

ALCOR LIFE EXTENSION FOUNDATION

A Non-Profit Organization

CRYONICS

OCTOBER 2014 · VOLUME 35:10

Viral-Induced Repair of Damaged Neurons

Page 8

Biological Repair Technologies

Page 5

Alcor Reduces Membership Dues and Adopts CMS Dues Waiver

Page 7

ISSN 1054-4305



\$9.95

Improve Your Odds of a **Good Cryopreservation**

You have your cryonics funding and contracts in place but have you considered other steps you can take to prevent problems down the road?

- ✓ Keep Alcor up-to-date about personal and medical changes.
- ✓ Update your Alcor paperwork to reflect your current wishes.
- ✓ Execute a cryonics-friendly Living Will and Durable Power of Attorney for Health Care.
- ✓ Wear your bracelet and talk to your friends and family about your desire to be cryopreserved.
- ✓ Ask your relatives to sign Affidavits stating that they will not interfere with your cryopreservation.
- ✓ Attend local cryonics meetings or start a local group yourself.
- ✓ Contribute to Alcor's operations and research.



Contact Alcor (1-877-462-5267) and let us know how we can assist you.

Visit the ALCOR FORUMS www.alcor.org/forums/

Discuss Alcor and cryonics topics with other members and Alcor officials.

- The Alcor Foundation
- Cell Repair Technologies
- Cryobiology
- Events and Meetings
- Financial
- Rejuvenation
- Stabilization

Other features include pseudonyms (pending verification of membership status) and a private forum.

Visit the ALCOR BLOG www.alcor.org/blog/

Your source for news about:

- Cryonics technology
- Cryopreservation cases
- Television programs about cryonics
- Speaking events and meetings
- Employment opportunities



Alcor is on Facebook

Connect with Alcor members and supporters on our official Facebook page:

www.facebook.com/alcor.life.extension.foundation

Become a fan and encourage interested friends, family members, and colleagues to support us too.

CRYONICS



COVER STORY: PAGE 8

Viral-Induced Repair of Damaged Neurons with Preservation of Long-Term Information Content

Cryonics magazine is extremely proud and excited to publish the first article-length proposal for the repair and revival of cryonics patients. This paper was originally presented by Jerome B. White (now an American Cryonics Society patient, stored at the Cryonics Institute) at the Second Annual Conference of the Cryonics Societies of America at the University of Michigan in April, 1969. Locating a copy of it was more challenging than expected. Though the paper was presented many years ago and was privately circulated in photocopy form, as far as we know this is the first time it has been published.

CONTENTS

22 Membership Statistics

How many members, associate members, and patients does Alcor have and where do they live?

24 Resuscitation Update

Mike Perry surveys the news and research to report on new developments that bring us closer to the resuscitation of cryonics patients.

28 Venturist Fundraiser Successful!

The Society for Venturism reports the successful conclusion of a fundraiser to cryopreserve the brain of an 88-year-old woman who recently deanimated without funding.

5 QUOD INCEPIMUS CONFICIEMUS

Biological Repair Technologies

Cryonics magazine editor Aschwin de Wolf uses Jerome White's paper on modified viruses as cell repair machines as a starting point to discuss the challenges and limitations of biological resuscitation technologies.

7 Alcor Reduces Membership Dues and Adopts CMS Dues Waiver

Starting in January, 2015, Alcor membership dues will be reduced by 10% and the annual \$180 CMS dues will be waived for members whose funding is \$20,000 above their cryopreservation minimums. Read the detail and other important decisions from the 2014 Annual Strategic Meeting.

Editorial Board

Saul Kent
Ralph C. Merkle, Ph.D.
R. Michael Perry, Ph.D.

Editor

Aschwin de Wolf

Contributing Writers

Aschwin de Wolf
R. Michael Perry, Ph.D.
Jerome B. White

Copyright 2014
by Alcor Life Extension Foundation
All rights reserved.
Reproduction, in whole or part, without
permission is prohibited.

Cryonics magazine is published monthly.

To subscribe to the printed edition
and/or change your address, please call
480.905.1906 x101 or visit the magazine
website:
www.alcor.org/magazine

Please note: If you change your address less than
a month before the magazine is mailed, it may
be sent to your old address.

Address correspondence to:

Cryonics Magazine
7895 East Acoma Drive, Suite 110
Scottsdale, Arizona 85260
Phone: 480.905.1906
Toll free: 877.462.5267
Fax: 480.922.9027

Letters to the Editor welcome:

aschwin@alcor.org

Advertising inquiries:

480.905.1906 x113
advertise@alcor.org
ISSN: 1054-4305

Visit us on the web at www.alcor.org

Alcor News Blog
<http://www.alcor.org/blog/>

2014 Annual Giving Program

Alcor provides a wide array of services for you the member, and the general public. We inform and educate, we protect and preserve, and we strive to remain at the forefront of cryonics technology.

Since its founding, Alcor has relied on member support to maintain its mission and attract new members. Your support, regardless of size, can provide a better future for all cryonicists. **Please act now.**

SUGGESTED GIVING LEVELS

\$20	FRIEND
\$60	JUNIOR SUPPORTER
\$120	SUSTAINING SUPPORTER
\$500	ADVOCATE SUPPORTER
\$1,000	LEADING SUPPORTER
\$2,500	VISIONARY SUPPORTER
\$5,000	SILVER SUPPORTER
\$10,000	GOLD SUPPORTER
\$25,000	TITANIUM SUPPORTER
\$50,000	VANGUARD SUPPORTER

We encourage every member to donate. Even if you can only afford \$5 right now, you will make a significant contribution to Alcor's future.

Donations may be made via the Donations button on the Alcor website or by contacting Alcor's Finance Director, Bonnie Magee, at bonnie@alcor.org. Your donation may be made as a lump sum or divided into easy monthly payments. ■

The James Bedford Society



Gifts have played a fundamental role in the cryonics movement since its earliest days. Dr. James Bedford, a man whose extraordinary vision led him to become the first person to be cryopreserved, and the first to make a bequest to a cryonics organization, exemplified the determination of the early pioneers of cryonics. We invite you to follow in his footsteps, and join the James Bedford Society.

The James Bedford Society recognizes those who make a bequest of any size to the Alcor Life Extension Foundation. If you have already provided a gift for Alcor in your estate, please send a copy of your relevant documents to Alcor's Finance Director, Bonnie Magee.

If you'd like to learn more about setting up a bequest, send an email to bonnie@alcor.org or call 480-905-1906 x114 to discuss your gift. ■



QUOD INCEPIMUS CONFICIEMUS



Photo: Cryo-Care Equipment Corporation at 2340 E. Washington St., Phoenix, AZ.
Dr. Bedford's "home" in 1970 or 1971.



BIOLOGICAL REPAIR TECHNOLOGIES By Aschwin de Wolf

While I believe it is very hard to irreversibly destroy information, I had become quite concerned that the earliest paper (presentation) about future cell repair technologies for cryonics patients might have become lost forever. Jerome "Jerry" White's paper, "Virus-Induced Repair of Damaged Neurons with Preservation of Long-Term Information Content," was frequently referred to in papers on the topic of revival technologies, but I had never seen the actual paper and was curious and determined to find it. When I discovered that even the people in cryonics who usually own (or can access) a wealth of historical cryonics materials (Mike Perry, Mike Darwin, Steve Bridge, etc.) were not able to track down a copy I became progressively pessimistic and even started questioning whether the presentation was actually transcribed at all. I wrote a column about the missing paper in which I put forward the sad possibility that the paper was lost to us forever. I never gave up though. Then, in September 2014, Mike Perry wrote me to tell that Alcor member Art Quaife was in possession of the paper and would send a copy to him. After receiving the paper, a PDF copy was soon produced and Mike also spent considerable time creating an editable text version.

The premise of White's paper is straightforward but ingenious (especially considering the fact that it was presented in 1969). We already know of biological "machines" that can enter the body of the patient and make modifications to cells and DNA. They are called viruses. When this is recognized it is not too far fetched to recognize the possibility of separating the virus as a biologically active delivery vehicle from its adverse health effects. The idea of using viruses to deliver genetic material has now become fully established in modern gene therapy. For example, the virus responsible for causing HIV and AIDS can be stripped of these properties but can still be used as a vehicle to modify genes within a cell. In his paper on biological cell repair, White proposed to modify viruses to engage in information gathering, gene modification, and cell repair.

"The idea of using viruses to deliver genetic material has now become fully established in modern gene therapy."

Space does not permit me here to analyze the paper in detail but I would like to briefly discuss two issues concerning the feasibility of biological cell repair for the revival of cryonics patients, namely, capabilities and temperature.

Modifying a virus to change genes is one thing, but rebuilding damaged cell membranes and intracellular organelles is another and it is not fully clear how a virus can be modified to accomplish this. In addition, for non-neural cells a case could be made that it is often more time- and cost-effective to simply destroy and remove cells and cell structures with severe damage (after gathering sufficient information about the cells and their organization). For brain cells there is a special difficulty in that the ultrastructure appears to be identity-critical in a way not expected in non-neural tissue. So the conservative approach here would dictate repairing these cells instead of replacing them. The challenge is that although human physiology already has endogenous mechanisms to maintain DNA integrity and repair damaged DNA, the human genome does not encode for wholesale repair of cells (including their genomic content) that have sustained substantial damage. This, combined with only limited neurogenesis in the brain, may explain why aging and dementia are strongly

correlated. One of the challenges of viral-induced repair of cells is that inserting new genetic information that allows for novel endogenous repair capabilities is itself dependent on the existence of viable cells in the body of the patient. This challenge is also identified in White's paper when he proposes to create artificial viruses that "carry out degrees of repair greater than those the cell in its damaged condition would itself provide."

"One of the challenges of viral-induced repair of cells is that inserting new genetic information that allows for novel endogenous repair capabilities is itself dependent on the existence of viable cells in the body of the patient."

An even bigger challenge for biological repair is temperature limitations. While it has been established that some enzymes still function (albeit at a slower pace) at low or even subzero temperatures, the temperatures that cryonics patients are stored at are substantially lower than that. This would seem to require that we first thaw the patient before conducting repairs. This course of action could create serious problems for the average cryonics patient. In the case of frozen patients, the ice will turn to water again and (damaged) biomolecules that were locked into place could dissolve into solution (which may constitute irreversible loss of identity-critical information). In the case of vitrified patients, ice nuclei that formed during the descent to cold temperatures (or continued forming during intermediate temperature storage) can organize themselves into ice during thawing. Another problem with conducting repairs after thawing is that ischemia will be permitted to continue, causing more damage. While White stipulates that "repair proceed faster than

deterioration, whatever the temperature" it is not likely that credible future repair scenarios will permit substantial deterioration to occur during, or prior to, repair.

Does this close the door on biological cell repair? Not necessarily. We can imagine breakthroughs in cryoprotectant design that reconcile negligible toxicity with extreme resistance to ice formation. Patients cryopreserved with such agents could be thawed without risk of ice damage. When temperatures are raised to a point where meaningful enzymatic activity is possible, various biological strategies (metabolic inhibition, reversible fixation) could be used to allow time for repairs. Another idea is to pursue a hybrid strategy in which (crude) nano-size mechanical machines are used to access and open the circulatory system while disrupting nucleation and/or delivering anti-nucleating molecules. After completing this task at cryogenic temperatures, the patient can be thawed and biological cell repair technologies introduced.

This discussion of the (potential) limitations of biological repair technologies draws attention to the relationship between cryopreservation technologies and repair technologies. We tend to think of preservation and repair technologies as independent endeavours but it has been shown here that the choice of cryoprotectant technology can influence the choice of the most effective repair technology. For example, if a cryoprotectant is just a moderately strong glass former, ice formation upon warming should be expected and mechanical repair technologies may be necessary for conducting the initial steps of repair (preventing ice formation). Or consider intermediate temperature storage. If we store patients just below the glass transition temperature of the vitrification solution, nucleation may still continue, which would favor ice formation upon warming, and thus, again, the need for initial mechanical cell repair technologies to stabilize the patient during the initial stages of repair.

Some people think that biological cell repair is an inefficient and impractical (if not impossible) task and the resuscitation

"While White stipulates that "repair proceed faster than deterioration, whatever the temperature" it is not likely that credible future repair scenarios will permit substantial deterioration to occur during, or prior to, repair."

of cryonics patients will require mechanical nanoscale repair devices. This may very well turn out to be the case, but demonstrating the technical feasibility of biological cell repair would further strengthen the case for cryonics. Let us hope that Jerry White, who is currently cryopreserved, will be one of the beneficiaries of such powerful technologies. ■

ALCOR 2014 ANNUAL STRATEGIC MEETING ANNOUNCEMENTS

ELECTIONS

At the September 13, 2014, Alcor board of directors meeting, by unanimous votes Max More was retained as President and R. Michael Perry as Secretary and Treasurer.

MEMBERSHIP DUES REDUCED BY 10%

We are pleased to announce that Alcor is reducing membership dues for the second consecutive year. Starting January 1, 2015, dues for Alcor cryopreservation members paying the full rate (currently \$590) will be reduced by 10% (rounded to \$530). Dues for members receiving any discount will not be changed.

We are able to do this thanks to strong finances. We hope and expect that this reduction in costs (especially combined with other measures about to be announced) will make it easier for financially stressed members to stay with us, and to attract new members. The resulting membership growth will result in economies of scale and therefore the probability of even lower membership costs.

CMS WAIVER

The Comprehensive Member Standby (CMS) fund enables Alcor to provide standby, stabilization, and transport services to all members in the United States and Canada. This is a critical part of the cryopreservation process.

The CMS has been funded by a fee of \$180 per year. At the September 13, 2014, board meeting, the Board unanimously voted in favor of the president's proposal to waive the CMS fee for all members who have at least \$20,000 in funding above current cryopreservation minimums.

Here is the motion that passed:

This is a Motion to create a new, optional CMS (Comprehensive Member Standby) payment mechanism:

- 1) Alcor will make available a new option on Attachment 1 to the Cryopreservation Agreement that will allow members to meet their obligation to make regular CMS payments by increasing their cryopreservation funding.
- 2) If a member selects this new option:
 - a) The member's cryopreservation funding minimum will be increased by \$20,000.
 - b) The member will not be required to pay regular CMS fees.
 - c) Upon the member's cryopreservation an additional \$20,000 will be paid from their cryopreservation fund to the CMS Fund.

- 3) Any member whose funding meets Alcor's current minimum requirements (including all applicable surcharges) can revise their membership agreement and select this new option at any time they so choose.
- 4) Following a 90 day reconsideration period, a member's selection of this new option cannot be reversed and will become permanent.
- 5) Existing allocations to CMS are unchanged, as are other allocations to other funds, and all other fees and payments.
- 6) The board will review the impact of this motion annually to determine if any further changes are needed.

OVERSEAS CHARGES REDUCED

Until now, Alcor has added surcharges for the cryopreservation minimum for members outside the USA and Canada to compensate for higher response and transport costs. After reevaluating these costs – and despite a recent commitment to providing a higher level of response – Alcor is reducing these surcharges. The former surcharges were \$15,000 for the UK and \$25,000 for other countries. The new, universal surcharge is \$10,000.

ALTERNATIVE FUNDING METHODS INTRODUCED

Until now, Alcor has accepted only highly-assured means of payment such as life insurance, trusts, or prepayment for cryopreservation minimums. We will accept, on a limited basis, alternative funding methods. Here is the proposal that was passed at the September 13, 2014, board meeting:

On an individual basis, Alcor will accept partial payment for cryopreservation from alternative funding methods such as real estate, 401(k) plans, and bequests, with a 50% discount from net assets to allow for risk. These alternative payment methods may be used only up to a maximum of 50% of current cryopreservation minimums. Acceptance of alternative funding methods in any individual case is subject to review by Alcor and will be approved, if at all, only after checking for possible conflicting claims, after attempting to verify the current value of assets, and while putting in place regular checks on future value. ■

Viral-Induced Repair of Damaged Neurons with Preservation of Long-Term Information Content

To be presented to the Second Annual Conference of the Cryonic Societies of America, University of Michigan at Ann Arbor, April 11-12, 1969, by J. B. White.

ABSTRACT

An organic cell, as an automaton, derives energy from the metabolism of its own constituents for self-maintenance under the guidance of its genetic control program, which will not function properly if damaged or if a certain level of environmental deprivation or interference is exceeded; if allowed to proceed, such conditions lead to complete degradation. Although they increment it, methods exist for virtually halting such deterioration by stopping all biochemical processes; other means will be required to restore or augment a control program, or enrich the environment to enhance repair ability. It has been proposed that appropriate genetic information be introduced by means of artificially constructed virus particles into a congenitally defective cell for remedy; similar means may be used for the repair of more general cell damage exceeding the functional limit. Progress is being made in relevant areas such as virus/cell specificity, temperature-sensitive viral mutants, identification of RNA and DNA codon sequences, *in vitro* DNA synthesis, viral disassembly and assembly, and metabolic pathway determination. Further work is needed also in isolation of viral capsid programs, specific cell function subprograms, metabolic repair pathways, identification of enriching nutrients, replication of repair virions, infection methods, and quality control. *In situ*, the repair program must use means such as protein synthesis and metabolic pathways to diagnose and repair any damage. Applied to brain neurons, this may destroy long-term information content, which appears to be stored ultimately in molecular form, often proposed to be in a feedback cycle

involving mRNA and protein synthesis. This information can be preserved by specifying that the repair program incorporate appropriate RNA tapes into itself upon entry and release them on termination of repair. This method of cell repair is applicable to many forms of brain damage and may be used as a research tool in investigating metabolic processes as well as information content and storage.

VIRAL-INDUCED REPAIR OF DAMAGED NEURONS WITH PRESERVATION OF LONG-TERM INFORMATION CONTENT

By Jerome B. White

ABSTRACT

An organic cell is a self-repairing automaton, but if environmental interference exceeds a certain limit, damage will become total. Freezing can be used to halt progressive damage along with all metabolism, but means are required to restore or augment the cellular genetic control program, or enrich the environment to enhance repair ability. It has been proposed that appropriate genetic information be introduced by means of artificially constructed virus particles into a congenitally defective cell for remedy; similar means may be used for the more general case of repair. Progress has been made in many relevant areas. The repair program must use means such as protein synthesis and metabolic pathways to diagnose and repair any damage. Applied to brain neurons, this might destroy long-term information content, which appears to be stored in molecular form, often suggested to be in a feedback cycle involving mRNA and protein. This information can be

preserved by specifying that the repair program incorporate appropriate RNA tapes into itself upon entry and release them on termination of repair.

CELLS AS AUTOMATA

In 1936, Alan Turing, British mathematician and one of the fathers of the modern electronic computer, wrote that it was possible to

compare a man in the process of computing a real number to a machine which is only capable of a finite number of conditions q_1, q_2, \dots, q_R which will be called "*m*-configurations." The machine is supplied with a "tape" (the analogue of paper) running through it, and divided into sections (called "squares") each capable of bearing a "symbol." At any moment there is just one square, say the *r*-th, bearing the symbol $S(r)$ which is "in the machine". We may call this square the "scanned square". The symbol on the scanned square may be called the "scanned symbol". The "scanned symbol" is the only one of which the machine is, so to speak, "directly aware." However, by altering its *m*-configuration the machine can effectively remember some of the symbols which it has "seen" (scanned) previously. The possible behaviour of the machine at any moment is determined by the *m*-configuration q_n and the scanned symbol $S(r)$. This pair $q_n, S(r)$ will be called the "configuration:" thus the

configuration determines the possible behaviour of the machine. In some of the configurations in which the scanned square is blank (i.e. bears no symbol) the machine writes down a new symbol on the scanned square: in other configurations it erases the scanned symbol. The machine may also change the square which is being scanned, but only by shifting it one place to right or left. In addition to any of these operations the m -configuration may be changed. (17, 231)¹

Each such machine will compute a mathematical function; its behavior may be specified by a standard description, or S.D. Turing further states that:

It is possible to invent a single machine which can be used to compute any computable sequence. If this machine U is supplied with a tape on the beginning of which is written the S.D. of some computing machine M , then U will compute the same sequence as M . (17, 241f)

This universal computing machine, as he calls it, will thus imitate the action of any specific computing machine.

An automaton is, roughly, an entity with these properties:

- a) it can take on any of a number of distinct internal configurations, or, states;
- b) it can be affected by any of a number of stimuli, or, inputs;
- c) it is affected by these inputs in that its internal state changes;
- d) depending upon the internal state, the input, and the resulting internal state, it may engage in one of a number of actions, or outputs.

It should be clear that a Turing machine corresponds to this definition. So does a

computer, and so do many familiar objects. Eventually, research turned to the theory of automata of generality greater than Turing machines. Investigations were made into automata which, apart from or in addition to printing or modifying tapes, would construct objects. In some cases, the object to be constructed would be an automaton. Specifically, the automaton to be constructed would be a replica of the constructor. Self-repairing and self-maintaining automata, as well as self-reproducing ones, have been investigated.

In 1948, John von Neumann lectured on self-reproducing automata. He showed that it was possible to describe an automaton on something resembling a tape, or one-dimensional chain:

Given any automaton X , let $f(X)$ designate the chain which represents X . Once you have done this, you can design a universal machine tool A which, when furnished with such a chain $f(X)$, will take it and gradually consume it, at the same time building up the automaton X from the parts floating around freely in the surrounding milieu. All this design is laborious, but it is not difficult in principle, for it's a succession of steps in formal logics. It is not qualitatively different from the type of argumentation with which Turing constructed his universal automaton. (19, 84)

Von Neumann also showed that there is a fundamental reason for having an automaton construct another, whether the latter is different from the former or not, by using a description rather than taking an example apart or copying. However, von Neumann requires "... that there exists an automaton B which has this property: If you provide B with a description of anything, it consumes it and produces two copies of this description." (19, 84)

I will let von Neumann summarize the construction of a self-reproducing automaton in his own words:

The general constructive automaton A produces only X when a complete description of X is furnished it, and on any reasonable view of what constitutes complexity, this description of X is as complex as X itself. The general copying automaton B produces two copies of $f(X)$, but the juxtaposition of two copies of the same thing is in no sense of higher order than the thing itself. Furthermore, the extra unit B is required for this copying.

Now we can do the following thing. We can add a certain amount of control equipment C to the automaton $A + B$. The automaton C dominates both A and B , actuating them alternately according to the following pattern. The control C will first cause B to make two copies of $f(X)$. The control C will next cause A to construct X at the price of destroying one copy of $f(X)$. Finally, the control C will tie X and the remaining copy of $f(X)$ together and cut them loose from the complex $(A + B + C)$. At the end the entity $X + f(X)$ has been produced.

Now choose the aggregate $(A + B + C)$ for X . The automaton $(A + B + C) + f(A + B + C)$ will produce $(A + B + C) + f(A + B + C)$. Hence auto-reproduction has taken place.

[The details are as follows. We are given the universal constructor $(A + B + C)$, to which is attached a description of itself, $f(A + B + C)$. Thus the process of self-reproduction starts with $(A + B + C) + f(A + B + C)$. Control C directs B to copy the description twice; the result is $(A + B + C) + f(A + B + C) + f(A + B + C)$. Finally, C ties the new automaton and its description together and cuts them loose. The final result consists of the two automata $(A$

¹ The first number indicates a bibliography entry, the second the page(s) thereof

+ B + C) and (A + B + C) + f (A + B + C). If B were to copy the description thrice, the process would start with one copy of (A + B + C) + f (A + B + C) and terminate with two copies of this automaton. In this way, the universal constructor reproduces itself.]

This is not a vicious circle. It is quite true that I argued with a variable X first, describing what C is supposed to do, and then put something which involved C for X. But I defined A and B exactly, before I ever mentioned this particular X, and I defined C in terms which apply to any X. Therefore, in defining A, B, and C, I did not make use of what X is to be, and I am entitled later on to use an X which refers explicitly to A, B, and C. The process is not circular. (19, 85)

Consider a self-reproducing automaton in a changing milieu. Such an automaton must of necessity be highly structured. High degrees of structure are susceptible to degradation through entropy if the components making them up are required to engage in activity simply because complex structure is very improbable and any change will tend toward states of greater probability, which have less structure. This entropy can be counteracted if external energy is available and the automaton's control program can utilize it to maintain the structure. Self-reproduction is activity; therefore, a self-reproducing automaton will tend to be degraded. In addition, any action, such as self-reproduction, requires energy. A self-reproducing automaton must have energy sources if it is to act and remain in existence. Energy conversion itself requires action, and so tends to degrade an automaton. Thus, to prevent eventual, and possibly rapid total collapse, an automaton must of necessity possess self-repair and self-maintenance abilities.

Biological cells, at various stages of development, are examples of self-reproducing and self-maintaining automata. The genes, or, the genome as they are

collectively called, are a cell's control program. They constitute a description of the cell's structure and action. Of course the genome itself possesses complex structure, the first determination of which was made in 1953 by James D. Watson and Francis Crick, who later received Nobel prizes for their contributions. It consists of deoxyribonucleic acid, DNA, made up of two interwoven chains of smaller molecules. The analogy to the tape of an automaton is obvious. When a cell reproduces, the two chains of the genome separate; a complementary other half is then synthesized for each. Thus, the original control program is destroyed and two others are constructed. This is precisely analogous to von Neumann's formulation, which was made more than four years before the structure of DNA was determined.

The analogy is highlighted by Watson's statement about the situation in 1951: "... I had worried about the possibility that the gene might be fantastically irregular. Now, however, I know that genes could crystallize; hence they must have a regular structure that could be solved in a straightforward fashion." (21, 28)

Von Neumann's model eventually diverges from self-reproduction as it occurs in cells, but the similarities are striking.

Some authors, like Carl R. Woese, emphasize the automaton-theoretic aspects of cell development:

In the present instance we are primarily concerned with only two classes of molecules in the cell: first, molecules whose primary structure has a high information content and whose secondary structures, and so forth, are in one sense of no real interest—that is, DNA, a large class of RNA, and most of the cell's protein; and, second, molecules that bring about the transfer of information from one kind of the *informational molecules* to another. The first class, we think of as tapes, and the second, because of the mode of action, as *tape readers*. To us, then, the cell becomes a conglomerate of tapes and tape readers.

In cellular tape-reading processes, an input tape feeds linearly through the tape reader; the reading in all cases consists of producing an output tape whose monomer units and mapping rules are characteristic of the tape reader but whose information content, of course, reflects exactly that of the input tape. The cell contains three basic kinds of tapes and three kinds of tape readers. The primary (ultimate reference) tape is DNA, which undergoes two kinds of tape-reading operations. One, called replication, results in an output of two tapes each identical to the input tape. The other, called transcription, results in an output tape that is an RNA copy of a particular strand of the input tape (DNA being double-stranded) in addition, of course, to the original input tape itself. Under normal conditions, all RNA of the cell appears to be produced by the process of transcription. A special subclass of RNA, appropriately called message RNA, becomes an input tape for the translation tape reader, whose output is the polypeptide tapes. The latter class of tapes is, of course, never subject to a tape-reading operation itself. ... It appears that the two remaining classes of RNA tapes, called ribosomal RNA and transfer RNA, are not themselves used as input tapes ... but are incorporated as parts of the translation tape-reader system. (22, 5f)

Proteins, more generally polypeptides, are *translated* from RNA tapes through a complex process involving the association of an amino acid with three consecutive RNA bases. The resulting polypeptide chain is folded into a characteristic biologically active form. (20, 298ff)

Prominent among the proteins produced by a cell are enzymes, which are biological catalysts. Their synthesis

... follows a double genetic control. The so-called structural genes determine the molecular organization of the proteins. Other, functionally specialized, genetic determinants, called regulator and operator genes, control the rate of protein synthesis through the intermediacy of cytoplasmic components or repressors. The repressors can be either inactivated (induction) or activated (repression) by certain specific metabolites. This system of regulation appears to operate directly at the level of the synthesis by the gene of a short-lived intermediate, or messenger, which becomes associated with the ribosomes where protein synthesis takes place. (9, 318)

DAMAGE AND GENETIC REPAIR

The proper function of a cell is dependent upon maintaining the normalcy of these factors:

1. physical environment; i.e., factors such as temperature, pressure, radiation, membrane integrity and so on;
2. chemical environment; i.e., the presence within certain limits of certain biologically active chemicals, ion concentrations, and so on, both within and without the cell membrane;
3. integrity of the control program.

There is an upper limit of interference from the environment such that if this limit is exceeded, the control program will not be able to continue repair or maintenance. This limit may be lowered if the control program is itself damaged or diminished, and it is reasonable to assume that it may be raised if the control program is augmented and/or the constituent milieu of the environment is enriched. If the upper limit of interference is either exceeded or is lowered until normal functions cannot proceed, damage occurs, which if not slowed, stopped, or reversed, leads to complete degradation. Ultimately, any form of damage is manifested on the molecular level, and we may

... outline the possible modes of molecular recovery in general terms. Three possible modes for dealing with damaged molecules in the cell might be listed as follows:

I. The damaged molecule or part of a molecule may be restored to its functional state *in situ*. This may be accomplished by the activity of some enzymatic mechanism or it may simply result from the "decay" of the damage to an innocuous form.

II. The damaged unit may be removed from the molecule or system which contains it and then be replaced with an undamaged unit to restore normal function.

III. The damage may remain unrepaired in the system, but for one reason or another the system may be able to bypass or ignore the damage.

All of these general modes have now been well documented ... (8, 2f)

It is one of the theses of the cryonic movement that a method of slowing and virtually halting progressive cell damage exists, though it contributes an increment to it. This method is controlled freezing and storage. Concrete proposals for carrying out repair on the molecular level are required. Such methods for eventually effecting repair, or inducing regenerative processes to begin and continue at a rate greater than those of degradation are needed. Since a cell is formed and maintained under genetic control, it is reasonable to suggest that genetic control also be used to carry out degrees of repair greater than those the cell in its damaged condition could by itself provide. For each degree of damage greater than the normal regenerative abilities of a cell, a suitable enriched environment and augmented control program should be provided. The control program should be augmented as such, in the form of additional genetic information which will enable the cell to carry out emergency repairs, such as of

a damaged membrane, gather nutrients from the environment, and restore normal functioning according to the standard control program.

All this will require that the cell be provided with a specifically enriched environment, and that supplementary genetic information be introduced into the cell. The latter occurs in the phenomenon known as transformation, defined as "the integration with the genome of a recipient cell of a small piece of exogenous genetic material, extracted from a donor cell and introduced into the reception as part of a free DNA particle." (12, 231)

It is of course not necessary that DNA used for repair purposes come from a donor cell; DNA has been synthesized (11, 78ff) (7, 2321ff), and synthetic DNA could be used for this purpose. Transformation has been studied in bacteria and higher organisms as well:

In transformation certain bacteria change their hereditary makeup by absorbing DNA molecules from their environment. The ability to do this is induced by a giant-molecule factor synthesized by the cell. ... The phenomenon of transformation in bacteria was first observed in 1928, led to the identification of DNA as the genetic material in 1944 and has since been recognized as a significant form of genetic intervention: a means whereby bacterial cells can acquire new genes (and thus new traits) with a frequency many orders of magnitude higher than if such changes occurred only through random mutation. ... In bacterial transformation a bit of DNA penetrates the boundary of a bacterial cell and becomes incorporated into the cell's genetic apparatus. (16, 38)

The situation is more complicated in higher organisms:

... increasing numbers of workers have studied

the possibility of genetic transformation mediated by nucleic acid in cells of higher organisms. *In vivo*, the difficulties encountered are numerous. In such systems, the injected DNA must be carried by the blood stream or by the plant sap to sites distant from the point of injection and the DNA molecules must pass several cell membranes before reaching their final site. (12, 231f)

Commenting on transformation, Tomasz states: "The importance of learning more about the mechanism is obvious, since the invasion of cells by extraneous genetic material is not restricted to the world of bacteria. Such events are the essence of all viral infections and may be responsible for the induction of some forms of cancer." (16, 38)

He also states:

Work is now in progress ... aimed at learning more about the mechanisms that somehow open and close the gates of cells to the entry of foreign genetic material. This work could eventually lead to better understanding of viral infection and could even contribute to the possibility of deliberate genetic intervention in higher organisms. (16, 44)

VIRUSES

Artificial viruses offer a possibility of transporting supplementary genetic information into a cell for repair purposes. Luria and Darnell define viruses as "entities whose genome is an element of nucleic acid, either DNA or RNA, which reproduces inside living cells and uses their synthetic machinery to direct the synthesis of specialized particles, the virions, which contain the viral genome and transfer it to other cells." (13, 3)

Expanding on this definition, they

... attempt to convey the two qualities of a virus: first, the possession of a genetic material

of its own which, inside a host cell, behaves as part of the cell; second, the possession of an extra-cellular infective state, represented by specialized objects, the virions, which are produced in the cell under the genetic control of the virus itself and serve as vehicles for introducing the viral genome into other cells. (13, 3)

Virus particles or virions consist basically of a control program in the form of a DNA or RNA tape, and an enclosing capsid which protects the program in the extra-host-cellular environment and administers the program to an appropriate host cell. The program, either in conjunction or not with the cell's control program, may use the intracellular environment to replicate additional virions. Some viruses do not so replicate: "Viruses are obligate parasites and in nature many of them give rise to latent infections causing little inconvenience to the host cell; only occasionally do they break out to produce symptoms of disease." (14, 15)

Watson expands on some such viruses:

Some bacterial viruses ... do not always multiply upon entering a host cell. Instead their chromosome sometimes becomes inserted into a specific section of a host chromosome. Then the viral chromosome is, for all practical purposes, an integral part of its host chromosome and is duplicated, like the bacterial chromosome, just once every cell generation. The virus chromosome when it is integrated into a host chromosome is called the *prophage*; those bacteria containing prophages are called *lysogenic bacteria*; and those types of virus whose chromosomes can become prophage are known as lysogenic viruses. In contrast, those viruses ... that always multiply when they enter a host cell are called *lytic viruses*. (20, 204f)

Besides lysogenic viruses, there also exist defective ones, which by themselves are unable to reproduce when infecting a host, but which can grow in the presence of another, helper virus, which is able to supply one or more of the functions that a defective virus lacks, thus enabling the latter to multiply. (20, 474ff)

These characteristic properties of lysogenic or defective viruses are of course determined by specificities in the control programs, and the genes determining them would be relevant in the synthesis of artificial repair viruses.

NEURAL INFORMATION CONTENT

Every cell in a higher organism, including man, contains the genetic specifications for the entire organism, so only a percentage is used to maintain a particular cell. In some cases of damage, then, it might be more feasible to replace a damaged portion with an artificial component or grow a new one from another cell. This alternative is not attractive in the case of the central nervous system, especially the brain, since essential information content regarding memory and personality is stored there. As Ungar and Irwin state:

The essential function of the nervous system is to receive, store, and retrieve information so as to modify behavior according to the changing conditions of the environment and past experience. Part of the information is built into the organism and stored in the genetic material: It determines the structure and organization of the system and directs the innate responses to stimuli. These responses vary in complexity from simple reflexes to the elaborate instinctive patterns of behavior observed in some species.

However, in almost all animals behavior is modified by acquired information. Operationally, memory and learning comprise everything that enables organisms to change their behavior as a result of experience. (18, 144)

Repair, rather than replacement, is thus most crucial in the case of damaged neurons. In addition, information content in neurons, assuming it has not been already damaged, is likely to be destroyed during any large-scale repair process unless specific steps are taken to preserve it.

One favorable factor in brain information storage is that there appears to be considerable redundancy:

It is well known that functionally identical information may be stored at multiple sites in the nervous system so that the system can function extremely well despite extensive ablation. This property of the nervous system is referred to as “redundancy.” (2, 164)

Even if information is destroyed in one part of the brain, redundancy may ensure that it will nonetheless not be lost; as Flexner and Flexner report from an experiment: “This result was interpreted to mean that large areas of the brain participate in longer-term memory but that a relatively small area is sufficient to sustain it.” (4, 1653)

Pribram theorizes on how redundancy may be achieved: “Experiments with monkeys have identified the brain areas involved in the recall of various learned tasks. Memory may take the form of interference patterns that resemble laser-produced holograms.” (15, 73)

He expands on this hologram-like storage:

... I believe there is now available a hypothesis about the nature of the memory trace that satisfies the known physiological requirements and that can be tested by experiment. It is perhaps not surprising that the brain may exploit, among other things, the most sophisticated principle of information storage yet known: the principle of the hologram. In a hologram the information in a scene is recorded on a photographic plate in the form

of a complex interference, or diffraction, pattern that appears meaningless. When the pattern is illuminated by coherent light, however, the original image is reconstructed. What makes the hologram unique as a storage device is that every element in the original image is distributed over the entire photographic plate. The hypothesis is attractive because remembering or recollecting literally implies a reconstructive process—the assembly of dismembered mnemonic events. (15, 73)

Flexner, Flexner, and Roberts discuss the nature of instinct, memory, and learning:

Memory is thought to consist of overlapping stages. In the first stage the essential process is believed to be the electrical activity of those nerve cells which participate in a learning procedure. In this stage memory can be destroyed by electroconvulsive shock which disrupts this selective electrical activity. The period when memory is vulnerable to electroconvulsive shock in the mammal varies greatly, with a minimal value of less than 1 minute.

The learning process also leads to changes of a permanent kind so that in man, for example, memory of an event in childhood may persist for life. Thus long-term memory appears to be a relatively stable condition reached as the outcome of events occurring in a period of consolidation. In this period electrical activity is transformed into a more permanent record. ... Further clues to the nature of the learning process and memory can be obtained by considering instinctive or inherited behavior. Such behavior must be attributed to certain stable patterns of gene expression which

become established during the development of the individual. These patterns of gene expression are dictated by the sequence of nucleotides in the DNA and are manifested during the complicated and mysterious process known as differentiation.

Behavioral patterns acquired by learning or training are so similar to instinctive ones that they are often difficult to distinguish. Accordingly it is reasonable to assume that well consolidated, long-term memory has the same fundamental basis as instinctive behavior, that is, it is the manifestation of a stable pattern of gene expression. Nature frequently uses the same mechanism for a variety of purposes. (6, 1377)

They go on to propose a theory of how information is stored in neurons:

We assume that an established memory of long duration depends, not on the continued presence of any protein or nucleic acid molecules, but on the establishment of a self-sustaining system for their synthesis. Such a system can occur whenever some of the products of a gene’s expression act as inducers (or derepressors) of that gene. If the gene is repressed, inducers are not synthesized and the gene stays repressed. On the other hand, if the gene is induced for a sufficient time, inducers will accumulate above a critical level and the gene will stay induced. If, however, the synthetic processes are inhibited for a sufficient time, the level of inducers will fall below the critical level and the gene will revert to its repressed state.

The processes involved in the establishment of a long-term memory can be described in terms of the self-inducing system. We assume that the initial

learning experience triggers the synthesis of one or more species of mRNA. This mRNA alters the synthetic rate of one or more proteins which are essential for the expression of memory. These proteins are thought to modify the characteristics of synapses concerned in a learning process so that the passage of impulses between nerve cells is facilitated. In turn, the proteins or their products act as inducers of their related mRNA; in this way the concentration of the inducer proteins is maintained. In this view, expression of memory depends upon changes in proteins, changes which are initiated and sustained by qualitative and quantitative changes in mRNA produced by a learning experience. Loss of this mRNA would lead to loss of essential protein with consequent permanent loss of memory. In the presence of an inhibitor of protein synthesis, the concentration of essential protein could fall to levels too low for expression of memory, but loss of memory would be temporary if mRNA were conserved to direct the synthesis of protein when the inhibitor had disappeared. (6, 1381f)

To be sure, no certainty can be accorded the theory:

Clearly only a beginning has been made in testing the hypothesis based on a self-sustaining system. The hypothesis is consistent with the results of Hydén and collaborators ... who demonstrated an increase in nuclear RNA following training. It is also consistent with the recent finding by Zemp *et al* ... that rate of synthesis of nuclear RNA is increased in a learning situation. There is, however, as yet no completely convincing demonstration that changes in

RNA and protein are fundamental to memory. (6, 1382)

And evaluating the results of another experiment, Flexner and Flexner conclude that it "raises the possibility that the basic memory trace of maze learning may depend upon a long-lasting normal peptide(s) and so may make unnecessary the postulation of a self-sustaining system requiring messenger RNA." (5, 927)

Certainly there are many theories on how information is stored in neurons; but it seems clear that in some form or other, long-term information content, the only type likely to be present in a cryonically suspended patient, must have a molecular basis. In what follows I will nonetheless assume the self-sustaining RNA theory, being confident that any molecular-based information storage will be amenable to preservation by an appropriately devised repair control program.

PROBLEMS IN VIRUS PRODUCTION

Nobel laureate Kornberg speculates on future areas for research in biology:

One is the exploration of the physical and chemical nature of DNA polymerase in order to understand exactly how it performs its error-free replication of DNA. Without this knowledge of the structure of the enzyme and how it operates under defined conditions in the test tube, our understanding of the intracellular behavior of the enzyme will be incomplete.

A second direction is to clarify the control of DNA replication in the cell and in the animal. Why is DNA synthesis arrested in a mature liver cell and what sets it in motion 24 hours after part of the liver is removed surgically? What determines the slow rate of DNA replication in adult cells compared with the rate in embryonic or cancer cells? The time is ripe for exploration of the factors that govern the initiation and rate of DNA synthesis in

the intact cell and animal. Finally, there are now prospects of applying our knowledge of DNA structure and synthesis directly to human welfare. (11, 78)

Of course, using artificial viruses for repair purposes necessitates being able to produce them, and much has already been done in the disassembly and reassembly of viruses, for instance:

If, on the other hand, the components of the virus that causes the mosaic disease of tobacco are gently dissociated and then brought together under the proper conditions, they do reassociate, forming complete, infectious virus particles. The tobacco mosaic virus consists of a single strand of ribonucleic acid with several thousand identical protein subunits assembled around it in a tubular casing. (25, 61)

Aside from tobacco mosaic virus, other viruses have been synthesized, such as ϕ X174. (7, 2321ff)

Wood and Edgar state some of the relationships involving protein synthesis in general and the process of assembling a virus:

Molecular biologists have now provided a fairly complete picture of how genes carry out their primary function: the specification of protein structure. The segment of nucleic acid (DNA or RNA) that constitutes a single gene specifies the chain of amino acids that comprises a protein molecule. Interactions among the amino acids cause the chain to fold into a unique configuration appropriate to the enzymatic or structural role for which it is destined. In this way the information in one gene determines the three-dimensional structure of a single protein molecule.

Where does the information come from to direct the next step: the assembly of many kinds of protein molecules into more complex structures? To build the relatively simple tobacco mosaic virus no further information is required; the inherent properties of the strand of RNA and the protein subunits cause them to interact in a unique way that results in the formation of virus particles. (25, 61)

They go on to conclude:

The problem has now reached a tantalizing stage. A partial sequence of gene-controlled assembly steps can be written, but the manner in which the corresponding gene products contribute to the process remains unclear ... Continued investigation ... can be expected to provide further insight into how genes control the building of biological structures. (25, 74)

Regarding viral assembly and its research possibilities, Kornberg states:

An obvious area for investigation would be the synthesis of the polyoma virus, a virus known to induce a variety of malignant tumors in several species of rodents. Polyoma virus in its infective form is made up of duplex circular DNA and presumably replicates in this form on entering the cell. On the basis of our experience it would appear quite feasible to synthesize polyoma virus DNA. If this synthesis is accomplished, there would seem to be many opportunities for modifying the virus DNA and thus determining where in the chromosome its tumor-producing capacity lies. With this knowledge it might prove possible to modify the virus in order to control its

tumor-producing potential. (11, 78)

I am surely not the first to propose the use of artificial viruses for one purpose or another; Kornberg suggests:

Our speculations can extend even to large DNA molecules. For example, if a failure in the production of insulin were to be traced to a genetic deficit, then administration of the appropriate synthetic DNA might conceivably provide a cure for diabetes. Of course, a system for delivering the corrective DNA to the cells must be devised. Even this does not seem inconceivable. The extremely interesting work of Stanfield Rogers at the Oak Ridge National Laboratory suggests a possibility. Rogers has shown that the Shope papilloma virus, which is not pathogenic in man, is capable of inducing production of the enzyme arginase in rabbits at the same time that it induces tumors. Rogers found that in the blood of laboratory investigators working with the virus there is a significant reduction of the amino acid arginine, which is destroyed by arginase. This is apparently an expression of enhanced arginase activity. Might it not be possible, then, to use similar nonpathogenic viruses to carry into man pieces of DNA capable of replacing or repairing defective genes? (11, 78)

The proposal set forth in this paper extends the use of artificial viruses to the more general case of repair of cell, especially neuron, damage. This will require artificial viruses which will infect neurons: "Viruses are selective in the cells they attack, the evidence indicating that this depends on whether the cells have available the particular receptors to which the viruses may attach themselves." (23, 7) It is known that there are many viruses capable of causing infection of the central nervous

system (23, 9), so appropriate portions of the control programs of such viruses should be included in the production of repair virions. In addition, it needs to be assured that the viruses are able to reach the cells in question, either along natural routes of infection (24, 11), since the ability to make effective contact with a host cell is essential to infection (24, 59), or through micro-surgical injection techniques. In some cases it might be feasible to inject naked genetic material directly into a cell rather than administer it from without by a virus.

Viral mutants which operate at unusual or restricted temperatures exist; the control program characteristics specifying this might be useful if it is determined that repair should proceed at other than normal biological temperature (24, 26); but the important factor is that repair proceed faster than deterioration, whatever the temperature.

PROBLEMS IN VIRAL-INDUCED REPAIR

The following is a summary, claiming no finality or completeness, of the problems on whose solution a technology of cell repair using artificial viruses depends:

Capsid programs need to be isolated or created to ensure that a particular artificial virus will be specific to the type of cell it is supposed to repair. Those portions of the cell genome dealing specifically with the cell's own function must be isolated and perhaps incorporated into the virus in case the cell's own program is damaged. The metabolic pathways necessary to effect repair of a certain degree of damage must be determined and coded into the repair program. Supplementary nutrients to assist repair of the same degree of damage must be determined, prepared, and suitably administered. A preparatory program designed to replicate repair virions in large numbers must be devised. Natural and mechanical methods of infecting all the cells in a damaged or possibly damaged area must be developed. Quality control of many batches of virions must be maintained. Non-replication within the cell must be assured. It must be ascertained whether or not repair should be carried out

by one virus, or by successive infection of several, each acting alone or in conjunction with earlier ones. Once *in situ*, the repair program should determine, by preliminary synthesis, or immediate reaction to specific abnormal products, the degree and kind of damage, if any. According to the diagnosis it should then shift to the appropriate subprogram and carry out the repair, organizing the resources available in the cell and in the enriched extracellular environment. It should determine when repair is complete, and provide for its own disposition. This method may be used to repair any type of cell, but I am interested especially in repair of neurons, where preservation of information content is critical.

PRESERVATION OF LONG-TERM INFORMATION CONTENT

Assuming the self-sustaining RNA theory, how will the control program preserve information content while repair is proceeding? This information can be preserved by requiring the repair program to incorporate the appropriate RNA tapes before large-scale repair is carried out, and, after it is complete, release them to function as before. A possibility for a technique of accomplishing this exists in the phenomenon known as hybridization. Watson discusses an experiment:

If a heated DNA solution is slowly cooled, a single strand can often meet its complementary strand and reform a regular double-helical molecule. This ability to renature DNA molecules permits us to show that artificial hybrid DNA molecules can be formed by slowly cooling mixtures of denatured DNA from two different species. For example, hybrid molecules can be formed containing one strand from a man and one from a mouse. (20, 266)

Of course, preservation of the information content here involves RNA, and DNA-RNA hybridization occurs; Watson mentions a special case in which "... the RNA product remains attached to

its DNA template, allowing the isolation of a hybrid DNA-RNA double helix." (20, 307) Such hybrids are often used in experiments, for instance "... to show the complementarity in nucleotide sequences between an RNA molecule and one of the two strands of its DNA template ..." (20, 310) In fact, Adair, Wilson, and Glassman discuss hybridization in conjunction with brain information content:

There remains the question of the function of RNA that shows the response to training. Since it has been shown that preribosomal RNA attaches to polysomes, the increase in radioactivity in polysomes reported here may reflect increased labeling of either messenger or ribosomal RNA. Regardless of whether mRNA, rRNA, or both are involved, however, the increase in radioactivity would seem to signal the beginning of the synthesis of either a new protein (or proteins) or of an increased rate of synthesis of proteins that are being made continuously. Tests to distinguish between these alternatives by using DNA-RNA hybridization techniques are underway. (1, 921f)

Kates and McAuslan discuss it in connection with viruses: "Viral messenger RNA was assayed by specific hybridization with RP [rabbit poxvirus] - DNA." (10, 316)

Since RNA molecules used for information storage are doubtless genetically specified, a repair control program might carry out DNA-RNA hybridization of all such molecules at the appropriate time after entry into a neuron, and then incorporate the resulting hybrids into its main program in much the same manner as prophage is incorporated into the genome of a lysogenic cell. When repair is complete, the hybrids would be detached, the RNA molecules released, and allowed to function as before.

CONCLUSION

The general method outlined here has its obvious use in the repair of nervous

tissues especially human. Repair of all types of damage—caused by factors mechanical, chemical, pathological, aging, freezing, thawing, and so on—is intended. The method may be partly realized by using its theoretical aspects as a research tool to investigate metabolic pathways in organisms such as bacteria as well as information content and storage in human and other neurons. As Darnell states:

... the most effective means to study animal cell biology is to choose an appropriate virus to introduce a controlled set of genes which perform or cause to be performed the set of events one wishes to analyse. The obvious limitation to this approach is that we do not know a virus which will cause any and every event of interest in animal cell biology. It is nevertheless true that a vast array of interesting problems can be attacked, through the analysis of virus functions at the level of molecular interactions. One possible example of such a problem is the study of the synthesis and entry into organized structures of membrane proteins derived from viral genes. (3, 160f)

I hope that the method cursorily outlined here is still concrete enough to encourage those who are concerned with problems of repair of brain damage, whatever its origin. ■

Special thanks go to Julia Allison for conducting much of the research and reviewing the content.

BIBLIOGRAPHY

1. Adair, Linda B., Wilson, John Eric, and Glassman, Edward, "Brain function and macromolecules, IV. Uridine incorporation into polysomes of mouse brain during different behavioral experiences," *Proceedings of the National Academy of Sciences*, 61 (1968).
2. Barondes, Samuel H. and Cohen, Harry D., "Delayed and sustained effect of acetoxycycloheximide on memory in mice," *Proceedings of the National Academy of Sciences*, 58 (1967).
3. Darnell, James E., "Considerations on virus-controlled functions," in *The Molecular Biology of Viruses*, the Eighteenth Symposium of the Society for General Microbiology, edited by L. V. Crawford and M. G. P. Stoker, Cambridge (1968).
4. Flexner, Josefa B. and Flexner, Louis B., "Restoration of expression of memory lost after treatment with puromycin," *Proceedings of the National Academy of Sciences*, 57 (1967).
5. Flexner, Louis B. and Flexner, Josefa B., "Studies on memory: the long survival of peptidyl-puromycin in mouse brain," *Proceedings of the National Academy of Sciences*, 60 (1968).
6. Flexner, Louis B., Flexner, Josefa B., and Roberts, Richard B., "Memory in mice analyzed with antibiotics," *Science*, 155 (1967).
7. Goulian, Mehran, Kornberg, Arthur, and Sinsheimer, Robert L., "Enzymatic synthesis of DNA, XXIV. Synthesis of infectious phage ϕ X174 DNA," *Proceedings of the National Academy of Sciences*, 58 (1967).
8. Hanawalt, Philip C., "Cellular recovery from photochemical damage," Biophysics Laboratory Report No. 192, W. W. Hansen Laboratories of Physics, Stanford University (1967).
9. Jacob, Francois and Monod, Jacques, "Genetic regulatory mechanisms in the synthesis of proteins," *Journal of Molecular Biology*, 3 (1961).
10. Kates, J. R. and McAuslan, "Messenger RNA synthesis by a coated viral genome," *Proceedings of the National Academy of Sciences*, 57 (1967).
11. Kornberg, Arthur, "The synthesis of DNA," *Scientific American*, 219, 4 (1968).
12. Ledoux, L., "Uptake of DNA by living cells," in *Progress in Nucleic Acid Research and Molecular Biology, Volume 4*, Academic Press, New York (1965).
13. Luria, S. E. and Darnell, James E., Jr., *General Virology*, 2nd edition, John Wiley & Sons, New York (1967).
14. Martin, E. M. and Kerr, I. M., "Virus-induced changes in host-cell macro-molecular synthesis," in *The Molecular Biology of Viruses*, the Eighteenth Symposium of the Society for General Microbiology, edited by L. V. Crawford and M. G. P. Stoker, Cambridge (1968).
15. Pribram, Karl H., "The neurophysiology of remembering," *Scientific American*, 220, 1 (1969).
16. Tomasz, Alexander, "Cellular factors in genetic transformation," *Scientific American*, 220, 1 (1969).
17. Turing, A. M., "On computable numbers, with an application to the Entscheidungsproblem," *Proceedings of the London Mathematical Society*, ser. 2, 42 (1936-7).
18. Ungar, Georges and Irwin, Louis N., "Chemical correlates of neural function," in *Neurosciences Research, Volume 1*, edited by S. Ehrenspreis and Othmar C. Solnitzky, Academic Press, London (1968).
19. Von Neumann, John, *Theory of Self-Reproducing Automata*, edited and completed by Arthur W. Burks, University of Illinois Press, Urbana (1966).
20. Watson, James D., *Molecular Biology of the Gene*, W. A. Benjamin, New York (1965).
21. Watson, James D., *The Double Helix*, New American Library, New York (1968).
22. Woese, Carl R., *The Genetic Code: The Molecular Basis for Genetic Expression*, Harper & Row, New York (1967).
23. Wolstenholme, G. E. W. and Cameron, Margaret P., editors, *Virus Meningo-Encephalitis*, Ciba Foundation Study Group No. 7, Little, Brown and Company, Boston (no date).
24. Wolstenholme, G. E. W. and O'Connor, Cecilia M., editors, *Virus Virulence and Pathogenicity*, Ciba Foundation Study Group No. 4, Little, Brown and Company, Boston (1960).
25. Wood, William B. and Edgar, R. S., "Building a bacterial virus," *Scientific American*, 217, 1 (1967).

Longevity and Genetics 2014 Conference

~ Featuring Dr. Aubrey De Grey ~

Vancouver, BC • November 15, 2014 • 11 am – 6 pm (PST)

The Lifespan Society of British Columbia is proud to present its third annual conference: Longevity and Genetics 2014. Join us as we explore recent developments in biotechnology, personal genomics and quantified-self. This event will be held at SFU's Segal building in downtown Vancouver, British Columbia. Vancouver is one of the most beautiful cities in the world, where the mountains meet the ocean. If you have not been to Vancouver before, this is your chance.



Our keynote speaker, **Dr. Aubrey de Grey**, will be presenting on the latest developments in biorejuvenation at SENS Research Foundation. Aubrey has not been to Vancouver in over 10 years so this is an exclusive experience. We asked Aubrey for an overview of what he will be presenting about:

“It may seem premature to be discussing the comprehensive medical conquest of human aging when so little progress has yet been made in even postponing it. However, two facts undermine this assessment. The first is that aging happens throughout our lives but only causes ill-health after middle age: this shows that we can postpone that ill-health without knowing how to prevent aging completely, but instead by molecular and cellular repair. The second is that regenerative medicine is now advancing from a futuristic twinkle in a few visionaries’ eyes to a realistic strategy for addressing numerous medical conditions. In this talk I will explain why therapies that can add 30 healthy years to the remaining lifespan of typical 60-year-olds may well arrive within the next few decades, with an emphasis on recent progress both in SENS Research Foundation’s own work and elsewhere.” - *Aubrey de Grey*

Our other speakers include Dr. Clinton Mielke, Dr. S. Jay Olshansky, Dr. Angela Brooks-Wilson and Ben Best. They come from different backgrounds and different parts of the world to present their findings to the public. Our speakers will speak on a variety of topics ranging from biorejuvenation, healthy aging, obesity genetics to personal genomics.

Dr. Clinton (Cosmo) Mielke completed his doctoral research at the Mayo Clinic on insulin signaling and resistance in skeletal

muscle. Cosmo’s current research interests include the genetic basis of obesity (specifically in genes that regulate overall metabolism), eating behavior, and sleep. He is the founder of infino.me, a non-profit organization that uses quantified-self equipment to gather information in order to identify and cure chronic diseases. Cosmo will be presenting a talk titled: “Genetic/Neurological Factors Underlying Health And Lifespan”



Dr. S. Jay Olshansky is a Professor in the School of Public Health at the University of Illinois at Chicago and Research Associate at the Center on Aging at the University of Chicago. The focus of his research to date has been on estimates of the upper limits to human longevity, exploring the health and public policy implications associated with individual and population aging, forecasts of the size, survival, and age structure of the population, pursuit of the scientific means to slow aging in people, and global implications of the re-emergence of infectious and parasitic diseases. Dr. Olshansky is on the Board of Directors of the American Federation of Aging Research and is the first author of *The Quest for Immortality: Science at the Frontiers of Aging*.

Dr. Angela Brooks-Wilson is the Head of Cancer Genetics at the Michael Smith Genome Sciences Centre at the BC Cancer Agency. She is also a professor in the Department of Biomedical Physiology and Kinesiology at Simon Fraser University. She has done research in a variety of areas including healthy aging. She is currently leading a team that studies the genetic factors that underlie



healthy aging and resistance to common age-related diseases such as cancer, cardiovascular and pulmonary disease. She also serves on the Ethics Advisory Board of Genome BC and a member of the CIHR Institute of Cancer Research Institute Advisory Board.

to see you there, so mark your calendars. If you would like to ask any questions about our event you can email Carrie Wong, Executive Director at carrie@lifespanbc.ca.



Ben Best is the Director of Research Oversight at the Life Extension Foundation. He is well-known within the life-extension community and has travelled to many longevity conferences. He evaluates life-extension related research proposals and makes recommendations on funding them. Ben has a background in pharmacology and has spoken on a number of topics ranging from cryobiology to biogerontology. He will be giving a talk on dietary supplements for health and lifespan.

After our speakers have made their presentations, there will be a panel where the audience can ask them questions. More information about our conference and which topics the speakers will be speaking on will be announced soon on our website: www.lifespanbc.ca. Early Bird Tickets are only \$40 and can be purchased here: www.lifespanbc.ca/2014 (Redirects to EventBrite). We hope

ABOUT THE LIFESPAN SOCIETY OF BRITISH COLUMBIA

The Lifespan Society of British Columbia is a small non-profit organization which was provincially incorporated in 2012. Lifespan's mission is to promote and protect access to science-based strategies for extending human lifespan. We advocate healthy living through education on optimal nutrition, integration of physical activities, and a broad range of existing and future treatments that encompass all aspects of longevity.

We believe the best years of your life are still ahead of you, and we make it our mission to help people improve upon that journey. Through a variety of community programs and events, we offer exciting insights into present and future healthcare technologies.

Lifespan Society of British Columbia believes that access to life extension technology is a fundamental human right. Together, we work to ensure Canadians have access to medical life extension treatments currently in development. To this end, we organize conferences and educational outreach events to stimulate informed and critical discussion on life extension issues. ■



The Lifespan Crew at Maker Faire Vancouver with their UV Photo Damage Booth (May 2014)

Preserving Minds, Saving Lives: 35 Years of the Best Cryonics Writing of The Alcor Life Extension Foundation

Available for Pre-Order NOW!

Featuring stimulating articles from the pages of CRYONICS Magazine by Steven Harris, Hugh Hixon, Saul Kent, Mike Darwin, Stephen Bridge, Thomas Donaldson, Aschwin de Wolf, Brian Wowk, Michael Perry, Ralph Merkle, and many others.

Here are some of the classic articles that shaped cryonics thought and Alcor policy over the past three decades.

Why We are Cryonicists

Notes on the First Human Freezing

Dear Dr. Bedford

How Cryoprotectants Work

How Cold is Cold Enough?

The Death of Death in Cryonics

The Society for The Recovery of Persons Apparently Dead

Frozen Souls: Can A Religious Person Choose Cryonics?

But What Will the Neighbors Think?!

Systems for Intermediate Temperature Storage for Fracture Reduction and Avoidance

You can't really understand cryonics today unless you can appreciate how we got here. The philosophy, the history, the science and technology, the debates, the PEOPLE of cryonics—it's all here in one indispensable volume. The book will be published in 2014.

Quantity: _____ Hardcover @ \$35.00 _____ Quality paperback @ \$20.00 = \$ _____

Add \$3.00 for Shipping (\$15.00 for non-US/Canada orders) = \$ _____

TOTAL: \$

CREDIT CARD INFORMATION

Card type: Discover Visa MasterCard AMEX

Name on card: _____ Billing Zip Code: _____

Credit card number: _____ Expiration date: _____

Signature: _____

SHIPPING INFORMATION

Name: _____

Address: _____ City: _____ State: _____ Zip: _____

Phone: _____ Email: _____

(Optional)

Send this form to:

Alcor Life Extension Foundation

7895 East Acoma Drive Suite 110

Scottsdale, Arizona 85260.

You can also order via PayPal by sending payment to bonnie@alcor.org or by calling Alcor at 1-877-462-5267 Ext. 114



Item # 01430

Advanced Resveratrol Formula

In 2003, the **Life Extension Foundation®** introduced a standardized **resveratrol** extract shown to favorably alter genes implicated in the aging process—many of the same genes that respond to **calorie restriction**.

Since then, we have identified additional compounds that simulate calorie restriction's ability to trigger youthful **gene expression**—the process by which genes transmit signals that slow certain aspects of aging.

Compelling evidence reveals that certain compounds found in berries, such as **pterostilbene** and **fisetin**, possess potent “longevity gene” activators that work in synergy with **resveratrol**. For example, **fisetin** (found in strawberries) has been shown to **stabilize** resveratrol in the body by shielding it from metabolic breakdown,¹⁻¹⁰ thus extending its beneficial effects.

CAUTION: If you are taking anti-coagulant or anti-platelet medications or have a bleeding disorder, consult your healthcare provider before taking this product.

References

1. *Cell*. 2006 Dec 15;127(6):1109-22.
2. *Endocrinology*. 2008 Jan;149(1):84-92.
3. *Crit Care Med*. 2004 Oct;32(10):2097-103.
4. *J Agric Food Chem*. 1999 Apr;47(4):1416-21.
5. *Arch Pharm Res*. 2002 Oct;25(5):561-71.
6. *Nutr Cancer*. 1999;35(1):80-6.
7. *Anticancer Agents Med Chem*. 2006 Sep;6(5):389-406.
8. *Nature*. 2006 Nov 16;444(7117):337-42.
9. *Nature*. 2004 Aug 5;430(7000):686-9.
10. *Xenobiotica*. 2000 Sep;30(9):857-66.

High-Potency Resveratrol with Synergistic Activators

Life Extension® members gain access to standardized **trans-resveratrol** combined with botanical extracts that favorably influence longevity gene expression. Unlike many commercial formulas, Life Extension standardizes to **trans-resveratrol**, which researchers contend is the most active constituent.

A bottle containing 60 vegetarian capsules of **Optimized Resveratrol with Synergistic Grape-Berry Actives** retails for \$46. If a member buys four bottles, the price is reduced to **\$31** per bottle.

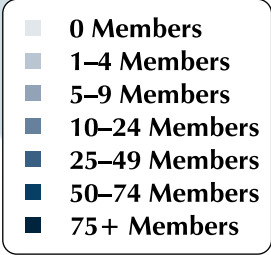
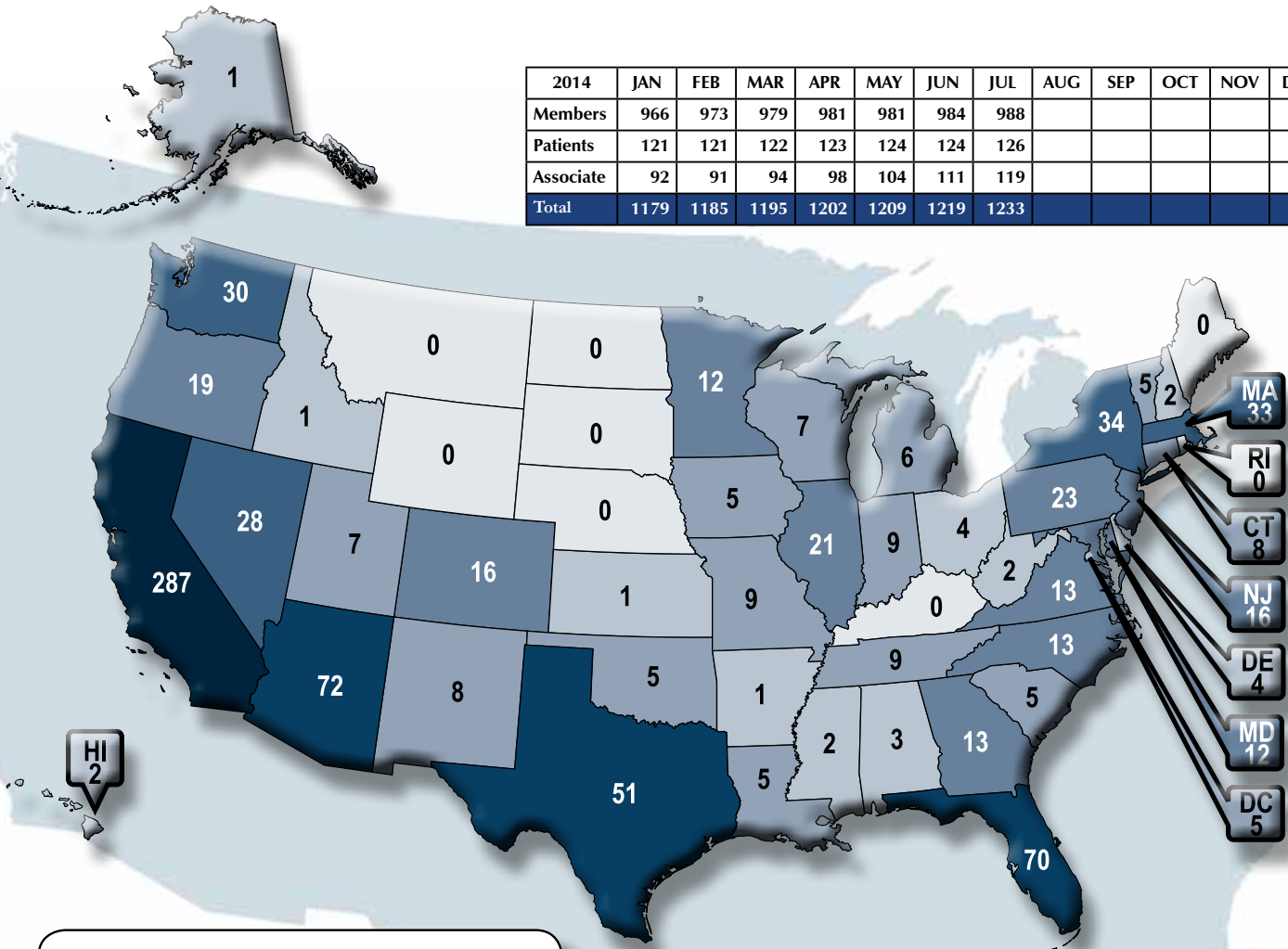
The suggested dose of one capsule a day provides:

Trans-Resveratrol	250 mg
Grape-Berry Actives	85 mg
Quercetin	60 mg
Trans-Pterostilbene	0.5 mg
Fisetin	10 mg

To order **Optimized Resveratrol with Synergistic Grape-Berry Actives**,
call 1-800-544-4440 or visit www.LifeExtension.com
Be sure to mention code PIM401X.

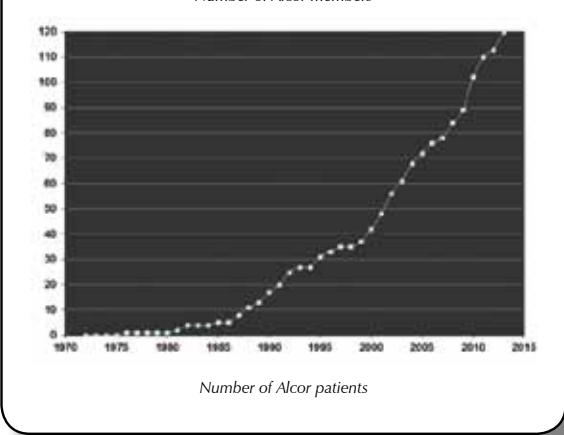
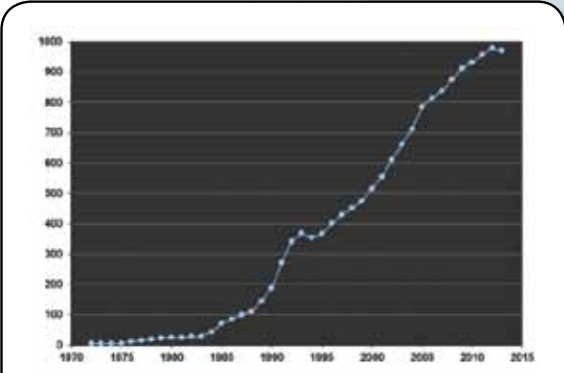
Membership Statistics

2014	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Members	966	973	979	981	981	984	988					
Patients	121	121	122	123	124	124	126					
Associate	92	91	94	98	104	111	119					
Total	1179	1185	1195	1202	1209	1219	1233					



International

Country	Members	Patients
Australia	10	3
Canada	43	2
Germany	4	0
Hong Kong	1	0
Israel	1	1
Italy	3	0
Japan	2	0
Lebanon	1	0
Mexico	4	0
Monaco	1	0
Netherlands	2	0
New Zealand	3	0
Norway	1	0
Portugal	4	0
Singapore	1	0
Spain	3	1
Thailand	3	0
United Arab Emirates	1	0
United Kingdom	21	2
TOTAL	109	9



Options for Safe, Secure and Legal Asset Preservation for Post-Resuscitation Access

The Sixth Annual Young Cryonicists Gathering

Teens & Twenties 6 2015: Getting to Know You - You Getting to Know Each Other - All While Being Updated On the Latest Scientific Research

Fri-Sun; April 24-26, '15 Las Vegas NV Host: Life Extension Foundation SCHOLARSHIPS AVAILABLE



Greetings to *Young Cryonicists*,

You are receiving this invitation because you are among the future leaders in cryonics.

All attention will be focused on:

our getting to know you and
you getting to know each other.

PLUS: an update on the latest emergency response technologies and revival strategies.

Who is Eligible?

Fully signed up young cryonicists from all cryonics organizations aged 13-30 as of March 27, 2015 - may apply to attend. Cryonicists aged 12-17 must be accompanied by their parent(s) or guardian. In Vegas those under 21 must room with someone over 21.

Parents/guardians of attendees aged 18-19 are also encouraged to accompany their child. All attending parents will be put in touch with each other should they choose to have their own "get together" during the "young cryonicists" gathering.

Program

Some individuals are social butterflies. This is not so for everyone. And we want everyone to meet everyone. Therefore, I have designed a diverse range of "getting to know you" activities. If you would enjoy participating in these various getting acquainted activities, all while being updated on the latest scientific research, then this is for you.

Enjoy this exciting & fulfilling weekend.

SCHOLARSHIPS:

Life Extension Foundation, through a generous education grant, is offering 40 scholarships that pay for ALL of the following:

- ◆ U.S. airfare to/from Las Vegas (or up to \$1000 for origin outside the U.S., \$1350 for Australia)
- ◆ Hotel accommodations for Friday and Saturday nights. Plus Thursday and Sunday for attendees who room together.
- ◆ Meals and beverages on Friday night, all day Saturday, & Sunday breakfast & lunch
- ◆ Registration fee - \$350 - also covered

Please click on this website for a full packet with details & application forms.

http://www.alcor.org/T2_6_2015_details.pdf

Forever,

Cairn Erfreuliche Idun
Founder/Director: T2

Bill Faloon: The Life Extension Foundation

Some attendees to T2 enjoy spending extra time in Las Vegas - especially since their flight is already paid for via their scholarship.

This is at their own expense for additional food and lodging.

We look forward to getting to know you.

Memory Relies on Astrocytes, the Brain's Lesser Known Cells

When you're expecting something—like the meal you've ordered at a restaurant—or when something captures your interest, unique electrical rhythms sweep through your brain. These waves, called gamma oscillations, reflect a symphony of cells—both excitatory and inhibitory—playing together in an orchestrated way. Though their role has been debated, gamma waves have been associated with higher-level brain function, and disturbances in the patterns have been tied to schizophrenia, Alzheimer's disease, autism, epilepsy and other disorders. Now, new research from the Salk Institute shows that little known supportive cells in the brain known as astrocytes may in fact be major players that control these waves. In a study published July 28 in the *Proceedings of the National Academy of Sciences*, Salk researchers report a new, unexpected strategy to turn down gamma oscillations, by disabling not neurons but astrocytes. In the process, the team showed that astrocytes, and the gamma oscillations they help shape, are critical for some forms of memory.

Salk Institute

28 Jul. 2014 http://www.salk.edu/news/pressrelease_details.php?press_id=2039

Program to Make Engineered Biological Systems More Robust and Stable

To date, work in synthetic biology has focused primarily on manipulating individual species of domesticated organisms to perform specific tasks such as producing medicines or fuels. These species tend to be both relatively fragile and relatively unstable. The costs of maintaining required environmental controls and detecting and compensating for genetic alterations are substantial and severely limit the widespread application of synthetic biology to U.S. national security missions. To help address

these challenges, DARPA has created the Biological Robustness in Complex Settings (BRICS) program. BRICS seeks to develop the fundamental understanding and component technologies needed to increase the biological robustness and stability of engineered organisms while maintaining or enhancing the safe application of those organisms in complex biological environments. The goal is to create the technical foundation for future engineered biological systems to achieve greater biomedical, industrial and strategic potential.

DARPA

29 Jul. 2014 <http://www.darpa.mil/NewsEvents/Releases/2014/07/29.asp>

Nanofibers Created Like Those of Living Cells

Researchers from Carnegie Mellon University have developed a novel method for creating self-assembled protein/polymer nanostructures that are reminiscent of fibers found in living cells. The work offers a promising new way to fabricate materials for drug delivery and tissue engineering applications. The findings were published in the July 28 issue of *Angewandte Chemie International Edition*. "We have demonstrated that, by adding flexible linkers to protein molecules, we can form completely new types of aggregates. These aggregates can act as a structural material to which you can attach different payloads, such as drugs. In nature, this protein isn't close to being a structural material," said Tomasz Kowalewski, professor of chemistry in Carnegie Mellon's Mellon College of Science. The building blocks of the fibers are a few modified green fluorescent protein (GFP) molecules linked together using a process called click chemistry.

Carnegie Mellon University

31 Jul. 2014 <http://www.cmu.edu/mcs/news/pressreleases/2014/0731-gfp-nanofibers.html>

Seeing Into Living Brains with Lasers and Nanotubes

By injecting carbon nanotubes into the bloodstream, scientists can use near-infrared lasers to see blood flow in a living animal's brain. The new technique, which is almost completely noninvasive, was developed for mice, but could offer insight into human ailments, such as strokes, migraines, and possibly Alzheimer's and Parkinson's diseases. Some of the most damaging brain diseases can be traced to irregular blood delivery in the brain. Current procedures for viewing blood flow are either overly invasive or less effective. Surgically removing part of the skull offers a clear view of activity at the cellular level. But the trauma can alter the function or activity of the brain or even stimulate an immune response. Noninvasive techniques such as CT scans or MRI can't visualize individual vessels or groups of neurons. The first step of the new technique, called near infrared-IIa imaging, or NIR-IIa, involves injecting water-soluble carbon nanotubes into a live mouse's bloodstream. The researchers then shine a near-infrared laser over the rodent's skull, to view about 3 millimeters under the scalp.

Futurity / Bjorn Carey, Stanford University

7 Aug. 2014 <http://www.futurity.org/brain-lasers-nanotubes-743932/>

On the Frontiers of Cyborg Science

No longer just fantastical fodder for sci-fi buffs, cyborg technology is bringing us tangible progress toward real-life electronic skin, prosthetics and ultraflexible circuits. Now taking this human-machine concept to an unprecedented level, pioneering scientists are working on the seamless marriage between electronics and brain signaling with the potential to transform our understanding of how the brain works—and how to treat its most devastating diseases.

Their presentation is taking place at the 248th National Meeting & Exposition of the American Chemical Society (ACS). "By focusing on the nanoelectronic connections between cells, we can do things no one has done before," says Charles M. Lieber, Ph.D. "We're really going into a new size regime for not only the device that records or stimulates cellular activity, but also for the whole circuit. We can make it really look and behave like smart, soft biological material, and integrate it with cells and cellular networks at the whole-tissue level. This could get around a lot of serious health problems in neurodegenerative diseases in the future."

American Chemical Society
10 Aug. 2014 <http://www.acs.org/content/acs/en/pressroom/newsreleases/2014/august/on-the-frontiers-of-cyborg-science.html>

Bioengineers Create Functional 3D Brain-like Tissue

Bioengineers have created three-dimensional brain-like tissue that functions like and has structural features similar to tissue in the rat brain and that can be kept alive in the lab for more than two months. As a first demonstration of its potential, researchers used the brain-like tissue to study chemical and electrical changes that occur immediately following traumatic brain injury and, in a separate experiment, changes that occur in response to a drug. The tissue could provide a superior model for studying normal brain function as well as injury and disease, and could assist in the development of new treatments for brain dysfunction. The brain-like tissue was developed at the Tissue Engineering Resource Center at Tufts University, Boston, which is funded by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) to establish innovative biomaterials and tissue engineering models. David Kaplan, Ph.D., Stern Family Professor of Engineering at Tufts University is director of the center and led the research efforts to develop the tissue.

National Institute of Biomedical Imaging and Bioengineering
11 Aug. 2014
<http://www.nibib.nih.gov/news-events/>

newsroom/bioengineers-create-functional-3d-brain-tissue

Manipulating Molecules to Make Memories

Researchers have created a genetically engineered mouse that allows them to observe the movement of molecules in the brain that may be involved in the formation of memories. The transgenic mouse carries a fluorescently labeled messenger RNA (mRNA) that can be visualized in cells without disrupting normal physiological processes. This new genetic tool allows observation of gene expression in real time in neurons where the movement of the fluorescently labeled beta-actin mRNA provides clues to the molecular changes in the brain involved in forming and storing memories. The research team is based at Albert Einstein College, Bronx, NY, with collaborators in Novara Italy, Hunter College in New York, and the Howard Hughes Medical Institute in Ashburn, Virginia. They report their findings in *Science* ("Visualization of dynamics of single endogenous mRNA labeled in live mouse"). The group used a series of genetic manipulations to create a mouse whose natural beta-actin gene creates an mRNA that is fluorescently labeled and so can be observed in real time in the cells of the mouse.

Nanowerk News
11 Aug. 2014 http://www.nanowerk.com/news2/biotech/newsid=36876.php?utm_source=feedburner&utm_medium=email&utm_campaign=Feed%3A+NanowerkEmergingTechnologiesNews+%28Nanowerk+Emerging+Technologies+News%29#ixzz3ABzG8YVB

Neuromorphic 'Atomic-Switch' Networks Function Like Synapses in the Brain

Researchers in the U.S. and Japan have developed a self-assembled neuromorphic (brain-like) device comprising more than a billion interconnected "atomic-switch" inorganic synapses embedded in a complex network of silver nanowires. The researchers are located at the California NanoSystems Institute (CNSI) at the

University of California, Los Angeles (UCLA) and the International Center for Materials Nanoarchitectonics (MANA) at the National Institute for Materials Science, Japan. The atomic switch, a recently developed nanoscale circuit element, has been shown to possess synapse-like properties in a purely inorganic device. The device uses a billion junctions per square centimeter incorporated into a densely interconnected network of silver nanowires. Like biological neural networks, these atomic switch networks (ASN) generate memristor-like emergent behaviors made up of their distributed, collective interactions. These emergent behaviors are a principal characteristic of biological neural networks and many other complex systems.

Kurzweil AI
19 Aug. 2014
<http://www.kurzweilai.net/neuromorphic-atomic-switch-networks-function-like-synapses-in-the-brain>

Nanoscale Biological Assembly Line Created

Researchers at ETH Zurich, Switzerland have realized a long-held dream: inspired by an industrial assembly line, they have developed a nanoscale production line for the assembly of biological molecules. On the nano assembly line, tiny biological tubes called microtubules serve as transporters for the assembly of several molecular objects. Cars, planes and many electronic products are now built with the help of sophisticated assembly lines. Mobile assembly carriers, on to which the objects are fixed, are an important part of these assembly lines. In the case of a car body, the assembly components are attached in various work stages arranged in a precise spatial and chronological sequence, resulting in a complete vehicle at the end of the line. The creation of such an assembly line at molecular level has been a long-held dream of many nanoscientists. "It would enable us to assemble new complex substances or materials for specific applications," says Professor Viola Vogel, head of the Laboratory of Applied Mechanobiology at ETH Zurich.

ETH Zurich

Practical Human Brain Implants Initiative

DARPA, on the back of the US government's BRAIN program, has begun the development of tiny electronic implants that interface directly with your nervous system and can directly control and regulate many different diseases and chronic conditions, such as arthritis, PTSD, inflammatory bowel diseases (Crohn's disease), and depression. The program, called ElectRx (pronounced *electric*), ultimately aims to replace medication with "closed-loop" neural implants, which constantly assess the state of your health, and then provide the necessary nerve stimulation to keep your various organs and biological systems functioning properly. The work is primarily being carried out with US soldiers and veterans in mind, but the technology will certainly percolate down to civilians as well. The ElectRx program will focus on a fairly new area of medical therapies called *neuromodulation*. As the name implies, neuromodulation is all about modulating your nervous system, to improve or fix an underlying problem. Notable examples of neuromodulation are cochlear implants ...

ExtremeTech
29 Aug. 2014 <http://www.extremetech.com/extreme/188908-darpas-tiny-implants-will-hook-directly-into-your-nervous-system-treat-diseases-and-depression-without-medication>

Animal Organ Grown from Lab-Created Cells

Scientists have grown a fully functional organ from transplanted laboratory-created cells in a living animal for the first time. The researchers have created a thymus—an organ next to the heart that produces immune cells known as T cells that are vital for guarding against disease. They hope that, with further research, the discovery could lead to new treatments for people with a weakened immune system. The team from

the MRC Centre for Regenerative Medicine at the University of Edinburgh took cells called fibroblasts from a mouse embryo. They turned the fibroblasts into a completely different type of cell called thymus cells, using a technique called reprogramming. The reprogrammed cells changed shape to look like thymus cells and were also capable of supporting development of T cells in the lab—a specialized function that only thymus cells can perform. When the researchers mixed reprogrammed cells with other key thymus cell types and transplanted them into a mouse, the cells formed a replacement organ with the same structure, complexity and function as a healthy adult thymus.

University of Edinburgh
4 Sep 2014 <http://www.ed.ac.uk/news/2014/livingorgan-250814>

Scientists Revert Human Stem Cells to Pristine State

Researchers at EMBL-EBI have resolved a long-standing challenge in stem cell biology by successfully "resetting" human pluripotent stem cells to a fully pristine state, at point of their greatest developmental potential. The study, published in **Cell**, involved scientists from the UK, Germany and Japan and was led jointly by EMBL-EBI and the University of Cambridge ("Resetting Transcription Factor Control Circuitry toward Ground-State Pluripotency in Human"). Embryonic stem (ES) cells, which originate in early development, are capable of differentiating into any type of cell. Until now, scientists have only been able to revert "adult" human cells (for example, liver, lung or skin) into pluripotent stem cells with slightly different properties that predispose them to becoming cells of certain types. Authentic ES cells have only been derived from mice and rats. "Reverting mouse cells to a completely 'blank slate' has become routine, but generating equivalent naïve human cell lines has proven far more challenging," says Dr Paul Bertone, Research Group Leader at EMBL-EBI and a senior author on the study.

Nanowerk News
11 Sep. 2014 http://www.nanowerk.com/news2/biotech/newsid=37322.php?utm_source=feedburner&utm_me

Therapy-Grade Stem Cells by Reprogramming Adult Cells

Researchers at the Hebrew University of Jerusalem have developed a new cocktail that is highly effective at coaxing adult cells to become quality pluripotent stem cells. Regenerative medicine is a new and expanding area that aims to replace lost or damaged cells, tissues or organs through cellular transplantation. Because stem cells derived from human embryos can trigger ethical concerns, a good solution is reprogramming adult cells back to an embryo-like state using a combination of reprogramming factors. The resulting cells, called induced pluripotent stem cells (iPSCs), could be used to replace those lost to damage or disease. However, scientists have discovered that the process of reprogramming adult cells can introduce genetic abnormalities that limit the cells' usefulness in research and medicine. The researchers have now developed a new cocktail of reprogramming factors that produce high-quality iPSCs. Dr. Yosef Buganim worked with scientists at the lab of Whitehead Institute founding member Rudolf Jaenisch.

ScienceDaily
16 Sep. 2014 <http://www.sciencedaily.com/releases/2014/09/140916111909.htm>

Key Discovery about Communication between Cells

When the body forms new tissues during the healing process, cells must be able to communicate with each other. For years, scientists believed this communication happened primarily through chemical signaling. Now researchers at Carnegie Mellon University and the University of Pittsburgh have found that another dimension—mechanical communication—is equally if not more crucial. The findings, published in this week's issue of the *Proceedings of the National Academy of Sciences*,

could lead to advancements in treatments for birth defects and therapies for cancer patients. "It's like 19th century scientists discovering that electricity and magnetism were the same force," said Lance Davidson, associate professor of bioengineering at the University of Pittsburgh, who co-lead the study. "The key here is using mechanical engineering tools and frameworks to reverse-engineer how these biological systems work, thereby giving us a better chance to develop methods that affect this cellular communication process and potentially treat various diseases related to tissue growth."

Carnegie Mellon University
24 Sep. 2014 http://www.cmu.edu/news/stories/archives/2014/september/september24_communicatingcells.html

Electronic Brain by 2023

Like a Manhattan Project, resources are coming together for the big push to simulate the human brain. Personnel on European Union (EU)'s Human Brain Project reported their progress toward the primary directive—an artificial brain by 2023—at the annual HBP Summit at the University of Heidelberg in Germany, yesterday, September 29. The 10-year-long Human Brain Project, funded to the tune of \$1 billion euro (US\$1.3 billion) by the European Commission Future and Emerging Technologies as one of its "Flagship Programs," aims to simulate the entire human brain on supercomputers first, then build a special hardware emulator that will reproduce its functions so accurately that diseases and their cures can be tried out on it. Ultimately, the long-term goal is

to build artificial brains that are inexpensive enough to outperform traditional von Neuman supercomputers at a fraction of the cost.

EETimes
30 Sep. 2014 http://www.eetimes.com/document.asp?doc_id=1324121&

A Roadmap to Resuscitation

Successful rejuvenation 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 list is a list of landmark papers and books that reflect ongoing progress towards the resuscitation 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.

Michael G. Darwin, "The Anabolocyte: A Biological Approach to Repairing Cryoinjury," *Life Extension*

Magazine (July-August 1977):80-83. Reprinted in *Cryonics* 29 (4th Quarter 2008):14-17.

Corey Noble, "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(January 1994):16-31 (Part I) & *Cryonics* 15(April 1994):20-32 (Part II).

Ralph C. Merkle, "Cryonics, Cryptography, and Maximum Likelihood Estimation," First Extropy Institute Conference, Sunnyvale CA, 1994.

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, pp. 685-805.

Chana de Wolf, "Reconstructive Connectomics," *Cryonics Magazine*, July 2013.

Elizabeth G. Pugliese

FUNDRAISER SUCCESSFUL!!

A few months ago your assistance was requested to help cryopreserve the brain of an 88-year-old woman who died and wanted to be cryopreserved. Happily, we can report that the necessary funds were raised and Elizabeth G. Pugliese became a patient at Alcor July 15. As is customary with brain-only cases starting with fixative preservation, she is now undergoing a lengthy process of slow, diffusive cryoprotection at low above-freezing temperature. This phase should be completed within a few months, to be followed by cooldown to cryogenic temperatures and long-term storage in liquid nitrogen. For now, a heartfelt thanks from The Venturists to those who made it all possible with your generous donations and to Alcor for their charitable willingness to help!



With son Ron Putirka, about 1948

THE VENTURISTS (SOCIETY FOR VENTURISM) | WWW.VENTURIST.INFO



Item# 01808

How Much Curcumin Are You Absorbing?

Curcumin is an active compound derived from the Indian spice **turmeric**. It has been widely acclaimed for its diverse health-promoting effects on nearly every organ system in the body,¹⁻⁶ including its support for the body's natural inflammatory response system.⁷ But most curcumin is neither *absorbed* well nor *retained* well in the blood—posing a challenge to those who wish to maximize its benefits.⁸

Life Extension® took the lead in resolving this issue several years ago by introducing **Super Bio-Curcumin®** containing **BCM-95®**, a patented, *bioenhanced* preparation of curcumin that has been shown to reach up to **7 times higher concentration** in the blood than standard curcumin.⁸

Now, an exciting **next generation** curcumin formula has become available! **Advanced Bio-Curcumin® with Ginger & Turmerones** provides additional compounds that **further** boost absorption of curcumin's highly beneficial phytonutrients!^{9,10}

UNRIVALED POTENCY AND ABSORBABILITY

In addition to **BCM-95®**, this **curcumin** formula contains:

- 1. Turmerones:** After curcumin is extracted from turmeric, what remains is **turmeric oil** rich in compounds called **turmerones**.^{11,12} Combining **BCM-95®** with a high content of **turmerones** provides health consumers with more beneficial **turmeric** compounds that further multiply absorption.⁹ Scientists have shown that these potent **turmerones** not only support curcumin absorption, but significantly increase the amount of curcumin **inside** the cell as well!⁹
- 2. Ginger:** Curcumin and **ginger** are close botanical relatives. Research demonstrates that they have overlapping and complementary health benefits,¹³ and scientists are focusing on the therapeutic effects of *combining* these two plants.^{14,15} **Advanced Bio-Curcumin® with Ginger & Turmerones** provides a supercritical extract of ginger standardized to the greatest concentration of ginger compounds—including beneficial gingerols and shogaols.
- 3. Phospholipids:** This new curcumin formula also contains **phospholipids**, a type of emulsifying molecule known to greatly enhance absorption of poorly soluble active compounds.¹⁰

The powerfully enhanced bioavailability and potency of **Advanced Bio-Curcumin® with Ginger & Turmerones** is superior to conventional curcumin supplements. This product represents the most powerful and cost-effective way to supplement with—and receive the full benefits of—this very critical nutrient.

The suggested daily dosage of one softgel of **Advanced Bio-Curcumin® with Ginger & Turmerones** provides:

Turmeric Phospholipid Blend	630 mg
BCM-95® Bio-Curcumin Turmeric 25:1 extract (rhizome) [total curcuminoids complex with essential oils (380 mg)], Turmeric oil (rhizome) [providing 60 mg total turmerones], Phospholipids	
Ginger CO₂ extract (root)	200 mg
[providing 60 mg gingerols]	

Each softgel of **Advanced Bio-Curcumin® with Ginger & Turmerones** provides **400 mg** of **BCM-95® Super Bio-Curcumin** plus an array of turmerones and phospholipids.

A bottle of 30 softgels of **Advanced Bio-Curcumin® with Ginger & Turmerones** retails for \$30. If a member buys four bottles, the price is reduced to **\$20.25** per bottle

Contains soybeans.

Bio-Curcumin® and **BCM-95®** are registered trademarks of Dolcas- Biotech, LLC.

ORDER NOW!

Toll-free 1-800-544-4440

www.LifeExtension.com

You must use Discount Code PIM401X to get these savings.

References

1. *Adv Exp Med Biol.* 2007;595:197-212.
2. *Biofactors.* 2013 Jan-Feb;39(1):2-13.
3. *Clin Exp Pharmacol Physiol.* 2012 Mar;39(3):283-99.
4. *Adv Exp Med Biol.* 2007;595:1-75.
5. *Trends Pharmacol Sci.* 2009 Feb;30(2):85-94.
6. *Curr Drug Targets.* 2011 Mar 1;12(3):332-47.
7. *J Clin Immunol.* 2007 Jan;27(1):19-35.
8. *Indian J Pharm Sci.* 2008 Jul-Aug;70(4):445-9.
9. *J Med Food.* 2012 Mar;15(3):242-52.
10. *Cancer Chemother Pharmacol.* 2007;60:171-7.
11. *J Agric Food Chem.* 1999 Oct;47(10):4297-300.
12. *Z Naturforsch C.* 2001 Jan-Feb;56(1-2):40-4.
13. *Osteoarth Cartilage.* 2003 Nov;11(11):783-9.
14. *Wound Repair Regen.* 2009 May-Jun;17(3):360-6.
15. Available at: http://www.umassmed.edu/hema_oncology/MDSInfo/curcuminandgingerol.aspx. Accessed September 25, 2013.

Caution: Do not take if you have gallbladder problems or gallstones. If you are taking anti-coagulant or anti-platelet medications, or have a bleeding disorder, contact your healthcare practitioner before taking this product.

MEETINGS

ABOUT THE ALCOR FOUNDATION

The Alcor Life Extension Foundation is a nonprofit tax-exempt scientific and educational organization dedicated to advancing the science of cryopreservation and promoting cryonics as a rational option. Being an Alcor member means knowing that—should the worst happen—Alcor's Emergency Response Team is ready to respond for you, 24 hours a day, 365 days a year.

Alcor's Emergency Response capability includes specially trained technicians and customized equipment in Arizona, northern California, southern California, and south Florida, as well as many additional certified technicians on-call around the United States. Alcor's Arizona facility includes a full-time staff, and the Patient Care Bay is personally monitored 24 hours a day.

ARIZONA

FLAGSTAFF:

Arizona without the inferno. Cryonics group in beautiful, high-altitude Flagstaff. Two-hour drive to Alcor. Contact eric@flagstaffcryo.com for more information.

PHOENIX

VALLEY OF THE SUN:

This group meets monthly, usually in the third week of the month. Dates are determined by the activity or event planned. For more information or to RSVP, visit <http://cryonics.meetup.com/45/> or email Lisa Shock at lisa@alcor.org.

AT ALCOR:

Alcor Board of Directors Meetings and Facility Tours—Alcor business meetings are generally held on the first Saturday of every month starting at 11:00 AM MST. Guests are welcome to attend the fully-public board meetings on odd-numbered months. Facility tours are held every Tuesday and Friday at 2:00 PM. For more information or to schedule a tour, call Marji Klima at (877) 462-5267 x101 or email marji@alcor.org.

CALIFORNIA

LOS ANGELES:

Alcor Southern California Meetings—For information, call Peter Voss at (310) 822-4533 or e-mail him at peter@optimal.org. Although monthly meetings are not held regularly, you can meet Los Angeles Alcor members by contacting Peter.

SAN FRANCISCO BAY:

Alcor Northern California Meetings are held quarterly in January, April, July, and October. A CryoFeast is held once a year. For information on Northern California meetings, call Mark Galeck at (650) 969-1671, (650) 534-6409 or email Mark_galeck@pacbell.net.

FLORIDA

Central Florida Life Extension group meets once a month in the Tampa Bay area (Tampa and St. Petersburg) for discussion and socializing. The group has been active since 2007. Email arcturus12453@yahoo.com for more information.

NEW ENGLAND

CAMBRIDGE:

The New England regional group strives to meet monthly in Cambridge, MA—for information or to be added to the Alcor NE mailing list, please contact Bret Kulakovich at 617-824-8982, alcor@bonfireproductions.com, or on FACEBOOK via the Cryonics Special Interest Group.

PACIFIC NORTHWEST

A Yahoo mailing list is also maintained for cryonicists in the Pacific Northwest at <http://tech.groups.yahoo.com/group/CryonicsNW/>.

BRITISH COLUMBIA (CANADA):

The contact person for meetings in the Vancouver area is Keegan Macintosh: keegan.macintosh@me.com.

OREGON:

The contact person for meetings in the Portland area is Aschwin de Wolf: aschwin@alcor.org

See also: <https://www.facebook.com/portland.life.extension>

ALCOR PORTUGAL

Alcor Portugal is working to have good stabilization and transport capabilities. The group meets every Saturday for two hours. For information about meetings, contact Nuno Martins at n-martins@n-martins.com. The Alcor Portugal website is: www.alcorportugal.com.

TEXAS

DALLAS:

North Texas Cryonauts, please sign up for our announcements list for meetings (<http://groups.yahoo.com/group/cryonauts-announce>) or contact David Wallace Croft at (214) 636-3790 for details of upcoming meetings.

AUSTIN/CENTRAL TEXAS:

We meet at least quarterly for training, transport kit updates, and discussion. For information: Steve Jackson, 512-447-7866, sj@sjgames.com.

UNITED KINGDOM

There is an Alcor chapter in England. For information about meetings, contact Alan Sinclair at cryoservices@yahoo.co.uk. See the web site at www.alcor-uk.org.

If you are interested in hosting regular meetings in your area, contact Alcor at 877-462-5267, ext. 113. Meetings are a great way to learn about cryonics, meet others with similar interests, and introduce your friends and family to Alcor members!

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 a 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.
- Finally:** After enrolling, you will wear emergency alert tags or carry a special card in your wallet. This is your confirmation that Alcor will respond immediately to an emergency call on your behalf.

Not ready to make full arrangements for cryopreservation? Then **become an Associate Member** for \$10/month (or \$30/quarter or \$120 annually). Associate Members will receive:

- *Cryonics* magazine by mail
- Discounts on Alcor conferences
- Access to post in the Alcor Member Forums
- A dollar-for-dollar credit toward full membership sign-up fees for any dues paid for Associate Membership

To become an Associate Member send a check or money order (\$10/month or \$30/quarter or \$120 annually) to Alcor Life Extension Foundation, 7895 E. Acoma Dr., Suite 110, Scottsdale, Arizona 85260, or call Marji Klima at (480) 905-1906 ext. 101 with your credit card information. You can also pay using PayPal (and get the Declaration of Intent to Be Cryopreserved) here: <http://www.alcor.org/BecomeMember/associate.html>



Call toll-free TODAY to start your application:

877-462-5267 ext. 132 • info@alcor.org • www.alcor.org

LifeExtension
Foundation for Longer Life®



You're going to great lengths to avoid death. Why not do something to prolong life.

Join the Life Extension Foundation® now so you can live a longer, healthier life. We'll give you all the support you need, starting with cutting-edge medical information.

You get it three ways. Through our monthly *Life Extension Magazine*® ... filled with cutting-edge research findings and global medical breakthroughs even your doctors may not know about. Through our *Disease Prevention and Treatment* book, filled with breakthrough protocols on over 130 different diseases of aging. And with free phone access to our **knowledgeable Health Advisors** (naturopaths, nurses, nutritionists, even personal trainers). They're available every day of the year to address your health concerns and guide you in structuring a personal regimen of diet, exercise and nutritional supplements designed to extend your healthy life span.

As a Life Extension® member, you'll save far more than money with **preventive blood screening** to head off health problems ... and **advanced nutritional supplements** that are light-years ahead of the commercial marketplace. These are formulas guaranteed for purity, potency and efficacy that you simply won't find anywhere else. All formulated to keep your body functioning youthfully for more years than you ever thought possible.

So while you're busy planning for the future, try spending a moment to prolong it. Call **1-866-820-4967** toll-free or visit www.lef.org/pim to join the Life Extension Foundation now.

LifeExtension
Foundation for Longer Life®

1-866-820-4967 • www.lef.org/pim

Your \$75 annual membership dues will fund innovative anti-aging research that will ultimately benefit you.

