffolds with Enhanced Supramolecular Motion Promote Recovery from Spinal Cord Injury

Z. Álvarez, A. N. Kolberg-Edelbrock, I. R. Sasselli, J. A. Ortega, R. Qiu, Z. Syrgiannis, P. A. Mirau, F. Chen, S. M. Chin, S. Weigand, E. Kiskinis, S. I. Stupp

Science, 11 Nov 2021, Vol 374, Issue 6569, 848-856, DOI: 10.1126/science.abh3602, accessed 15 Nov 2021.

Abstract

The signaling of cells by scaffolds of synthetic molecules that mimic proteins is known to be effective in the regeneration of tissues. Here, we describe peptide amphiphile supramolecular polymers containing two distinct signals and test them in a mouse model of severe spinal cord injury. One signal activates the transmembrane receptor β1-integrin and a second one activates the basic fibroblast growth factor 2 receptor. By mutating the peptide sequence of the amphiphilic monomers in nonbioactive domains, we intensified the motions of molecules within scaffold fibrils. This resulted in notable differences in vascular growth,

axonal regeneration, myelination, survival of motor neurons, reduced gliosis, and functional recovery. We hypothesize that the signaling of cells by ensembles of molecules could be optimized by tuning their internal motions.

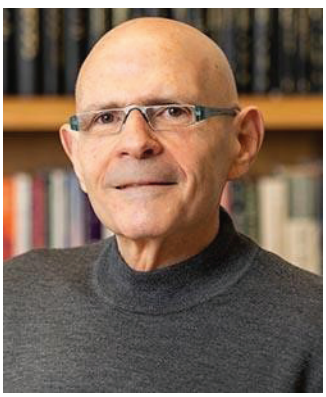
From: 'Dancing molecules' Successfully Repair Severe Spinal Cord Injuries

Amanda Morris, Northwestern Now, 11 Nov 2021, https://news.northwestern.edu/stories/2021/11/dancing-molecules-successfully-repair-severe-spinal-cord-injuries/, accessed 15 Nov 2021.

Northwestern University researchers have developed a new injectable therapy that harnesses "dancing molecules" to reverse paralysis and repair tissue after severe spinal cord injuries. In a new study, researchers administered a single injection to tissues surrounding the spinal cords of paralyzed mice. Just four weeks later, the animals regained the ability to walk.

By sending bioactive signals to trigger cells to repair and regenerate, the breakthrough therapy dramatically improved severely injured spinal cords in five key ways: (1) The severed extensions of neurons, called axons, regenerated; (2) scar tissue, which can create a physical barrier to regeneration and repair, significantly diminished; (3) myelin, the insulating layer of axons that is important in transmitting electrical signals efficiently, reformed around cells; (4) functional blood vessels formed to deliver nutrients to cells at the injury site; and (5) more motor neurons survived.

After the therapy performs its function, the materials biodegrade into nutrients for the cells within 12 weeks and then completely disappear from the body without noticeable side effects. This is the first study in which researchers controlled the collective motion of molecules through changes in chemical structure to increase a therapeutic's efficacy.



Samuel Stupp

"Our research aims to find a therapy that can prevent individuals from becoming paralyzed after major trauma or disease," said Northwestern's Samuel I. Stupp, who led the study. "For decades, this has remained a major challenge for scientists because our body's central nervous system, which includes the brain and spinal cord, does not have any significant capacity to repair itself after injury or after the onset of a degenerative disease. We are going straight to the FDA to start the process of getting this new therapy approved for use in human patients, who currently have very few treatment options."

"Currently, there are no therapeutics that trigger spinal cord regeneration," said Stupp, an expert in regenerative medicine. "I wanted to make a difference on the outcomes of spinal cord injury and to tackle this problem, given the tremendous impact it could have on the lives of patients. Also, new science to address spinal cord injury could have impact on strategies for neurodegenerative diseases and stroke."

The secret behind Stupp's new breakthrough therapeutic is tuning the motion of molecules, so they can find and properly engage constantly moving cellular receptors. Injected as a liquid, the therapy immediately gels into a complex network of nanofibers that mimic the extracellular matrix of the spinal cord. By matching the matrix's structure, mimicking the motion of biological molecules and incorporating signals for receptors, the synthetic materials are able to communicate with cells.

"Receptors in neurons and other cells constantly move around," Stupp said. "The key innovation in our research, which has never been done before, is to control the collective motion of more than 100,000 molecules within our nanofibers. By making the molecules move, 'dance' or even leap temporarily out of these structures, known as supramolecular polymers, they are able to connect more effectively with receptors.

"The central nervous system tissues we have successfully regenerated in the injured spinal cord are similar to those in the brain affected by stroke and neurodegenerative diseases, such as ALS, Parkinson's disease and Alzheimer's disease," Stupp said. "Beyond that, our fundamental discovery about controlling the motion of molecular assemblies to enhance cell signaling could be applied universally across biomedical targets."

Computed Structures of Core Eukaryotic Protein Complexes

Ian R. Humphreys, Jimin Pei, Minkyung Baek, Aditya Krishnakumar, Ivan Anishchenko, Sergey Ovchinnikov, Jing Zhang, Travis J. Ness, Sudeep Banjade, Saket R. Bagde, Viktoriya G. Stancheva, Xiao-Han Li, Kaixian Liu, Zhi Zheng, Daniel J. Barrero, Upasana Roy, Jochen Kuper, Israel S. Fernández, Barnabas Szakal, Dana Branzei, Josep Rizo, Caroline Kisker, Eric C. Greene, Sue Biggins, Scott Keeney, Elizabeth A. Miller, J. Christopher Fromme, Tamara L. Hendrickson, Qian Cong, David Baker

Science,11 Nov 2021, First Release DOI: 10.1126/science.abm4805, accessed 16 Nov. 2021.

Abstract

Protein-protein interactions play critical roles in biology, but the structures of many eukaryotic protein complexes are unknown, and there are likely many interactions not yet identified. We take advantage of advances in proteome-wide amino

acid coevolution analysis and deep-learning-based structure modeling to systematically identify and build accurate models of core eukaryotic protein complexes within the S*accharomyces cerevisiae* proteome. We use a combination of RoseTTAFold and AlphaFold to screen through paired multiple sequence alignments for 8.3 million pairs of yeast proteins, identify 1,505 likely to interact, and build structure models for 106 previously unidentified assemblies and 806 that have not been structurally characterized. These complexes, which have as many as 5 subunits, play roles in almost all key processes in eukaryotic cells and provide broad insights into biological function.

From: AI Cracks the Code of Protein Complexes – Providing a Road Map for New Drug Targets

Robert F. Service, Science News, 11 Nov. 2021, https://www.science.org/content/article/ai-cracks-code-protein-complexes-providing-road-map-new-drug-targets, accessed 16 Nov 2021.

The artificial intelligence (AI) revolution in protein structure prediction continues. Only 1 year ago, software programs first succeeded in modeling the 3D shapes of individual proteins as accurately as decades-old experimental techniques can determine them. This summer, researchers used those AI programs to assemble a near-complete catalog of human protein structures. Now, researchers have upped the ante once again, unveiling a combination of programs that can determine which proteins are likely to interact with one another and what the resulting complexes – crucial engines of the cell – look like.

"It's a really cool result," says Michael Snyder, a systems biologist at Stanford University. "Everything in biology works in complexes. So, knowing who works with who is critical." Those relationships were hard to reach with previous techniques. The new ability to predict them, he says, should yield an array of insights into cell biology and possibly reveal new targets for the next generation of therapeutic drugs.

Mapping proteins' shapes down to the atomic scale has until recently required costly and slow experimental techniques, such as x-ray crystallography and nuclear magnetic resonance spectroscopy. Those experimental techniques, if they work at all, typically only produce individual protein structures.

Computer modeling experts have worked for decades to speed things up. Their recent success has depended on deep learning algorithms, which use databases of experimentally solved protein structures to train software programs how to predict structures for proteins based on their amino acid sequences.

Last year, two groups, one from a U.K. company called DeepMind and the other led by David Baker at the University of Washington, Seattle, created rival AI programs that both now churn out predicted protein structures by the thousands. The software also produced structures for a handful of known protein complexes, mostly in bacteria. But in eukaryotes – organisms from yeast to people – the interacting partners are often unknown. Identifying them and predicting how they come together in a complex was too high a bar for the original programs.

Now, both research groups have tweaked their programs so they can solve structures of protein complexes by the hundreds. In *Science*, Baker and his colleagues use a combination of AI techniques to solve the structures of 712 complexes in eukaryotes.

To find proteins that may form complexes together, the team began by comparing the amino acid sequence of all 6000 yeast proteins to those from 2026 other fungi and 4325 other eukaryotes. The comparisons allowed the researchers to track how those proteins changed over the course of evolution and identify sequences that appeared to change in tandem in different proteins. The researchers reasoned that those proteins might form complexes, and that they changed in step to maintain their interactions. Then the team used its AI program, called RoseTTAFold, along with DeepMind's AlphaFold, which is publicly available, to attempt to solve the 3D structures of each set of candidates. Out of 8.3 million identified coevolving yeast protein pairs, the AI programs identified 1506 proteins that were likely to interact and successfully mapped the 3D structures of 712, or about half.

"These interactions span all processes of eukaryotic cells," says team member Qian Cong, a biomedical informatics expert at the University of Texas Southwestern Medical Center. Among the highlights, Cong and Baker say, are structures for protein complexes that allow cells to repair damage to their DNA, translate RNA into proteins in ribosomes, pull chromosomes apart during cell reproduction, and ferry molecules through the cell membrane.

More are likely on the way.

A Roadmap to Revival

Successful revival of cryonics patients will require three distinct technologies: (1) A cure for the disease that put the patient in a critical condition prior to cryopreservation; (2) biological or mechanical cell repair technologies that can reverse any injury associated with the cryopreservation process and long-term care at low temperatures; (3) rejuvenation biotechnologies that restore the patient to good health prior to resuscitation. OR it will require some entirely new approach such as (1) mapping the ultrastructure of cryopreserved brain tissue using nanotechnology, and (2) using this information to deduce the original structure and repairing, replicating or simulating tissue or structure in some viable form so the person "comes back."

The following is a list of landmark papers and books that reflect ongoing progress towards the revival of cryonics patients:

Jerome B. White, "**Viral-Induced Repair of Damaged Neurons with Preservation of Long-Term Information Content**," Second Annual Conference of the Cryonics Societies of America, University of Michigan at Ann Arbor, April 11-12, 1969, by J. B. White. Reprinted in *Cryonics* 35(10) (October 2014): 8-17.

Michael G. Darwin, "**The Anabolocyte: A Biological Approach to Repairing Cryoinjury**," *Life Extension Magazine* (July-August 1977):80-83. Reprinted in *Cryonics* 29(4) (4th Quarter 2008):14-17.

Gregory M. Fahy, "**A 'Realistic' Scenario for Nanotechnological Repair of the Frozen Human Brain**," in Brian Wowk, Michael Darwin, eds., *Cryonics: Reaching for Tomorrow*, Alcor Life Extension Foundation, 1991.

Ralph C. Merkle, "**The Molecular Repair of the Brain**," *Cryonics* 15(1) (January 1994):16-31 (Part I) & *Cryonics* 15(2) (April 1994):20-32 (Part II).

Ralph C. Merkle, "**Cryonics, Cryptography, and Maximum Likelihood Estimation**," First Extropy Institute Conference, Sunnyvale CA, 1994, updated version at http://www.merkle.com/cryo/cryptoCryo.html.

Aubrey de Grey & Michael Rae, "**Ending Aging: The Rejuvenation Breakthroughs That Could Reverse Human Aging in Our Lifetime**." St. Martin's Press, 2007.

Robert A. Freitas Jr., "**Comprehensive Nanorobotic Control of Human Morbidity and Aging**," in Gregory M. Fahy, Michael D. West, L. Stephen Coles, and Steven B. Harris, eds, *The Future of Aging: Pathways to Human Life Extension*, Springer, New York, 2010, 685-805.

Chana Phaedra, "**Reconstructive Connectomics**," *Cryonics* 34(7) (July 2013): 26-28.

Robert A. Freitas Jr., "**The Alzheimer Protocols: A Nanorobotic Cure for Alzheimer's Disease and Related Neurodegenerative Conditions**," *IMM Report* No. 48, June 2016.

Ralph C Merkle, "**Revival of Alcor Patients**," *Cryonics*, 39(4) & 39(5) (May-June & July-August 2018): 10-19, 10-15.

What is Cryonics?

Cryonics is an attempt to preserve and protect human life, not reverse death. It is the practice of using extreme cold to attempt to preserve the life of a person who can no longer be supported by today's medicine. Will future medicine, including mature nanotechnology, have the ability to heal at the cellular and molecular levels? Can cryonics successfully carry the cryopreserved person forward through time, for however many decades or centuries might be necessary, until the cryopreservation process can be reversed and the person restored to full health? While cryonics may sound like science fiction, there is a basis for it in real science. The complete scientific story of cryonics is seldom told in media reports, leaving cryonics widely misunderstood. We invite you to reach your own conclusions.

How do I find out more?

The Alcor Life Extension Foundation is the world leader in cryonics research and technology. Alcor is a non-profit organization located in Scottsdale, Arizona, founded in 1972. Our website is one of the best sources of detailed introductory information about Alcor and cryopreservation (www.alcor.org). We also invite you to request our FREE information package on the "Free Information" section of our website. It includes:

- A fully illustrated color brochure
- A sample of our magazine
- An application for membership and brochure explaining how to join
- And more!

Your free package should arrive in 1-2 weeks. (The complete package will be sent free in the U.S., Canada, and the United Kingdom.)

How do I enroll?

Signing up for cryopreservation is easy!

Step 1: Fill out an application and submit it with your $90 application fee.
Step 2: You will then be sent a set of contracts to review and sign.
Step 3: Fund your cryopreservation. While most people use life insurance to fund their cryopreservation, other forms of prepayment are also accepted. Alcor's Membership Coordinator can provide you with a list of insurance agents familiar with satisfying Alcor's current funding requirements.
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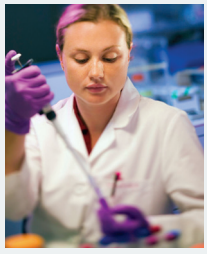

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