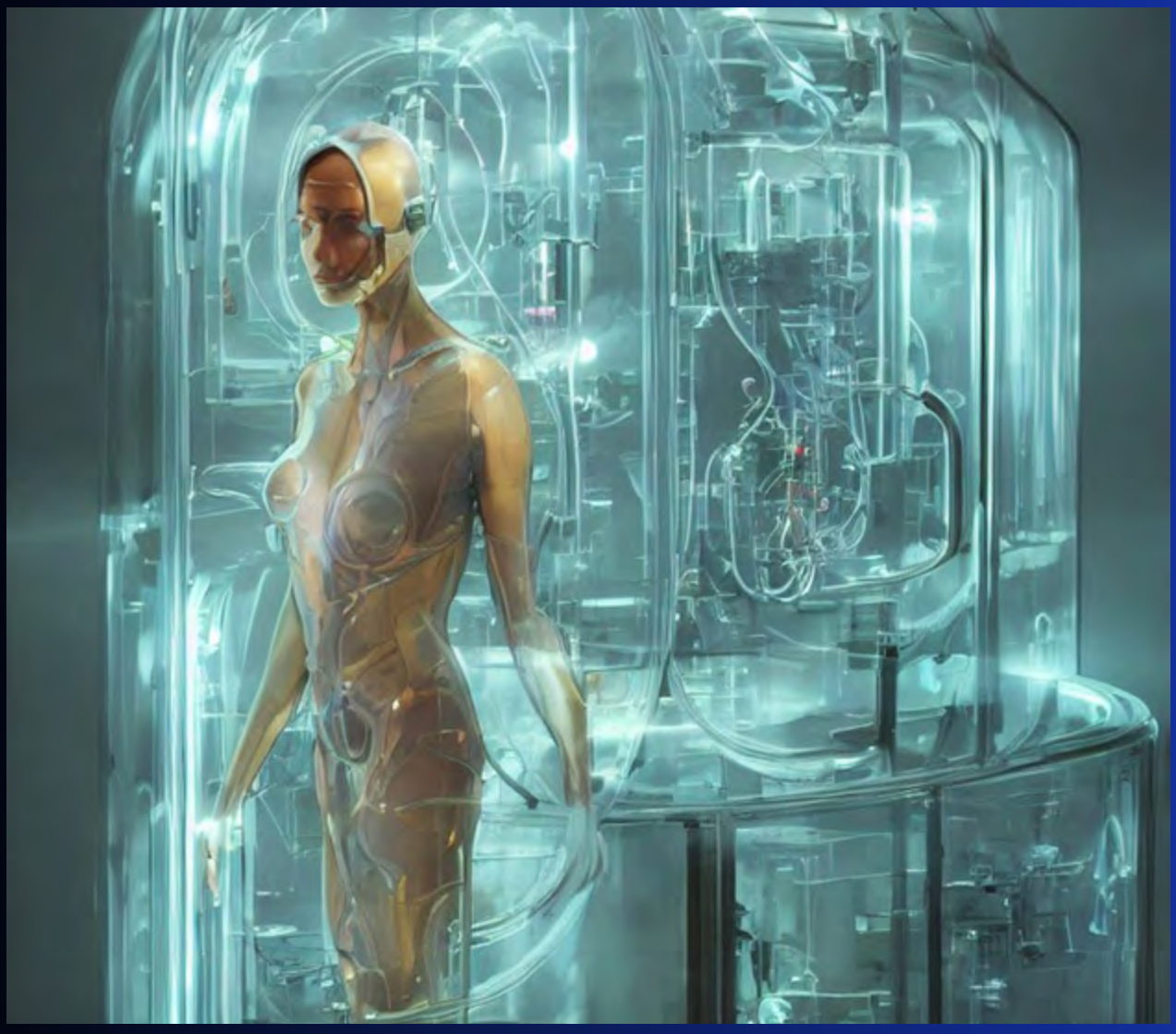
PUBLISHED BY THE CRYONICS INSTITUTE

ISSUE 03 | 2022

CRYONICS INSTITUTE NEWSLETTER

Cryonics insights and information for members and friends of the Cryonics Institute



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CI PRESIDENT'S REPORT

Hello All,

We have another AGM successfully behind us and I want to thank everyone who attended both in-person and online, as well as our speakers and behind-the-scenes team who helped organize and run the event.

For those of you who missed it, a video of the entire presentation is available **here.**

People seemed to enjoy having presentations from both Suspended Animation, Inc. and ICE (International Cryomedicine Experts) who both provide Professional Standby Services for cryonics. That said, we will certainly consider inviting both organizations back for the 2023 AGM.

CI does have a special arrangement in place with SA for our members, and we are exploring the possibility of also negotiating a similar arrangement with ICE.

Of course, we will also continue offering training materials and education to help with local standby arrangements for those who prefer that option. With that in mind, I encourage you to check out our Groups List and see if there is a cryonics group near you that assists with Standby. Several groups have been formed specifically with Standby in mind for their members, so it is worth looking into to see if one of those groups is near you and to contact them for more information.

On the topic of Standby Education, I'm looking forward to seeing what happens with **Transvision Madrid**, coming up on November 10 in Madrid Spain. This will be the first BFR (Biostasis First Response) training to be organized in Spain, after some smaller similar events during previous years in Germany, the Netherlands, Switzerland and the United Kingdom.

The BFR training will be a hands-on experience with theoretical and practical training, using human dummies and the special NL ambulance that will come from Amsterdam to Madrid. The event is being organized by José Cordeiro, PhD who has a long history with cryonics. We will be in contact with Dr Cordeiro to see if any video of the training or speakers will be made available post-summit and share that information here.

Back to the AGM, I'm pleased to report the results of our 2022 Board of Directors Elections. We saw all three of the current incumbents re-elected, and Alan Mole's vacant postion will be filled by new Board Member Jim Broughton. I'm looking forward to working with Jim and the rest of our outstanding Directors moving forward.

The tallies were as follows:

* Jim Broughton : 132
* Kevin Doyle : 102
* Debbie Flemming : 91
* Nicholas Van Der Meulen : 80

Nicolas Lacombe : 36
Vivien Gruss : 13

Congratulations to all the winners, and a special thanks to Nicholas Lacombe and Vivien Gruss for their candidacies. To drive home a point I often make, even if you aren't on the Board, there are still opportunities to assist CI by donating or by volunteering. That said, I want to extend my thanks to Nicholas Lacombe for recently pitching in to help with required updates to the CI Emergency Notification App. Nicholas joins the app team of Michael Harrop, Michael Gill and team lead, Douglas Golner. Thanks to all for pitching in.

An easy way you can help CI is by exploring arrangements to pay your monthly or annual dues either by check or via a direct bank transfer rather than by credit card or PayPal, both of which are very convenient for you and for CI, but also incur transaction fees which amount to a sizable annual cost. We are actively looking for ways to simplify the payment process that doesn't involve these fees, but is still easy to use and convenent for our members and our staff. If you are an ecommerce or banking wizard and have some additonal ideas on what we can do to help mitigate these costs, please contact me at dennis@cryonics.org with any suggestions.

Speaking of memberships, it's also worth noting, in the case of family members, CI offers a special membership for the children of current members. All children under the age of 18 of active and funded members can sign up for free life membership at CI. We also offer discounts for spouses and other close adult family members of active members. We're all excited about the opportunity to live again in the future, so why not encourage our families and friends to join us? Personally, I don't really like the idea of a future without my family so my wife and sons are all members.

CI has recently reformed our scientific advisory board with the mission of reviewing and discussing progress in science and technology as it relates to cryonics. The goal of this board is to stay up to date with trends by reviewing breakthrough news and scientific journals and meeting up via email to recommend changes or staying the course with research and/or protocol changes that affect the cryonics procedure. The board will look for research that has actionable results or benefits the cryonics cause both directly and indirectly. We hope to collaborate and share knowledge with the other major cryonics organizations in the same spirit as conventional medicine and so as to not duplicate efforts with scarce resources. I encourage all professionals with a scientific background to apply to this board and all members in general to share news and events with the advisory board. Two CI members with relevant backgrounds have already agreed to step up and start this board. I welcome Dr Don Kleinsek and Jim Broughton to head the reformed CI scientific advisory board. In addition I have spoken with Dr Adam Higgins who will continue to share his expertise in the field of cryobiology .

In closing, I am happy to see the continued progress and volunteerism that we are seeing in cryonics. The grass roots local standby from Minnesota Cryonics Rapid Response is yet another example of cryonicists from different organizations pulling together to have a measurable and positive impact in their region. This group and others are setting an example for us all. If we want cryonics to be better its simple — we must get involved and put in time or money. You can debate cryonics all day in social media or within the forums or you can take action and do something to make a difference. Remember actions speak louder then words. The Members Readiness Checklist in every magazine and on our website of steps to take as a CI Member is an excellent start.

Best wishes and good luck!

Dennis Kowalski
CI President

CRYONICS INSTITUTE MAGAZINE

The digital newsletter of the Cryonics Institute
24355 Sorrentino Ct.
Clinton Township, MI 48035-3239

Phone: 1 (586) 791-5961
Toll-free: 1 (866) 288-2796 (North America)
FAX: 1 (586) 792-7062
Email: **info@cryonics.org**

ARTICLE SUBMISSIONS

Cryonics Institute or cryonics-related articles are welcome. Submissions: **dg@cryonics.org**

E-SUBSCRIPTIONS

* As a CI member, you are automatically added to our email reminder list. To unsubscribe, please use the "unsubscribe" link at the bottom of your email.

Cover Art

This issue's cover art was created using online AI image creator, Free Image Generator. (https://freeimagegenerator.com/) To submit your own work for consideration, please contact dg@cryonics.org.

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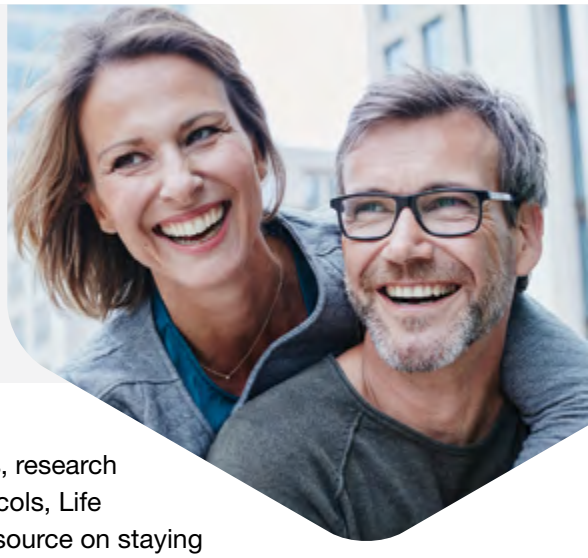

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Or, log on to **LifeExtension.com/CI**

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Membership Benefits

Why join the Cryonics Institute?

The choice is clear: Irreversible physical death, dissolution and decay, or the possibility of a vibrant and joyful renewed life. Don't you want that chance for yourself, your spouse, parents and children?

1) A Second Chance at Life

Membership qualifies you to arrange and fund a vitrification (anti-crystallization) perfusion and cooling upon legal death, followed by long-term storage in liquid nitrogen. Instead of certain death, you and your loved ones could have a chance at rejuvenated, healthy physical revival through cryopreservation.

2) Affordable Cryopreservation

The Cryonics Institute (CI) offers full-body cryopreservation for as little as $28,000.

3) Affordable Membership

Become a Lifetime Member for a one-time payment of only $1,250, with no dues to pay. Or join as a Yearly Member with a $75 inititation fee and dues of just $120 per year, payable by check, credit card or PayPal.

4) Lower Prices for Spouses and Children

The cost of a Lifetime Membership for a spouse of a Lifetime Member is half-price and minor children of a Lifetime Member receive membership free of charge.

5) Quality of Treatment

CI employed a Ph.D level cryobiologist to develop CI-VM-1, CI's vitrification mixture which can help prevent crystalline formation at cryogenic temperatures.

6) Standby Options and Assistance

CI's use of Locally-Trained Funeral Directors means that our members can get knowledgeable, licensed care. Or members can arrange for professional cryonics standby and transport by subcontracting with **Suspended Animation, Inc** or **International Cryomedicine Experts** (I.C.E.) Ci also offers Standby Training Materials and Kits for members who choose to perform Local Standby.

7) Affordable Funding Options

Cryopreservation with CI can be funded through life insurance policies issued in the USA or other countries. Prepayment and other options for funding are also available to CI members.

8) Cutting-Edge Cryonics Information

Members receive a free e-subscription to the Cryonics Institute Newsletter, as well as access to our Facebook page, Twitter feed, YouTube channel and an official members-only forum.

9) Helpful, Professional Support

CI's professional staff is available to answer any questions and address any concerns you may have about CI, your membership or Cryopreservation.

10) Additional Preservation Services

CI offers a sampling kit, shipping and long-term liquid nitrogen storage of tissues and DNA from members, their families or pets for just $98.

11) Support Education and Research

Membership fees help CI to fund important cryonics research and public outreach, education and information programs to advance the science of cryonics.

12) Member Ownership and Control

CI Members are the ultimate authority in the organization and own all CI assets. They elect the Board of Directors, from whom are chosen our officers. CI members also can change the Bylaws of the organization (except for corporate purposes).

CRYONICS INSTITUTE
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To get started, contact us at:

(586) 791-5961 • email: info@cryonics.org

Visit us online at www.cryonics.org

CI NEWS

What's happening at the Cryonics Institute

New LN2 Bulk Tank Installed at CI

The Lee Contracting company recently completed the install of our new 6,000 gallon tank at the main facility. The new tank is 30 feet tall, double the size of the old one, and will only require filling once per month.

The existing 3,000 gallon tank was moved to the new facility and given a thorough cleaning. Some light weathering and rust stains near the top and on the footing were removed, and now it looks brand new. Great job by the Facilities Team!.

CI NEWS

What's happening at the Cryonics Institute

New Cryonics Survey

A new cryonics survey is available online that is open to the entire cryonics community. The survery is available here:

CRYONICS SURVEY
(https://bit.ly/cryosurvey2022)

Here's what the web survey site has to say:

Cryonics Survey 2022

~Quick notes~

This survey is intended for Cryonicists, the Cryonics-adjacent, and those who find the idea worth considering but haven't yet signed up.

The goal of this survey is to learn more about the background, mindset, and motivations of this rare subset of the population. Where do these folks get their information? What do they think about important issues in the field? What philosophical positions undergird their mental frameworks?

The information you provide in this survey will help the Cryonics industry to provide higher quality services while making better use of limited time and resources available. Thank you for helping to make this possible.

A few quick notes:

All information provided is anonymous. We don't ask for names, membership IDs (if you're signed up), or the like. However, you're free to skip questions if you feel uncomfortable answering them.

We have $100 worth of amazon gift cards to give to three lucky folks who complete the survey and answer one last optional question. Check the final page for details on how to win.

Anonymous and aggregated results will be shared with the community. We'll publish an analysis of the results and post a link in public Cryonics forums like The Cryosphere, Cryonics subreddit, etc, when it is ready.

CI NEWS

What's happening at the Cryonics Institute

2022 AGM Photos

Enjoy this selction of photos from the 2022 AGM Facility Tour and meeting. Tours were conducted at both the main and secondary facilities prior to the meeting. More AGM photos are available on **Google Drive**.

For a video of the entire presentation, please visit our web site or watch it on **YouTube**.


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CI NEWS

What's happening at the Cryonics Institute

2022 Board of Directors Election

2022 | WINNERS

Jim Broughton
132 Votes
New Director

Kevin Doyle
102 Votes
Incumbent

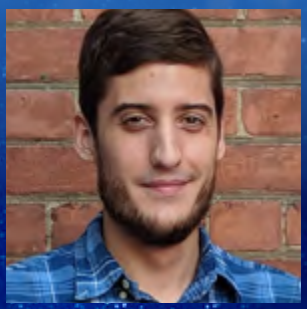
Debbie Fleming
91 Votes
Incumbent

Nicholas Van Der Mulen
80 Votes
Incumbent

Congratulations to all the winners!

RUNNERS UP

Thanks to both for running.



Nicolas Lacombe
:36 Votes

Vivien Gruss
13 Votes

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Member Readiness Checklist

You've signed up for cryonics - what are the next steps?

Welcome Aboard! You have taken the first critical step in preparing for the future and possibly ensuring your own survival. Now what should you do? People often ask "What can I do to make sure I have an optimal suspension?" Here's a checklist of important steps to consider.

- ☐ Become a fully funded member through life insurance or easy pre-payments

  Some members use term life and invest or pay off the difference at regular intervals. Some use whole life or just prepay the costs outright. You have to decide what is best for you, but it is best to act sooner rather then later as insurance prices tend to rise as you get older and some people become uninsurable because of unforeseen health issues. You may even consider making CI the owner of your life insurance policy.

- ☐ Keep CI informed on a regular basis about your health status or address changes. Make sure your CI paperwork and funding are always up to date. CI cannot help you if we do not know you need help.

- ☐ Keep your family and friends up to date on your wishes to be cryopreserved. Being reclusive about cryonics can be costly and cause catastrophic results.

- ☐ Keep your doctor, lawyer, and funeral director up to date on your wishes to be cryopreserved. The right approach to the right professionals can be an asset.

- ☐ Prepare and execute a Living Will and Power of Attorney for Health Care that reflects your cryonics-related wishes. Make sure that CI is updated at regular intervals as well.

- ☐ Review the CI Standby Manual and other materials designed to help you with you Standby Planning. Also, consider joining or forming a local standby group to support your cryonics wishes. This may be one of the most important decisions you can make after you are fully funded. As they say-"Failing to plan is planning to fail".

- ☐ Always wear your cryonics bracelet or necklace identifying your wishes should you become incapacitated. Keep a wallet card as well. If you aren't around people who support your wishes and you can't speak for yourself a medical bracelet can help save you.

- ☐ Get involved! If you can, donate time and money. Cryonics is not a turnkey operation. Pay attention and look for further tips and advice to make both your personal arrangements and cryonics as a whole a success. The stronger our organization is, the stronger your chances of success.

- ☐ Keep your records, contact information and contracts up to date. It is recommended you review your relevant information annually at a minimum. One way is to schedule time to review all your materials at the same time you submit your required Annual Proof of Funding to CI. Also, Be especially aware of easy to forget things like a new email, phone number or address. Remember, you can also contact us at any time to ask if you have any outstanding paperwork or other info that needs to be updated.

  The online CI Members' Information Form is a great resource for updating your current information on file.

CI NEWS

What's happening at the Cryonics Institute

Scale Model Cryostats Now Available for Sale

CI Board Member Nicholas Van Der Mulen is offering these highly-detailed scale model Cryonics Institute cryostats for sale. Each custom-made model is approximately 6 1/4" tall and about 9" wide ,including the catwalk assembly.

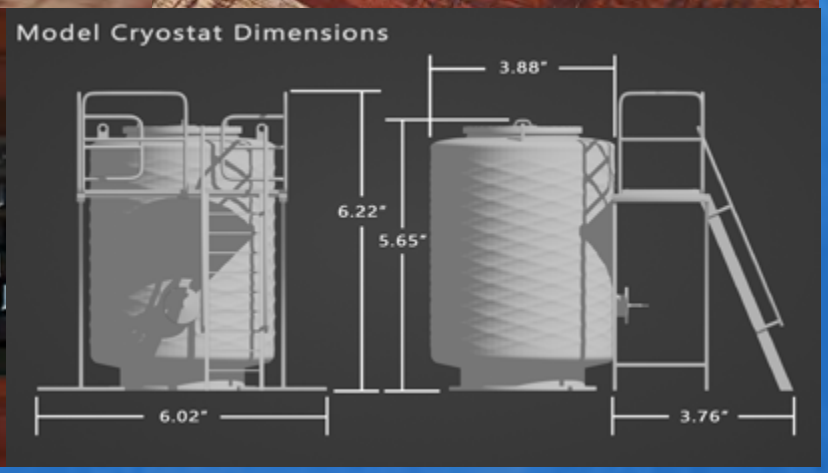
Nick has graciously offered to make his outstanding Cryostat models available for sale by individual commission to fellow cryonics enthusiasts. Each model is an individual hand-crafted piece, which includes 3D printing, assembly and painting. Nick is doing these models at just a little over his costs and also plans to make a donation to CI from every model purchased.

Please note, these models are not being produced or sold by the Cryonics Institute. Any transactions are solely between the buyer and Nicholas Van Der Muelen as individual commissions. Any additional terms and arrangements are also strictly between the buyer (yourself) and the seller (NIcholas Van Der Muelen.)

The estimated cost of each model is expecetd to be about $75US, plus shipping and handling, but the price has not been fixed at this time. To request a quote for having a piece commissioned for yourself or as a truly one-of-a-kind Christmas Gift for your favorite cryonicist, please contact Nick at nickvdm@att.net.

CI NEWS

What's happening at the Cryonics Institute



CI NEWS

What's happening at the Cryonics Institute

Pet Cryosuspension Services Available

Did you know CI Members can take advantage of our cryonic suspension services for their pets? Instead of burial or cremation, you can give a loyal and beloved pet the same second chance at life that we have through cryopreservation.

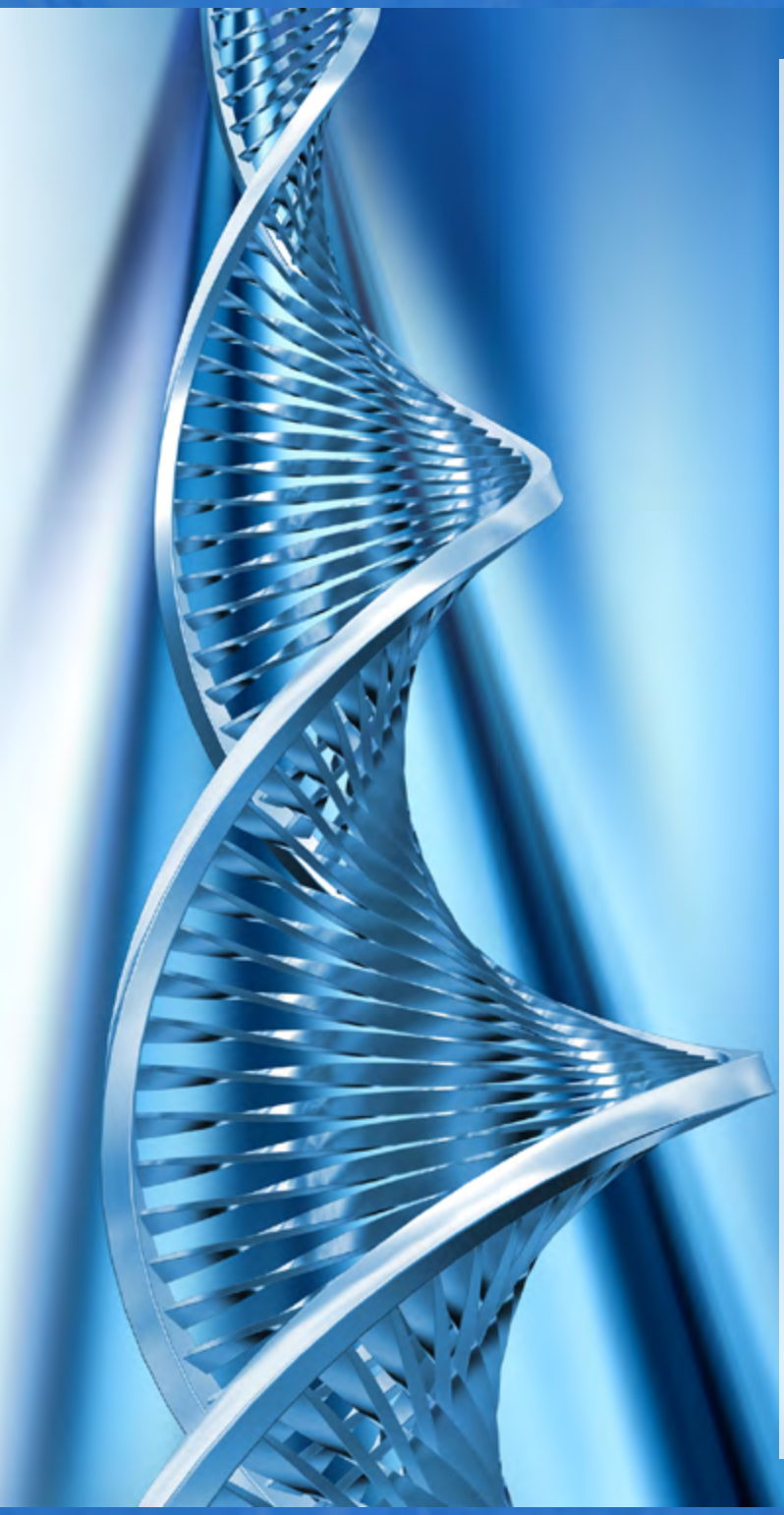
Many members who have preserved their pets say it's a comforting thought that their longtime animal companions now have the same chance to live again in a better future. Ci currently has nearly 200 pets in cryosuspension.

Cryopreservation of pets is only available to Lifetime and Yearly Members of the Cryonics Institute. Excluding the cost of Membership, the typical cost of cryopreserving a cat or dog is $5,800 up to 15 pounds in weight plus $150 per pound for every pound above 15 for dogs. This does not include shipping and veterinarian expenses. CI will also preserve other types of pets and pricing is similarly by the size and weight scale for dogs. Please contact us to inquire about specific pricing and procedures for pet patients, or visit https://www.cryonics.org/resources/pet-cryopreservation for more complete details.

Image by hoàng hon nguyen from Pixabay

CI NEWS

What's happening at the Cryonics Institute



DNA and Tissue Sample Preservation Services

Lifetime and Annual Members of the Cryonics Institute can have DNA / Tissue Samples cryopreserved by CI. Annual Members must have fully paid for no less than one year, i.e. have paid $120 yearly dues (plus the initial $75 initiation fee if it is their first year) for a full year's Membership.

CI provides a DNA sampling kit for hair, skin, and/or inner cheek samples from living persons or pets. Tissue samples may be extracted from a deceased person or pet by a funeral director or veterinarian, respectively. A CI Member may store DNA/tissue for $98 for four samples that will each fit into a 1.8ml sample vial. Some members choose to store larger samples, which cost more and that cost is calculated based on the sze of the sample. The cost includes a DNA sampling kit which consists of four 1.8-milliliter nalgene vials, swabs, instructions, tissue storage contracts and labels that can be placed on the vials, along with a mailing envelope. Each nalgene vial can be individually labeled for content. Each full kit is labeled, identified by a tissue storage contract and stored in liquid nitrogen at the Cryonics Institute.

Tissue samples need not be sent to CI in the DNA sampling kit. Any small vial or container can be used, and CI will transfer samples to nalgene vials for storage in liquid nitrogen.

For more information on DNA and Tissue Storage Cryopreservation, please contact us at info@cryonics.org or visit cryonics.org:

CI NEWS

What's happening at the Cryonics Institute

Visiting Hours For Family Members of CI Patients

Monday:	2:00pm - 4:00pm
Tuesday	2:00om - 4:00pm
Wednesday	2:00pm - 4:00pm
Thursday	2:00pm - 4:00pm

We ask that visitors kindly give us at least **one month advance notice** to ensure there are no scheduling conflicts. We cannot guarantee that the facility will be accessible to visitors who have not scheduled their visit in advance.

**** These visiting hours ar subject to change without notice due to patient or pet emergencies. ****

These requiirements have been established for multiple reasons, but most importantly for protecting our patients, members and facility.

Questions regarding visitation can be directed to Andy Zawacki, Facility Manager at info@cryonics.org or 1-586-791-5961.

Thank you!

Worldwide Cryonics Groups

AUSTRALIA: The Cryonics Association of Australasia offers support and information for Australia & nearby countries. caalist@prix.pricom.com.au. Their Public Relations Officer is Philip Rhoades. **phil@pricom.com.au** GPO Box 3411, Sydney, NSW 2001 Australia. Phone: +6128001 6204 (office) or +61 2 99226979 (home.)

BELGIUM: Cryonics Belgium is an organisation that exists to inform interested parties and, if desired, can assist with handling the paperwork for a cryonic suspension. The website can be found at **www.cryonicsbelgium.com**. To get in touch, please send an email to **info@cryonicsbelgium.com**.

BHUTAN: Can help Cryonics Institute Members who need help for the transport & hospital explanation about the cryonics procedure to the Dr and authorities in Thimphou & Paro. Contacts : Jamyang Palden & Tenzin Rabgay / Emails : **palde002@umn.edu** or **jamgarnett@hotmail.co** Phones : Jamyang / 975-2-32-66-50 & Tenzin / 975-2-77-21-01-87

CANADA: This is a very active group that participated in Toronto's first cryopreservation. President, Christine Gaspar; Vice President, Gary Tripp. Visit them at: **http://www.cryocdn.org/**. There is a subgroup called the Toronto Local Group. Meeting dates and other conversations are held via the Yahoo group. This is a closed group. To join write: **csc5@cryocdn.org**

BRITISH COLUMBIA: The Lifespan Society advocates for radical life extension. They also organize conferences and educational outreach events on life extension issues. Lifespan welcomes all Canadians as members, although voting in the society is open to BC residents. Contact Carrie Radomski, President at **carrie@lifespanbc.ca**. Web site **www.lifespansociety.com**

QUEBEC: Contact: Stephan Beauregard, C.I. Director & Official Administrator of the Cryonics Institute Facebook Page. Information about Cryonics & perfusion services in Montreal for all cryonicicts. Services available in French & English: **stephan@cryonics.org**

CHILE: Community oriented to provide reliable information on human cryopreservation, as far as technical scientific as well as other practical aspects. Dissemination, awareness and education on issues related to the extension of life in general and cryonics in particular. Contact José Luis Galdames via **galdamesh.jl@gmail.com.**

FINLAND: The Finnish Cryonics Society, (KRYOFIN) was established in 2008 and is an organization collaborating with all nearby groups and organizations. Contact them at: **kryoniikka.fi** Their President is Ville Salmensuu **ville@salmensuu.fi**

FRANCE: SOCIETE CRYONICS DE FRANCE is a non profit French organization working closely with European cryonics groups. For more information: J.Roland Missionnier: phone: 33 (0) 6 64 90 98 41 or email: **cryonicsnews.inpi@gmail.com** • **Facebook group**

Francecryonics-Webnode Vivien Gruss, member of Cryonics Institute, has opened a web site for the information of persons interested in cryonic suspension.

GERMANY: DGAB There are a number of Cryonicists in Germany. Their Organization is called "Deutsche Gesellschaft für Angewandte Biostase e.V.", or short "DGAB". More information on their homepage at **www.biostase.de**. If there are further questions, contact their Board at **vorstand@biostase.de**

GERMANY: CRYONICS-GERMANY is an active group providing cryonics support, including a special 8-member

Standby Response Team. Members from Germany or Internationally are welcome to join. at **http://cryonics-germany.org**. Direct inquiries to **contact@cryonics-germany.org**.

INDIA: Can help Cryonics Institute Members who need help for the transport & hospital explication about the cryonics procedure to the Dr and authority in Bangalore & Vellore Area. Contacts : Br Sankeerth & Bioster Vignesh / Email : **vicky23101994@gmail.com** Phones : Bioster / 918148049058 & Br Sankeerth / 917795115939

ITALY: The Italian Cryonics Group (inside the Life Extension Research Group (LIFEXT Research Group)) **www.lifext.org** and relative forum: **forum.lifext.org**. Contact Giovanni Ranzo at: **giovanni1410@gmail.com**

Kriorus Italy: Representative Filippo Polistena, email: filippopolistena45@gmail.com. phone: +39 334 298 9378

JAPAN: Hikaru Midorikawa is President Japan Cryonics Association. Formed in 1998, our goals are to disseminate cryonics information in Japan, to provide cryonics services in Japan, and eventually, to allow cryonics to take root in the Japanese society. Contact **mid_hikaru@yahoo.co.jp** or **http://www.cryonics.jp/**

NEPAL: Can help Cryonics Institute Members who need help for the transport & hospital explanation about the cryonics procedure to the Dr and authorities in Kathmandu. Contact : Suresh K. Shrestha / Email : **toursuresh@gmail.com** Phone : 977-985-1071364 / PO Box 14480 Kathmandu.

THE NETHERLANDS: Dutch Cryonics Organization is the local support group since 2002 and able to provide advice, standby, perfusion and shipment 24/7, in case of need. We are an active group utilizing the latest equipment. New members from The Netherlands welcome.

E-mail: **info@cryonisme.nl**
website: **http://www.cryonisme.nl**

NORWAY : Can help Cryonics Institute Members who need help for the transport & hospital explication about the cryonics procedure to the Dr, funeral home and authority at Sandvika. Contacts : Gunnar Hammersmark Sandvika Begegravelsesbyraa / Phones : 011-47-2279-7736

RUSSIA: KrioRus is a Russian cryonics organization operating in Russia, CIS and Eastern Europe that exists to help arrange cryopreservation and longterm suspension locally, or with CI or Alcor. Please contact **kriorus@gmail.com** for additional information or visit **http://www.kriorus.ru**. Phone: +7 962 947-50-79

SWEDEN: **www.kryonik.se** or Facebook: Svenska Kryonikföreningen. Initially, the society will focus on providing information and assistance to those who wish to sign up for cryonics. Eventually, we also hope to provide practical assistance in cases, possibly in collaboration with other European groups.

SWITZERLAND: **www.cryosuisse.ch**

CRYOSUISSE The Swiss Society for Cryonics is an active group with over 30 members. To join, **email info@cryosuisse.ch**

UNITED STATES:

Minnesota: Minnesota Cryonics Rapid Response (MCRR) is a nonprofit standby, stabilization and transport group based in Minneapolis, Minnesota. We have a strong, longstanding working relationship with local funeral directors, and have successfully participated in significantly more-timely suspension efforts in Minnesota in cooperation with both Alcor and the Cryonics Institute. Contact: President, Chuck Bartl, **chuckbartl@yahoo.com**.

UNITED KINGDOM: Cryonics UK is a nonprofit UK based standby group. **www.cryonics-uk.org** Cryonics UK can be contacted via the following people: Tim Gibson: phone: 07905 371495, email: **tim.gibson@cryonics-uk.org**. Victoria Stevens: phone: 01287 669201, email: **vicstevens@hotmail.co.uk**. Graham Hipkiss: phone: 0115 8492179 / 07752 251 564, email: **ghipkiss@hotmail.com**. Alan Sinclair: phone: 01273 587 660 / 07719 820715, email: **cryoservices@yahoo.co.uk**

Can help Cryonics Institute Members who need help, funeral home, transport at London. Contact : F.A. Albin & Sons / Arthur Stanley House Phone : 020-7237-3637

INTERNATIONAL: The Cryonics Society is a global cryonics advocacy organization. **www.CryonicsSociety.org**. They publish an e-newsletter *FutureNews*. Phone: 1-585-643-1167.

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Please send any corrections or changes to the address below. If you know of, or are considering starting a support, standby or other cryonics-related group in your area, please send details to

dg@cryonics.org.

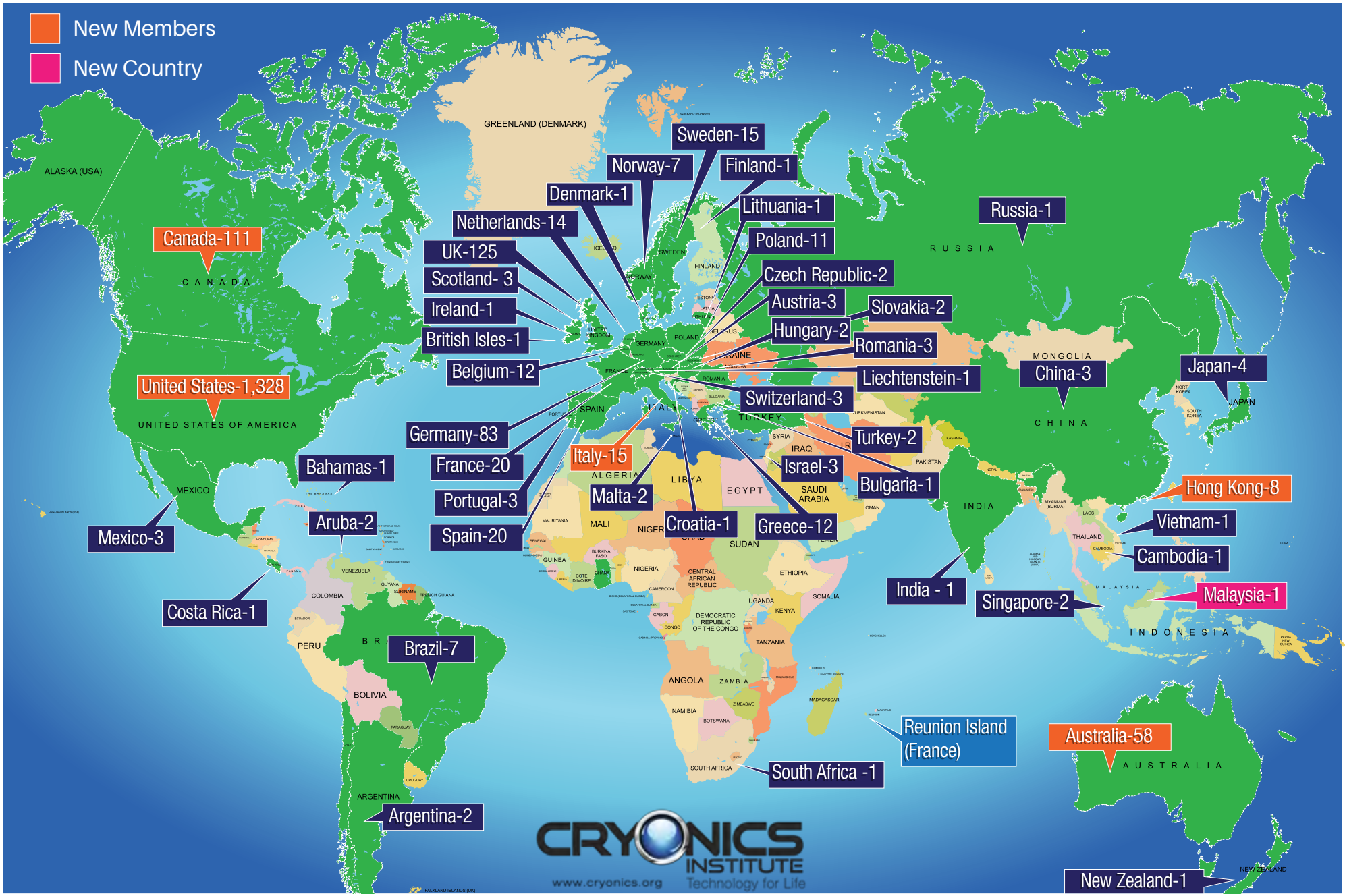
Please note, this list is provided as an information resource only. Inclusion on the list does not constitute an endorsement by the Cryonics Institute or our affiliated organizations. We urge our readers to use this list as a starting point to research groups that may meet their own individual needs. We further note that readers should always use their own informed judgment and a reasonable amount of caution in dealing with any organization and/or individual listed.

CI MEMBERSHIP

NOVEMBER 2022

Members	1,906	Pets	229
Patients	233	DNA/Tissue	340
		SA	316

TOTAL **2,139**



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Life suspended:
The past and future of cryopreservation

ME doctoral student Shen Ren works with professor Dayong Gao on advancing technology for preserving human and biological samples. Photo by Olivia Hagan / University of Washington

The idea of freezing and many years later thawing out the human body has been a favorite of storytellers for decades, including for popular characters like Captain America and Austin Powers. But the science of cryopreservation may be even more interesting.

Dayong Gao

Dayong Gao is the Origincell Endowed Professor of Mechanical Engineering and an internationally recognized scientist in cryo-biomedical engineering. Recently, the Society for Cryobiology created the Dayong Gao Young Investigator Award to recognize the field's best early career researchers.

ME's Andy Freeberg interviewed Gao on his research and attempted to separate the science from the fiction.

How did scientists get started freezing biological samples?

Scientists proposed the idea of keeping cells dormant by freezing them a long time ago. This was based on the scientific principle that life is a biochemical process with a temperature-dependent rate. The rate slows as you cool down until eventually all of life's processes stop. However,

there's a big contradiction between that concept and the experimental findings. At very low temperatures bioactivity does indeed stop, but early scientists found cells and tissues were killed by the freezing and thawing process itself.

The first successful preservation of mammalian cells didn't occur until 1949, when Christopher Polge discovered that glycerol can prevent freezing injury. Polge was studying rooster sperm and using glycerol to add viscosity to some samples to study sperm motion. Separately he was using liquid nitrogen to freeze other samples and look at their structure. But he accidentally confused a sample with glycerol in it and put it in the liquid nitrogen. After the sample warmed back up, he was surprised to see sperm that were still moving – at that point no one had reported that sperm could be frozen without killing them.

When he figured out what he had done, he repeated the experiment and showed that glycerol is what we now call a cryoprotective agent, or CPA. That really kicked this all off.

How did you get interested in cryopreservation?

That brings us to another major milestone in cryopreservation by Peter Mazur, who in the late 60s and early 70s reported on the actual mechanism for freezing injury due to ice crystallization. Mazur showed that each kind of cell has its own optimal freezing and thawing rate. Freeze it too fast and you get intracellular ice formation, which kills the cell. Freeze it too slow and you get severe dehydration damage.

I was a postdoctoral fellow under Mazur and John Critser, but my undergraduate training was in physics and mechanical engineering. My own interest arose from the challenges of biology. Whenever I asked a question in physics class the teachers could always give me the answer. But when I went to an introductory biology class, I couldn't get a clear answer to even "simple" questions. So that's why I got into biomedical engineering; it's applying physics, mechanics and mathematics into biology and health.

What have been the most important recent advances in cryopreservation and what effect have they had?

We now know that the optimal freezing and thawing rates are specific to each cell type. However, when you start to consider whole organs, embryos or tissues, this becomes a problem. These samples have different cell types. How do you make sure that the surface cooling is the same as the interior? And it turns out that even if all the cells survive, the ways the cells communicate may not.

So the new hope for cryopreservation is something called vitrification, or "glassification." It's not actually freezing at all, because there's no ice crystal formation. Instead the water molecules simply become solid in their disordered, amorphous state.

The key to vitrification is that we eliminate ice crystal induced damage. As a result, vitrification is the most promising cryopreservation method for larger tissues, organs, and reproductive samples like embryos and eggs.

However, despite some successes, vitrification still has two big challenges. To make it work, you need either a cooling rate of over a million degrees per minute, which is basically impossible for a large sample, or you need a very high concentration of CPAs to make the sample viscous and prevent ice crystal formation. But that much CPA becomes toxic to the cells. These are the things we're working on now.

What kinds of developments are happening in your lab?

We've been investigating an array of areas in cryopreservation, including some of the fundamental problems I've mentioned as well as a number of new potential applications. One of our most exciting recent advances involves re-warming frozen or vitrified cells and organs.

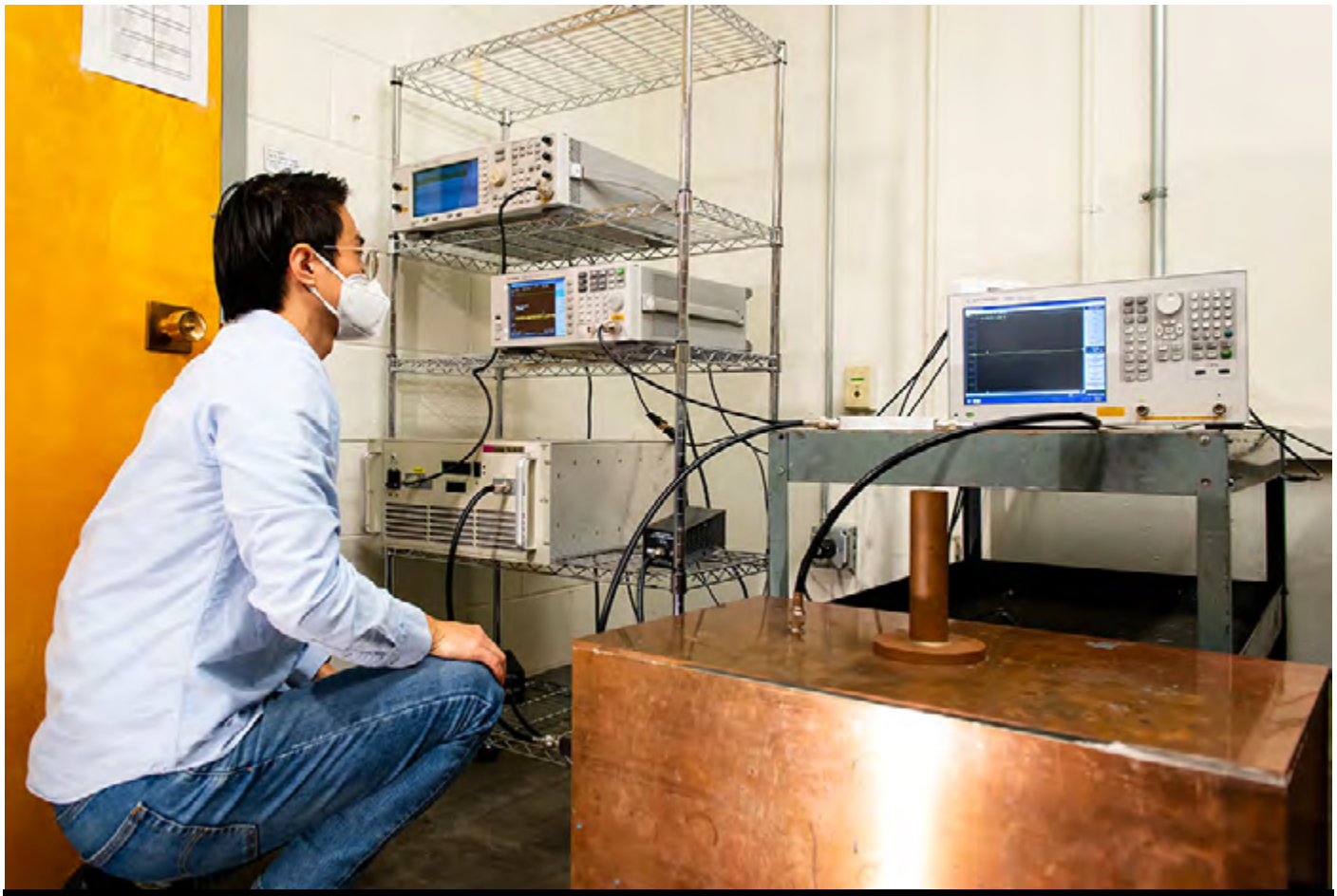
The conventional rewarming method, using a hot water bath, doesn't work for larger samples. Its heating is slow and uneven and irreparably damages the samples. We have been developing a new kind of single-mode electromagnetic resonance technology.

When you use your microwave at home, you're using electromagnetic warming. But a microwave oven generates hundreds of modes, or frequencies. Our single mode system can add energy rapidly and is much easier to control.

What's next? Will the science fiction idea of freezing someone and thawing them out years later ever come true?

Freezing human bodies in the hope of future revival is something people always ask me about. There are companies that do this, they mimic what we're doing in cryobiology and attempt to preserve people who have recently passed away. Hundreds of bodies are currently cryopreserved in liquid nitrogen tanks even though there's no rewarming method now that would ensure their survival after thawing.

If you had asked me the question 20 years ago, I would've told you it's pure science fiction. But now I have to tell you, in the future I think anything is possible. Cryopreservation and biobanking have already become indispensable in modern



A new single-mode electromagnetic resonance system developed by Gao's team uses electromagnetic energy to rewarm cryopreserved samples. Photo by Olivia Hagan / University of Washington

medicine and across industries like healthcare, agriculture, environmental conservation and biotech. In our labs we're developing new technology to meet urgent needs in cellular and gene therapy, regenerative medicine, tissue engineering, stem cell and organ transplantation, new vaccine and drug development, disease screening, and fertility treatments. Plus, this is the biological information age – the preservation of genes, seed banks, the gametes of endangered species, and so on. When you think about all of these things taken together it's very exciting.

Find out more

Gao's team's paper "Investigation of Electromagnetic Resonance Rewarming Enhanced by Magnetic Nanoparticles for Cryopreservation" was published last year in the journal Langmuir.

To learn more about the history of cryopreservation, see a 2009 article penned by Gao and two colleagues titled "Cryopreservation: An emerging paradigm change."

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Artificial intelligence used to uncover the cellular origins of Alzheimer's disease and other cognitive disorders

September 20, 2022 | Source: The Mount Sinai Hospital / Mount Sinai School of Medicine

Deep learning models represent 'an entirely new paradigm for studying dementia.

Image by Gerd Altmann from Pixabay

Mount Sinai researchers have used novel artificial intelligence methods to examine structural and cellular features of human brain tissues to help determine the causes of Alzheimer's disease and other related disorders. The research team found that studying the causes of cognitive impairment by using an unbiased AI-based method -- as opposed to traditional markers such as amyloid plaques -- revealed unexpected microscopic abnormalities that can predict the presence of cognitive impairment. These findings were published in the journal Acta Neuropathologica Communications on September 20.

"AI represents an entirely new paradigm for studying dementia and will have a transformative effect on research into complex brain diseases, especially Alzheimer's disease," said co-corresponding author John Crary, MD, PhD, Professor of Pathology, Molecular and Cell-Based Medicine, Neuroscience, and Artificial Intelligence and Human Health, at the Icahn School of Medicine at Mount Sinai. "The deep learning approach was applied to the prediction of cognitive impairment, a challenging problem for which no current human-performed histopathologic diagnostic tool exists."

The Mount Sinai team identified and analyzed the underlying architecture and cellular features of two regions in the brain, the medial temporal lobe and frontal cortex. In an effort to improve the standard of postmortem brain assessment to identify signs of diseases, the researchers used a

weakly supervised deep learning algorithm to examine slide images of human brain autopsy tissues from a group of more than 700 elderly donors to predict the presence or absence of cognitive impairment. The weakly supervised deep learning approach is able to handle noisy, limited, or imprecise sources to provide signals for labeling large amounts of training data in a supervised learning setting. This deep learning model was used to pinpoint a reduction in Luxol fast blue staining, which is used to quantify the amount of myelin, the protective layer around brain nerves. The machine learning models identified a signal for cognitive impairment that was associated with decreasing amounts of myelin staining; scattered in a non-uniform pattern across the tissue; and focused in the white matter, which affects learning and brain functions. The two sets of models trained and used by the researchers were able to predict the presence of cognitive impairment with an accuracy that was better than random guessing.

In their analysis, the researchers believe the diminished staining intensity in particular areas of the brain identified by AI may serve as a scalable platform to evaluate the presence of brain impairment in other associated diseases. The methodology lays the groundwork for future studies, which could include deploying larger scale artificial intelligence models as well as further dissection of the algorithms to increase their predictive accuracy and reliability. The team said, ultimately, the goal of this neuropathologic research program is to develop better tools for diagnosis and treatment of people suffering from Alzheimer's disease and related disorders.

"Leveraging AI allows us to look at exponentially more disease relevant features, a powerful approach when applied to a complex system like the human brain," said co-corresponding author Kurt W. Farrell, PhD, Assistant Professor of Pathology, Molecular and Cell-Based Medicine, Neuroscience, and Artificial Intelligence and Human Health, at Icahn Mount Sinai. "It is critical to perform further interpretability research in the areas of neuropathology and artificial intelligence, so that advances in deep learning can be translated to improve diagnostic and treatment approaches for Alzheimer's disease and related disorders in a safe and effective manner."

Lead author Andrew McKenzie, MD, PhD, Co-Chief Resident for Research in the Department of Psychiatry at Icahn Mount Sinai, added: "Interpretation analysis was able to identify some, but not all, of the signals that the artificial intelligence models used to make predictions about cognitive impairment. As a result, additional challenges remain for deploying and interpreting these powerful deep learning models in the neuropathology domain."

Researchers from the University of Texas Health Science Center in San Antonio, Texas, Newcastle University in Tyne, United Kingdom, Boston University School of Medicine in Boston, and UT Southwestern Medical Center in Dallas also contributed to this research. The study was supported by funding from the National Institute of Neurological Disorders and Stroke, the National Institute on Aging, and the Tau Consortium by the Rainwater Charitable Foundation.

Story Source:

Materials provided by The Mount Sinai Hospital / Mount Sinai School of Medicine. Note: Content may be edited for style and length.

Journal Reference:

Andrew T. McKenzie, Gabriel A. Marx, Daniel Koenigsberg, Mary Sawyer, Megan A. Iida, Jamie M. Walker, Timothy E. Richardson, Gabriele Campanella, Johannes Attems, Ann C. McKee, Thor D. Stein, Thomas J. Fuchs, Charles L. White, Jean-Paul Vonsattel, Andy F. Teich, Marla Gearing, Jonathan Glass, Juan C. Troncoso, Matthew P. Frosch, Bradley T. Hyman, Dennis W. Dickson, Melissa E. Murray, Johannes Attems, Margaret E. Flanagan, Qinwen Mao, M.-Marsel Mesulam, Sandra Weintraub, Randy L. Woltjer, Thao Pham, Julia Kofler, Julie A. Schneider, Lei Yu, Dushyant P. Purohit, Vahram Haroutunian, Patrick R. Hof, Sam Gandy, Mary Sano, Thomas G. Beach, Wayne Poon, Claudia Kawas, María Corrada, Robert A. Rissman, Jeff Metcalf, Sara Shuldberg, Bahar Salehi, Peter T. Nelson, John Q. Trojanowski, Edward B. Lee, David A. Wolk, Corey T. McMillan, C. Dirk Keene, Caitlin S. Latimer, Thomas J. Montine, Gabor G. Kovacs, Mirjam I. Lutz, Peter Fischer, Richard J. Perrin, Nigel J. Cairns, Erin E. Franklin, Ping Shang, Jeff Harris, Chan Foong, Kurt Farrell, John F. Crary. Interpretable deep learning of myelin histopathology in age-related cognitive impairment. Acta Neuropathologica Communications, 2022; 10 (1) DOI: 10.1186/s40478-022-01425-5

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The James Webb Space Telescope found signs of carbon dioxide in the atmosphere of the gas giant exoplanet WASP-39 b (illustrated, with its star). NASA, ESA, CSA AND J. OLMSTED/STSCI

The James Webb telescope spotted CO^2 in an exoplanet's atmosphere

It's the first definitive detection of the greenhouse gas at a planet outside the solar system

By Lisa Grossman - AUGUST 26, 2022

The James Webb Space Telescope has gotten the first sniff of carbon dioxide in the atmosphere of a planet in another solar system.

"It's incontrovertible. It's there. It's definitely there," says planetary scientist and study coauthor Peter Gao of the Carnegie Institution for Science in Washington, D.C. "There have been hints of carbon dioxide in previous observations, but never confirmed to such an extent."

The finding, submitted to arXiv.org on August 24, marks the first detailed scientific result published from the new telescope. It also points the way to finding the same greenhouse gas in the atmospheres of smaller, rockier planets that are more like Earth.

The planet, dubbed WASP-39b, is huge and puffy. It's a bit wider than Jupiter and about as massive as Saturn. And it orbits its star every four Earth days, making it scorching hot. Those features make it a terrible place to search for evidence of extraterrestrial life (SN: 4/19/16). But that combination of puffy atmosphere and frequent passes in front of its star makes it easy to observe, a perfect planet to put the new telescope through its paces.

James Webb, or JWST, launched in December 2021 and re-

leased its first images in July 2022 (SN: 7/11/22). For about eight hours in July, the telescope observed starlight that filtered through the planet's thick atmosphere as the planet crossed between its star and JWST. As it did, molecules of carbon dioxide in the atmosphere absorbed specific wavelengths of that starlight.

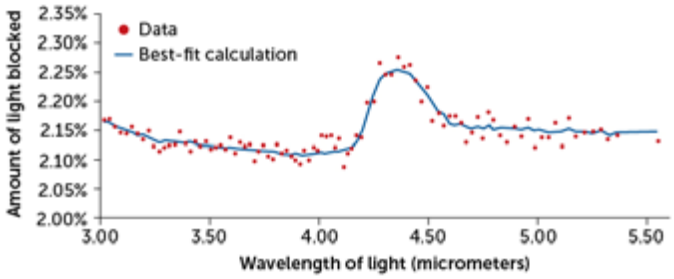
Previous observations of WASP-39b with NASA's now-defunct Spitzer Space Telescope had detected just a whiff of absorption at that same wavelength. But it wasn't enough to convince astronomers that carbon dioxide was really there.

"I would not have bet more than a beer, at most a six pack, on that weird tentative hint of carbon dioxide from Spitzer," says astronomer Nicolas Cowan of McGill University in Montreal, who was not involved with the new study. The JWST detection, on the other hand, "is rock solid," he says. "I wouldn't bet my firstborn because I love him too much. But I would bet a nice vacation."

The JWST data also showed an extra bit of absorption at wavelengths close to those absorbed by carbon dioxide. "It's a mystery molecule," says astronomer Natalie Batalha of the University of California, Santa Cruz, who led the team behind the observation. "We have several suspects that we are interrogating."

Carbon dioxide bump

The spectrum of light that filtered through the atmosphere of exoplanet WASP-39 b shows strong evidence for containing carbon dioxide. The large bump in the middle of the spectrum shows that the planet's atmosphere absorbed light with wavelengths around 4.3 micrometers — a clear



sign of CO2. A smaller bump (shown as three dots above the best-fit line) to the left of the CO2, around 4 micrometers, could represent a mystery molecule.

NASA, ESA, CSA, LEAH HUSTAK AND JOSEPH OLMSTED/STSCI

The amount of carbon dioxide in an exoplanet's atmosphere can reveal details about how the planet formed (SN: 5/11/18). If the planet was bombarded with asteroids, that could have brought in more carbon and enriched the atmosphere with carbon dioxide. If radiation from the star stripped away some of the planet atmosphere's lighter elements, that could make it appear richer in carbon dioxide too.

Despite needing a telescope as powerful as JWST to detect it, carbon dioxide might be in atmospheres all over the galaxy, hiding in plain sight. "Carbon dioxide is one of the few molecules that is present in the atmospheres of all solar system planets that have atmospheres," Batalha says. "It's your front-line molecule."

Eventually, astronomers hope to use JWST to find carbon dioxide and other molecules in the atmospheres of small rocky planets, like the ones orbiting the star TRAPPIST-1 (SN: 12/13/17). Some of those planets, at just the right distances from their star to sustain liquid water, might be good places to look for signs of life. It's yet to be seen whether JWST will detect those signs of life, but it will be able to detect carbon dioxide.

"My first thought when I saw these data was, 'Wow, this is gonna work,'" Batalha says.

CITATIONS

The JWST Transiting Exoplanet Community Early Release Science Team. Identification of carbon dioxide in an exoplanet atmosphere. arXiv:2208.11692. Submitted August 24, 2022.

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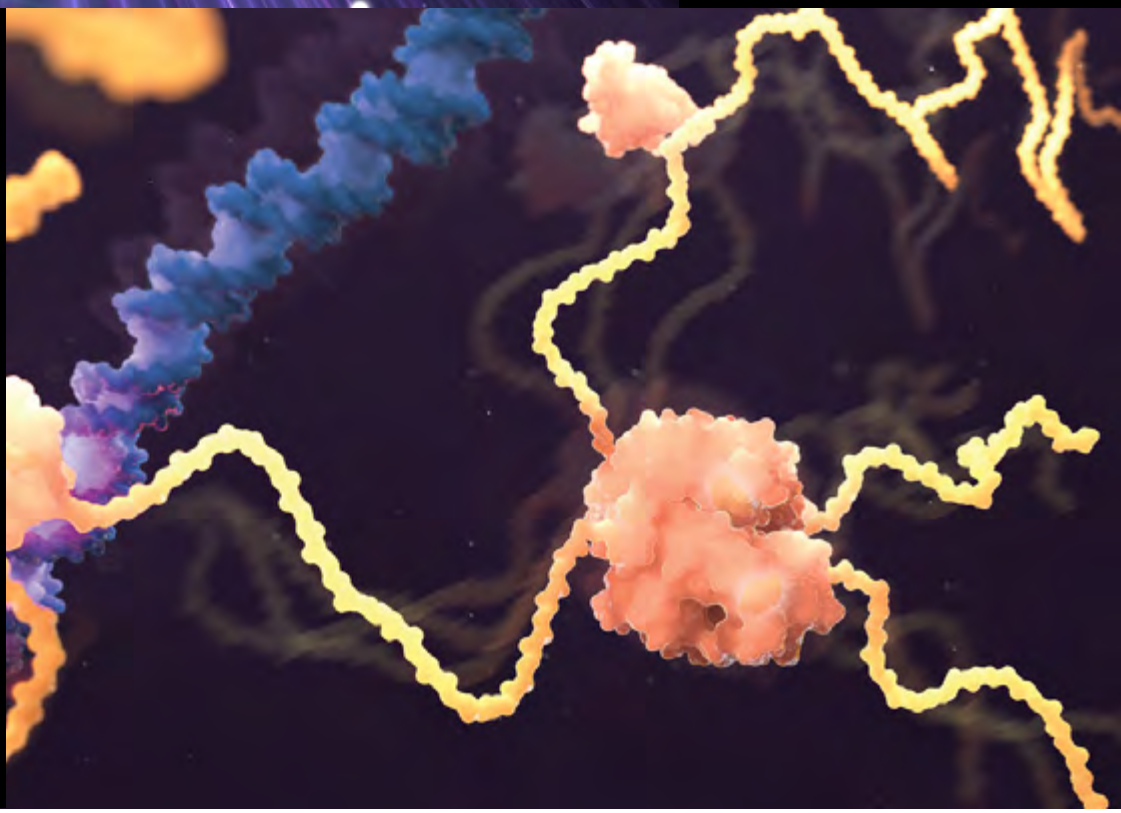


AlphaFold, a deep-learning artificial intelligence system, predicted the structure of the estrogen receptor protein, seen in this illustration binding to DNA (purple). The predicted protein has some parts folded into precise structures (pink) and other areas that resemble free-flowing spaghetti (yellow).

VERONICA FALCONIERI HAYS/ SCIENCE SOURCE

Has AlphaFold actually solved biology's protein-folding problem?

The system's predictions of millions of proteins' structures aren't without limits, some say

By Tina Hesman Saey | SEPTEMBER 23, 2022

A s people around the world marveled in July at the most detailed pictures of the cosmos snapped by the James Webb Space Telescope, biologists got their first glimpses of a different set of images — ones that could help revolutionize life sciences research.

The images are the predicted 3-D shapes of more than 200 million proteins, rendered by an artificial intelligence system called AlphaFold. "You can think of it as covering the entire protein universe," said Demis Hassabis at a July 26 news briefing. Hassabis is cofounder and CEO of DeepMind, the London-based company that created the system. Combining several deep-learning techniques, the computer program is trained to predict protein shapes by recognizing patterns in structures that have already been solved through decades of experimental work using electron microscopes and other methods.

The AI's first splash came in 2021, with predictions for 350,000 protein structures — including almost all known human proteins. DeepMind partnered with the European Bioinformatics Institute of the European Molecular Biology Laboratory to make the structures available in a public database.

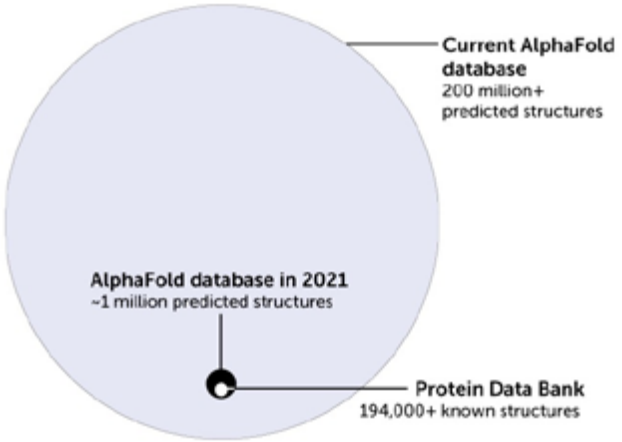
July's massive new release expanded the library to "almost every organism on the planet that has had its genome sequenced," Hassabis said. "You can look up a 3-D structure of a protein almost as easily as doing a key word Google search."

These are predictions, not actual structures. Yet researchers have used some of the 2021 predictions to develop potential new malaria vaccines, improve understanding of Parkinson's disease, work out how to protect honeybee health, gain insight into human evolution and more. DeepMind has also focused AlphaFold on neglected tropical diseases, including Chagas disease and leishmaniasis, which can be debilitating or lethal if left untreated.

Expanding the protein universe

Decades of slow-going experiments have revealed the structure of more than 194,000 proteins, all housed in the Protein Data Bank. In 2021, the AlphaFold project released predicted structures for about 1 million proteins, including almost all known human proteins. This year, the AlphaFold database exploded with predicted structures for more than 200 million proteins.

Total number of protein structures identified and predicted



T. TIBBITTS

The release of the vast dataset was greeted with excitement by many scientists. But others worry that researchers will take the predicted structures as the true shapes of proteins. There are still things AlphaFold can't do — and wasn't designed to do — that need to be tackled before the protein cosmos completely comes into focus.

Having the new catalog open to everyone is "a huge benefit," says Julie Forman-Kay, a protein biophysicist at the Hospital for Sick Children and the University of Toronto. In many cases, AlphaFold and RoseTTAFold, another AI researchers are excited about, predict shapes that match up well with protein profiles from experiments. But, she cautions, "it's not that way across the board."

Predictions are more accurate for some proteins than for others. Erroneous predictions could leave some scientists thinking they understand how a protein works when really, they don't. Painstaking experiments remain crucial to understanding how proteins fold, Forman-Kay says. "There's this sense now that people don't have to do experimental structure determination, which is not true."

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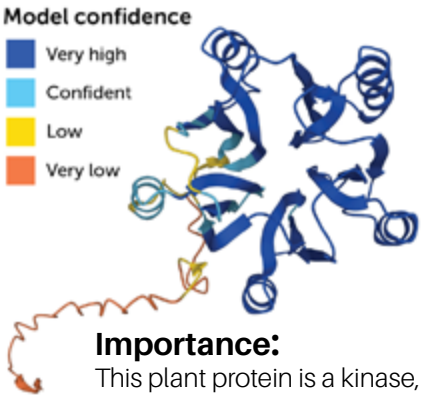


Source organism:
Thale cress *(Arabidopsis thaliana)*

Importance:
This plant protein is a kinase, which tacks phosphates onto other molecules, potentially changing their functions.

DEEP MIND

NOTE: THE CONFIDENCE LEVEL OF ALPHAFOLD'S PREDICTIONS VARY WITHIN EACH PROTEIN. DARK BLUE AND LIGHT BLUE REGIONS ON A PREDICTED STRUCTURE MEAN THE ALGORITHM IS RELATIVELY SURE. LESS CERTAIN PREDICTIONS ARE COLORED YELLOW AND ORANGE.

Plodding progress

Proteins start out as long chains of amino acids and fold into a host of curlicues and other 3-D shapes. Some resemble the tight corkscrew ringlets of a 1980s perm or the pleats of an accordion. Others could be mistaken for a child's spiraling scribbles.

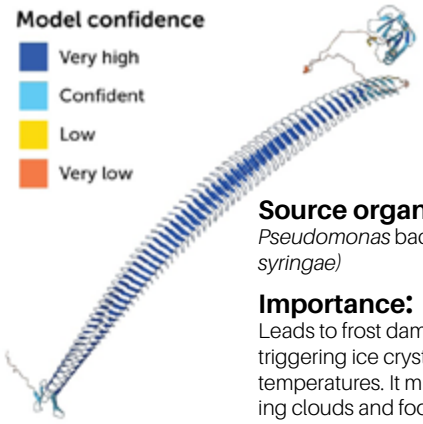
A protein's architecture is more than just aesthetics; it can determine how that protein functions. For instance, proteins called enzymes need a pocket where they can capture small molecules and carry out chemical reactions. And pro-

teins that work in a protein complex, two or more proteins interacting like parts of a machine, need the right shapes to snap into formation with their partners.

Knowing the folds, coils and loops of a protein's shape may help scientists decipher how, for example, a mutation alters that shape to cause disease. That knowledge could also help researchers make better vaccines and drugs.

For years, scientists have bombarded protein crystals with X-rays, flash frozen cells and examined them under high-powered electron microscopes, and used other methods to discover the secrets of protein shapes. Such experimental methods take "a lot of personnel time, a lot of effort and a lot of money. So it's been slow," says Tamir Gonen, a membrane biophysicist and Howard Hughes Medical Institute investigator at the David Geffen School of Medicine at UCLA.

Ice nucleation protein



Source organism:
Pseudomonas bacteria *(Pseudomonas syringae)*

Importance:
Leads to frost damage on plants by triggering ice crystals at relatively high temperatures. It might be used for seeding clouds and food preservation.

DEEP MIND

Such meticulous and expensive experimental work has uncovered the 3-D structures of more than 194,000 proteins, their data files stored in the Protein Data Bank, supported by a consortium of research organizations. But the accelerating pace at which geneticists are deciphering the DNA instructions for making proteins has far outstripped structural biologists' ability to keep up, says systems biologist Nazim Bouatta of Harvard Medical School. "The question for structural biologists was, how do we close the gap?" he says.

For many researchers, the dream has been to have computer programs that could examine the DNA of a gene and predict how the protein it encodes would fold into a 3-D shape.

Here comes AlphaFold

Over many decades, scientists made progress toward that AI goal. But "until two years ago, we were really a long way from anything like a good solution," says John Moult, a computational biologist at the University of Maryland's Rockville campus.

Moult is one of the organizers of a competition: the Critical Assessment of protein Structure Prediction, or CASP. Organizers give competitors a set of proteins for their algorithms to fold and compare the machines' predictions against experimentally determined structures. Most AIs failed to get close to the actual shapes of the proteins.

Then in 2020, AlphaFold showed up in a big way, predicting the structures of 90 percent of test proteins with high accuracy, including two-thirds with accuracy rivaling experimental methods.

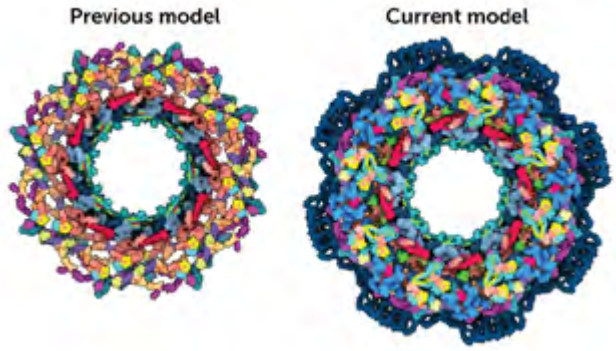
Deciphering the structure of single proteins had been the core of the CASP competition since its inception in 1994. With AlphaFold's performance, "suddenly, that was essentially done," Moult says.

Since AlphaFold's 2021 release, more than half a million scientists have accessed its database, Hassabis said in the news briefing. Some researchers, for example, have used AlphaFold's predictions to help them get closer to completing a massive biological puzzle: the nuclear pore complex. Nuclear pores are key portals that allow molecules in and out of cell nuclei. Without the pores, cells wouldn't work properly. Each pore is huge, relatively speaking, composed of about 1,000 pieces of 30 or so different proteins. Researchers had previously managed to place about 30 percent of the pieces in the puzzle.

The nuclear pore

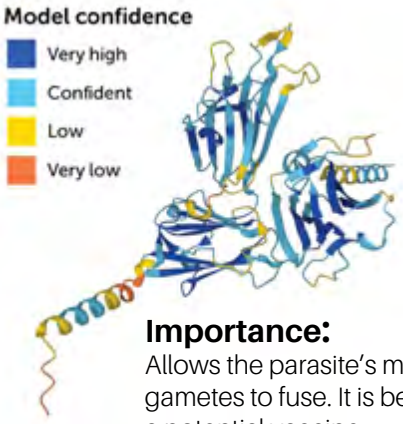
Researchers previously solved about 30 percent of the 1,000-piece puzzle that is the nuclear pore complex. AlphaFold helped make sense of experimental data to complete 60 percent of the structure.

The nuclear pore



S. MOSALAGANTI ET AL/SCIENCE 2022

Gametocyte surface antigen 48/45



Source organism:
Malaria parasite *(Plasmodium falciparum)*

Importance:
Allows the parasite's male and female gametes to fuse. It is being developed as a potential vaccine.

DEEP MIND

That puzzle is now almost 60 percent complete, after combining AlphaFold predictions with experimental techniques to understand how the pieces fit together, researchers reported in the June 10 Science.

Now that AlphaFold has pretty much solved how to fold single proteins, this year CASP organizers are asking teams to work on the next challenges: Predict the structures of RNA molecules and model how proteins interact with each other and with other molecules.

For those sorts of tasks, Moult says, deep-learning AI methods "look promising but have not yet delivered the goods."

Where AI falls short

Being able to model protein interactions would be a big advantage because most proteins don't operate in isolation. They work with other proteins or other molecules in cells. But AlphaFold's accuracy at predicting how the shapes of two proteins might change when the proteins interact are "nowhere near" that of its spot-on projections for a slew of single proteins, says Forman-Kay, the University of Toronto protein biophysicist. That's something AlphaFold's creators acknowledge too.

The AI trained to fold proteins by examining the contours of known structures. And many fewer multiprotein complexes than single proteins have been solved experimentally.

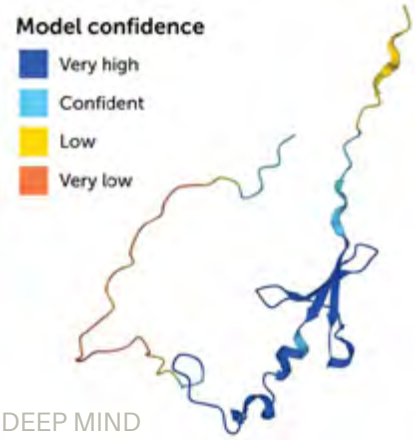
Forman-Kay studies proteins that refuse to be confined to any particular shape. These intrinsically disordered proteins are typically as floppy as wet noodles (SN: 2/9/13, p. 26). Some will fold into defined forms when they interact with other proteins or molecules. And they can fold into new shapes when paired with different proteins or molecules to do various jobs.

AlphaFold's predicted shapes reach a high confidence level for about 60 percent of wiggly proteins that Forman-Kay and colleagues examined, the team reported in a preliminary study posted in February at bioRxiv.org. Often the program depicts the shapeshifters as long corkscrews called alpha helices.

Forman-Kay's group compared AlphaFold's predictions for three disordered proteins with experimental data. The structure that the AI assigned to a protein called alpha-synuclein resembles the shape that the protein takes when it interacts with lipids, the team found. But that's not the way the protein looks all the time.

For another protein, called eukaryotic translation initiation factor 4E-binding protein 2, AlphaFold predicted a mishmash of the protein's two shapes when working with two different partners. That Frankenstein structure, which doesn't exist in actual organisms, could mislead researchers about how the protein works, Forman-Kay and colleagues say.

Eukaryotic translation initiation factor 4E-binding protein 2



Source organism:
Malaria parasite *(Plasmodium falciparum)*

Importance:
Allows the parasite's male and female gametes to fuse. It is being developed as a potential vaccine.

AlphaFold may also be a little too rigid in its predictions. A static "structure doesn't tell you everything about how a protein works," says Jane Dyson, a structural biologist at the Scripps Research Institute in La Jolla, Calif. Even single proteins with generally well-defined structures aren't frozen in space. Enzymes, for example, undergo small shape changes when shepherding chemical reactions.

If you ask AlphaFold to predict the structure of an enzyme, it will show a fixed image that may closely resemble what scientists have determined by X-ray crystallography, Dyson says. "But [it will] not show you any of the subtleties that are changing as the different partners" interact with the enzyme.

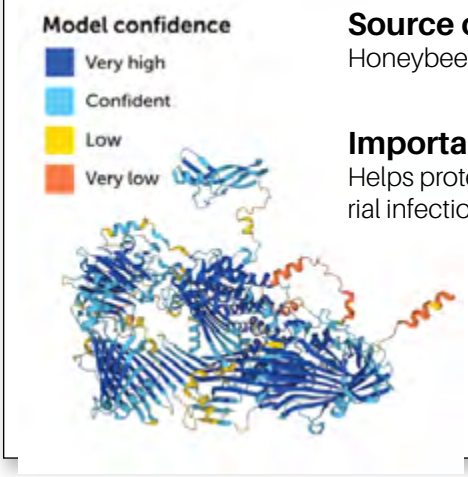
"The dynamics are what Mr. AlphaFold can't give you," Dyson says.

A revolution in the making

The computer renderings do give biologists a head start on solving problems such as how a drug might interact with a protein. But scientists should remember one thing: "These are models," not experimentally deciphered structures, says Gonen, at UCLA.

He uses AlphaFold's protein predictions to help make sense of experimental data, but he worries that researchers will accept the AI's predictions as gospel. If that happens, "the risk is that it will become harder and harder and harder to justify why you need to solve an experimental structure." That could lead to reduced funding, talent and other resources for the types of experiments needed to check the computer's work and forge new ground, he says.

Vitellogenin



Source organism:
Honeybee (Apis mellifera)

Importance:
Helps protect against bacterial infections.

Harvard Medical School's Bouatta is more optimistic. He thinks that researchers probably don't need to invest experimental resources in the types of proteins that AlphaFold does a good job of predicting, which should help structural biologists triage where to put their time and money.

"There are proteins for which AlphaFold is still struggling," Bouatta agrees. Researchers should spend their capital there, he says. "Maybe if we generate more [experimental] data for those challenging proteins, we could use them for retraining another AI system" that could make even better predictions.

He and colleagues have already reverse engineered AlphaFold to make a version called OpenFold that researchers can train to solve other problems, such as those gnarly but important protein complexes.

Massive amounts of DNA generated by the Human Genome Project have made a wide range of biological discoveries possible and opened up new fields of research (SN: 2/12/22, p. 22). Having structural information on 200 million proteins could be similarly revolutionary, Bouatta says.

In the future, thanks to AlphaFold and its AI kin, he says, "we don't even know what sorts of questions we might be asking."

READ SOURCE ARTICLE ONLINE

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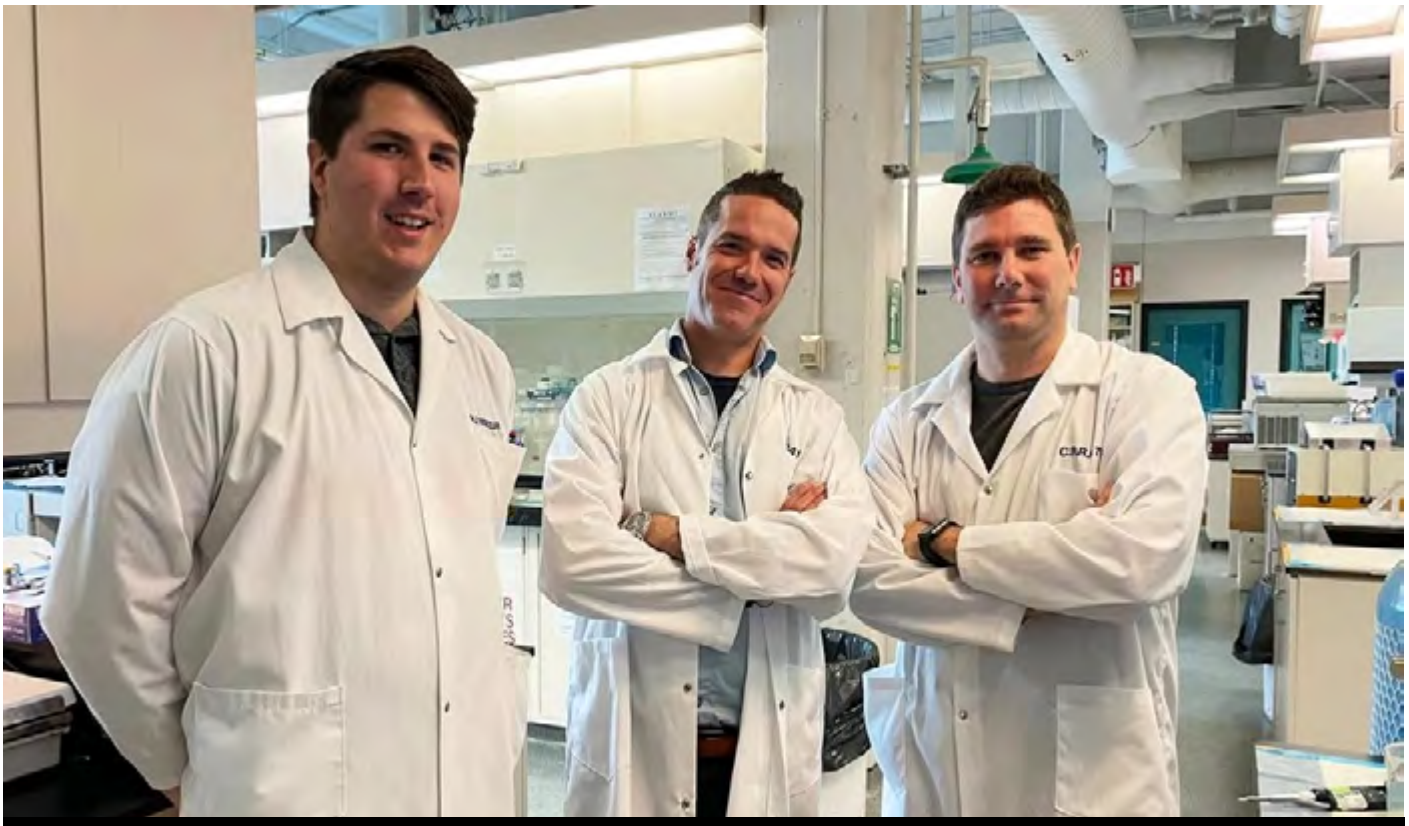
Mitochondrial transplant therapy appears to make immune systems younger

Author: Danny Sullivan | Last updated: October 12, 2022

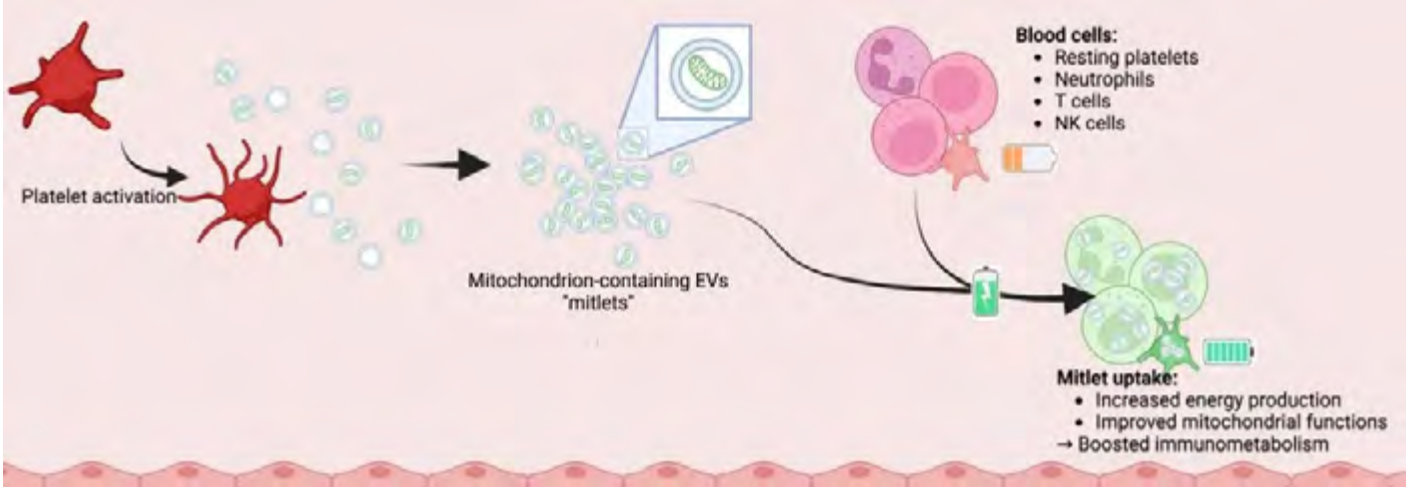


Dr Eric Boilard (centre) and some of his team in the lab.

DISCLOSURE: Longevity.Technology (a brand of First Longevity Limited) has been contracted by the company mentioned in this article to support its current funding round. Qualifying investors can find out more via the Longevity.Technology investment portal.

Scientists at Californian longevity biotech start-up Mitrix Bio are testing a new therapy to boost immune system strength using tiny particles called "mitlets" that contain mitochondria. The company says that injections of mitlets in animal models appear to reverse immune weakness, making old immune systems temporarily young again. In multiple tests, old or sick animals receiving the injections showed reduced cytokine storms and significantly improved survival against bacterial and viral infections.

Longevity.Technology: Mitochondria are the power generators within our cells, and their dysfunction is linked to a wide range of age-related diseases. The longevity potential of mitochondrial transplantation is an interesting area, and the mitlets technology being developed by Mitrix is something on which we've been keeping a close eye. This latest an-



nouncement from the company represents a shift in focus towards immunotherapy. With papers submitted for review, we look forward to hearing more from Mitrix on the detail of these animal studies.

Naming the treatment HISET (short for Human Immune System Energetic Transplantation Therapy), Mitrix says that it expects the therapy to be compatible with other immunotherapies such as CAR-T, monoclonal antibodies and checkpoint inhibitors. Following completion of animal testing, Mitrix expects to move HISET into human trials.

"If the results we are seeing translate to humans, the results would be roughly equivalent to making the human immune system 30 years younger," said Tom Benson, CEO of Mitrix. "This potentially gives doctors another tool to fight infectious disease such as COVID, pneumonia, sepsis, and blood infections. HISET could not only provide supplemental mitochondria during illness but could potentially help longer-term treatment of other conditions, notably in the battle against cancer."

Dr Eric Boilard from University Laval in Canada initially discovered mitlets in 2014, and the technology has been further researched by Mitrix.

Mitlets are mitochondria-containing extracellular vesicles that platelets, T cells, NK cells, neutrophils, and other immune components are believed to exchange to conserve energy. Mitrix uses special bioreactors to grow young mitlets, which are injected into the body, where immune cells absorb them and use the mitochondria inside. After a few days, the new mitochondria seem to be discarded so the benefit wears off, but Mitrix suggests that multiple injections could potentially be used to extend the effect.

"Mitlets can be compared to rechargeable battery packs which can be swapped back and forth between power tools we buy at the hardware store," says Boilard. "Mitlets enable immune components to work harder and last longer – a clever evolutional adaptation that helps our immune systems better fight infections."

Mitrix is based in Pleasanton, California and boasts a scientific advisory board including Dr. Michael Snyder, Chair of the Genetics Department at Stanford University, and Dr. Thomas Rando, Director of the UCLA Broad Stem Cell Research Center and former director of the Glenn Center for the Biology of Aging at Stanford University.

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ScienceDaily

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Clusters of genes help mice live longer

Date: October 12 2022 | Source: University of Texas Health Science Center at San Antonio

Researchers have announced the discovery of multiple candidate genes that influence longevity. The discovery of genetic loci that influence longevity only in females is interesting and important, according to the researchers. Genetic loci are clusters of between 10 and 100 genes..

Researchers from the National Institute on Aging (NIA)-funded Interventions Testing Program recently reported the discovery of multiple candidate genes that influence longevity. The three Interventions Testing Program sites -- The University of Texas Health Science Center at San Antonio, The University of Michigan at Ann Arbor and The Jackson Laboratory at Bar Harbor, Maine -- collaborated on the study with the labs of Robert W. Williams, PhD, of the University of Tennessee Health Science Center at Memphis and Johan Auwerx, MD, PhD, of the École Polytechnique Fédérale de Lausanne in Lausanne, Switzerland.

"Some candidate genes impacted female life span while others affected the male life span," said Randy Strong, PhD, of the Sam and Ann Barshop Institute for Longevity and Aging Studies at UT Health San Antonio. "One cluster of genes increased longevity of both sexes. In a rarity for these types of studies, the findings were made in a population of mice with genetic diversity comparable to human populations."

The high-impact journal Science published the findings Sept. 30. Strong directs the Interventions Testing Program site at the Barshop Institute, which first attracted National Institute on Aging (NIA) grant funding for the Interventions Testing Program in 2003 and is in its 19th year of the NIA funding.

Genetic smorgasbord

"The study models what happens in people," said research coauthor James Nelson, PhD, of the Barshop Institute. "Unlike mice in many other studies, mice in this newly reported research are not all the same. Each has different genetic variants, resulting in slightly different proteins that do slightly

different things, which together can impact aging."

Even subtle differences can lead to different health outcomes as we age. Slight variations in the hemoglobin gene, for example, can cause the hemoglobin protein in red blood cells to be less effective at binding to oxygen and transferring it from the lungs to the body's tissues, Nelson noted. Anemia is one effect.

Female longevity

The discovery of genetic loci that influence longevity only in females is interesting and important, Strong said. Genetic loci are clusters of between 10 and 100 genes.

"Females and males differ in almost every aspect of aging you can explore," Strong said. "They each must be studied, both to understand aging in the two sexes and to develop effective treatments. If we offer the same drug therapies to females that we offer to males, and females' aging is caused by different genes, we are not going to be as effective in our treatments."

Confirmation in roundworms

The next steps are scrutinizing these candidate genes to find ones that are responsible for increased longevity. In the final part of the Science article, the team reported doing this. The researchers tested candidate genes in roundworms, which are often used in aging research because of their short life span. "A number of the candidate genes did affect longevity in the worms," Nelson said.

That doesn't prove that those same genes in humans are going to affect human life span, the researchers said. But it's another part of the case for continuing to study the genetic basis of longevity.

Powerful study design

As envisioned when the Interventions Testing Program began, having three sites where studies are conducted ensures statistical power and rigor and reproducibility of findings, Strong said.

The study is unique in that it is based on a large sample size of animals numbering several thousand, the authors said. "It is among the largest number of mice of any study that has attempted to identify genes that influence life span," Nelson said.

Barshop Institute excellence

The Interventions Testing Program is one of several NIA-funded centers at the Sam and Ann Barshop Institute. Among them, the Nathan Shock Center of Excellence in the Basic Biology of Aging provides core services to enhance research of the fundamental biological questions of aging. The Claude D. Pepper Older Americans Independence Center, named for the late U.S. representative, is a center of excellence aimed at increasing scientific knowledge to develop better ways of maintaining or restoring independence in senior adults. The Barshop Institute is the only institute or university in the nation to have these three centers.

Strong is a tenured professor of pharmacology in the Joe R. and Teresa Lozano Long School of Medicine at UT Health San Antonio. Nelson is a tenured professor of cellular and integrative physiology in the Long School of Medicine.

Story Source:

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Journal Reference:

Maroun Bou Sleiman, Suheeta Roy, Arwen W. Gao, Marie C. Sadler, Giacomo V. G. von Alvensleben, Hao Li, Saunak Sen, David E. Harrison, James F. Nelson, Randy Strong, Richard A. Miller, Zoltán Kutalik, Robert W. Williams, Johan Auwerx. Sex- and age-dependent genetics of longevity in a heterogeneous mouse population. Science, 2022; 377 (6614) DOI: 10.1126/science.abo3191

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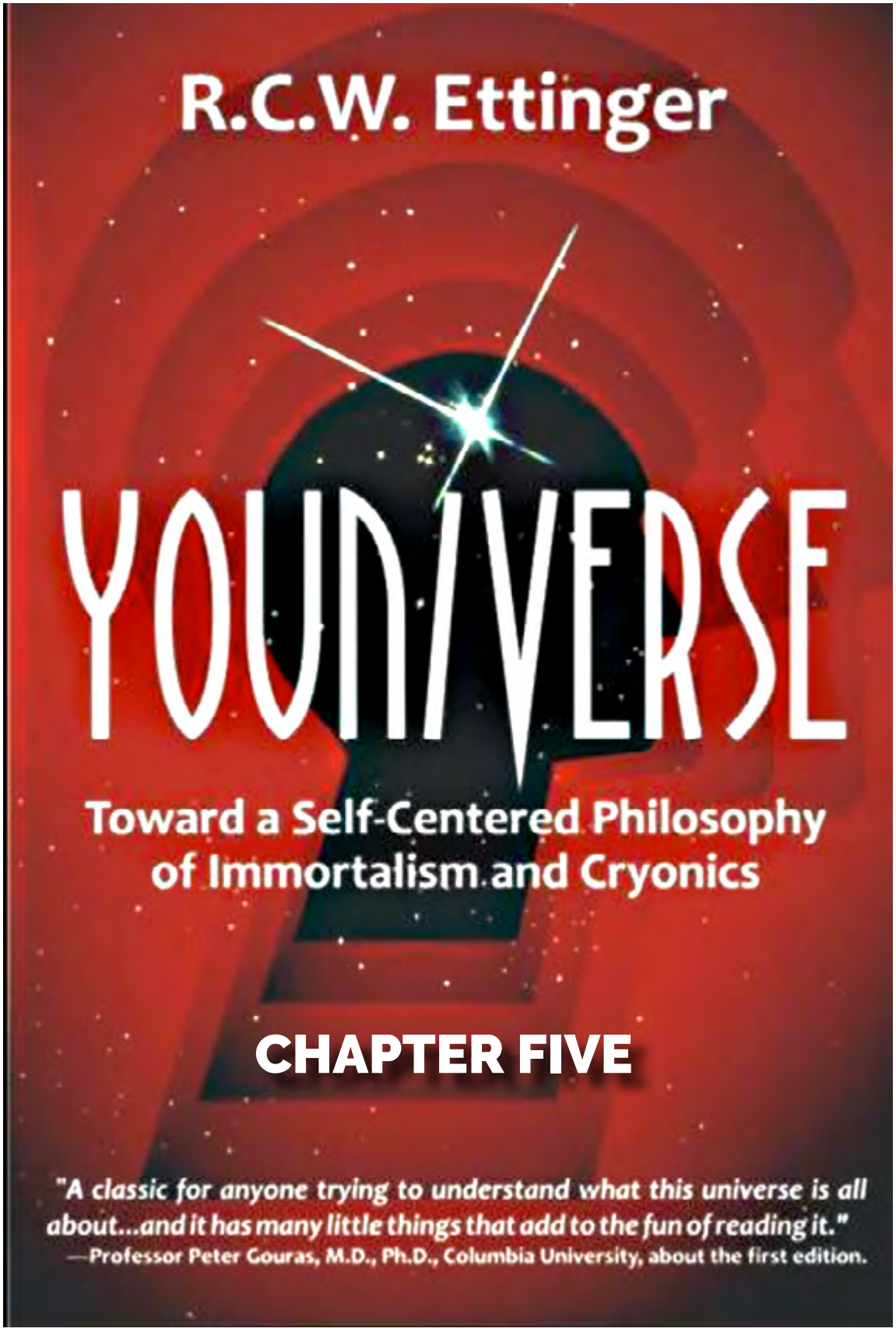

Chapter 5
Me-First & Feel-Good Foundations of Value

> Can one desire too much of a good thing?—*As You Like It*
>
> Good is better than evil, because it's nicer. —*Mammy Yokum*

I am a hedonist, and so are you... and so were all the saints, even if they would howl or sputter in indignation and rend their rags at the notion.

Of course, we may have to tinker a bit with the dictionary definitions of hedonism. Webster's New World Dictionary of American English, Third College Edition gives three definitions:

1. "In philosophy, the ethical doctrine that pleasure, variously conceived of in terms of happiness of the individual or of society, is the principal good and the proper aim of action."

   The "happiness" of "society" is not a clear concept, and my direct concern is only for the individual.

2. "In psychology, the theory that a person always acts in such a way as to seek pleasure and avoid pain."

   This is somewhat flawed, since it is obvious that we do not always act in this way, not to mention that "pleasure" and "pain" are left vague, as are time scales.

3. "The self indulgent pursuit of pleasure as a way of life."

This is the popular notion of hedonism, with its nasty connotations of gluttony, orgies, opium dens, etc. It arose because the original hedonists in ancient Greece, and almost all their successors, to this very day, were very poor at public relations and had very limited understanding of psychology and physiology.

The actual words of (3) above are not wrong or offensive—only the connotations or misinterpretations. So—with a different interpretation than that intended in the dictionary—(3) above is one way to express my definition of hedonism. Or we could use (2) above, modified to refer to motivated behavior, not all behavior, as shown a bit later on.

My modest aim is to derive a *rigorous* system of personal philosophy, centered on my version of hedonism. This cannot presently be done in a complete or certain way, since its success depends on information we do not yet have—information about the structure and functions of the brain, as well as the laws of physics including the nature of space and time. But we can take several steps along the way, settling some old questions and raising some new ones.

Satisfaction: First we remember the lamentation of the old song, "I don't get no satisfaction."

Then we remember that a famous labor leader (Was it the UAW's Walter Reuther? The UMW's John L. Lewis?) was asked what the workers wanted, and his answer was honest and exquisitely succinct:

"More."

As to more what, well—mostly money or the equivalent in various guises, plus job security and better working conditions. Nothing very

obscure or subtle.

But the individual, looking at life in the large, asking himself what he wants, if he gives an honest and thoughtful answer, must say *satisfaction*. This is very similar to the "pleasure principle" but avoids some of the traps in those words.

We often choose pain over pleasure in the short term, if this means "doing your duty". Not only that, but the masochist apparently finds pleasure *in* pain. For that matter, many ordinary people enjoy "handkerchief movies" involving suffering or sorrowing protagonists, i.e., the moviegoer likes to be made to weep. So instead of saying "pleasure" we say "satisfaction", and instead of saying "pain" we say "dissatisfaction". I have not yet found anyone willing to say that he would seek dissatisfaction or eschew satisfaction.

Maybe I should append a note to that last. Philosophers have an inordinately high quibble quotient, and one of them is certain to say, sure we sometimes seek dissatisfaction. We seek challenges, don't we? And doesn't a challenge situation imply some sort of temporary dissatisfaction? And isn't this another case of the road to Good being paved with Bad? I leave the answers as exercises for the reader.

"Ought" from "Is": Many respected philosophers—including David Hume, who had most things right—have said, "You can't derive an 'ought' from an 'is'." (But he also more or less contradicted himself elsewhere.) A.J. Ayer also said that "normative" statements (about what is good or bad, right or wrong) are meaningless. In other words, you can't derive values from facts—there is nothing about the objective world that can tell us what we ought to do. The implication is that values are arbitrary, and one set is as much justified as another, or maybe none is justified. Or in some cases, these writers mean that your values just happen to be there, through accidents of birth and nurture, and you are stuck with them.

There is a bit of truth in that last, as we shall see, but as usually formulated, it is very misleading. The error usually lies in failing to recognize that higher-level values are derivative and in principle analyzable into more primitive components. There is also endless confusion in the failure to distinguish social values from individual values. It is the latter that concern me.

For example, some people value honesty more than others. Everyone knows that views on honesty evolve, at least in part, from the experiences of individuals and their training or indoctrination. Other things equal, you are more likely to prize honesty if you have been taught that, and if you have been rewarded for honesty or/and punished (directly or indirectly, externally or internally) for dishonesty. Less frequently, you may arrive at a high regard for honesty by the intellectual route, proving to yourself that honesty usually pays, when the internal and external consequences are systematically examined.

What has been generally missing is the explicit recognition that values are rooted in biology —and I don't mean evolutionary biology in the usual sense. I mean that sentient creatures—systems with feeling or the capacity for subjective experience —have built-in needs or desires which represent or constitute values. Out of these grow derivative or subsidiary values, which in humans may culminate in highly abstract or rarefied drives, such as those of patriotism or music appreciation.

Groundwork: *Values* may be thought of as generic

aims—the general goals or guidelines behind specific goals. More simply put, values are *wants*.

An investigation of values, then, is just a matter of asking *who wants what, and for whom*.

It turns out that the "what" is simple—in principle!—and the "who" and "whom" also, on one level. But there are other levels, and what is simple in principle may be daunting in practice.

For starters then, in principle; (1) the wanter and the beneficiary are both *me*; (2) what I want is to *feel good*.

In what follows, once more, I believe some repetitiveness is justified by the difficulty most people experience with the concepts.

1. Me-First is an essential foundation of all value systems. This reminds us *whom* we are trying to benefit.

This ought to be seen as a truism, but most people cannot overcome their conditioning and genetic programming without extended and many-faceted discussion (if ever!)—and after that comes the hard part, the tricky interpretation and application.

There is nothing new about the doctrine of enlightened self-interest as the basis of value, but most proponents go at it haphazardly and half-heartedly, missing crucial points, and are finally unconvincing.

Perhaps we can convince a few people just by phrasing the proposition neatly:

"If you do something because *you* want it, then you are doing it for yourself. What could be simpler or more obvious?"

"It is *physically* impossible not to be motivated by self interest, because the only thing that can possibly matter to you—directly —is what goes on in your own head." (Because this is where you live, where you experience, where the stimuli are interpreted, where the preferences arise and where the judgments are formed.)

"It is impossible to be motivated by anything other than self interest, because motivation *means* what is important to the self."

"All motivated behavior (as opposed to that which is random or accidental) is based on self interest, since it is the interest of the self that constitutes the motivation."

"There is no such thing as true self-sacrifice or true altruism. If I 'sacrifice' my life or my apparent interests for someone else, or for a 'cause' or a principle, that simply means that one of my values, or one aspect of my personality, was dominant at the moment and others had to be subordinated. The choice can be a miscalculation—it may not really serve your logical longterm self interest—but it is still *your* preference at the time."

If a mother runs back into a burning building to save her baby, it isn't because she values the baby above herself; it is because she values her feelings about the baby above her other feelings. At the moment, at least, she would suffer more by abandoning the baby than by running into the fire, or so she feels."

Surprise—it really isn't quite that simple, for complex and subtle reasons, which we will get into eventually. But this "simple" formulation nevertheless represents for most people a profound and (probably) valid insight and a

radical shift in viewpoint.

CAUTION: The doctrine of me-first as it is used here must not be confused with vulgar and simple-minded slogans of

"looking out for number one" or

"situation ethics" or primitive hedonism or simple self-indulgence. All these latter are based on superficial analysis, at best. The successful application of a genuine philosophy of me-first and feel-good is very demanding in both intellectual analysis and self-discipline, as we shall see. (Calvinists, rejoice; the good life is a hard life.)

2. Feel-Good is the other basis of value. It reminds us what benefit we are trying to obtain. With me-first and feel-good together, we know what we want and for whom we want it.

We need only ask—what do we want, in the most basic and necessary and general sense? *We want to feel good*. The one

and only conscious goal of every individual is to feel good. (If you aren't convinced, stick around.)

This was more or less recognized, in a primitive way, by many of the classic philosophers. Certain schools of hedonists, epicureans and utilitarians had an initial partial handle on it, but quickly let it slip. The problem, of course, is that there are many different ways of feeling good, some of them inconsistent with each other or even ultimately self-destructive, and these difficulties have baffled all previous philosophers, or at least the well known ones.

I can't solve the problem with assured completeness or finality either, because, as previously noted, we still lack important information about the nature

of the brain and about crucial features of the physical world, especially time. But I can go further than others have gone, and with more clarity.

Popper's Error: I have said that all consciously motivated behavior is necessarily selfish or egoistic, because our choices stem from *our* needs or wants, those dominant at the moment. Karl Popper, among others, has said this is unscientific because it us unfalsifiable, not capable of verification or confutation by observation or experiment.

In a sense, Popper is wrong because he is right. The point is that my claim is not a theory, but just a way of drawing attention to a definition. The definition of "conscious motivation" is not mine alone, but the generally accepted one.

In slightly more detail, Popper *et al.* frequently add to the confusion by talking about "doing" what you want, and deeds do not always arise from bona fide wants. In fact, much of your behavior is just habit—sometimes based on real needs or logic, sometimes not. Some of your behavior is merely accidental. Another large bloc arises from conditioning, which means you are doing what you have been trained to think you want, or what you have been told is your duty.

It isn't a question necessarily of what you do, but of what you choose (since not all actions result from conscious choices). Not all choices are conscious, and not all conscious choices are well considered, and not all well considered choices are sound. And what you choose will usually be a compromise among various possibilities, so things are seldom as clear-cut as we would like.

More importantly, once more, the anti-egoists are misrepresenting my position. I do say that—when consciously motivated—we choose what we want, and therefore choose to please ourselves. The *meaning* of motivation is what moves the self, i.e., what appeals to the wants of the individual, and I didn't invent that definition. And then, I don't just let it lie there, which would be tantamount to suggesting that any old want is as good as any other. Rather, I point out that biology is beginning to allow us insights into

our real, basic needs and their hierarchies and relationships to derivative needs or wants; and also that, even with the

crude introspective tools now at hand, we can often review and improve our value systems. It is when we get into specifics that the worth of my approach becomes most evident.

Utility: I have not solved the problem of hedonic calculus, and cannot provide a rigorous and systematic approach to assessment of value. I can and will offer a lot of clues (as many others have also done), but will first just lay out some aspects of the problem.

The term *utility* in economics is closely related to the most fundamental problem of philosophy, the problem of what you ought to want, and therefore of what you ought to do.

The word "utility" of course means usefulness, and in economics, its meaning is roughly that of equivalent money value. "Roughly" because it is difficult, and in many cases seemingly impossible, to assign a monetary value to subjective gratification. Most people think that satisfactions are not fungible.

Certainly the difficulty has often been overplayed. For example, it is commonplace to hear that one cannot put a dollar value on human life, or on aesthetic enjoyment—yet we do it all the time.

For example, certain professions, such as lumberjack, have substantially higher than average mortality risk, and are paid accordingly—both employer and employee implicitly agree on the dollar value of life. Automobiles vary in safety, and with other things equal, the cars with more safety features cost more, and the buyer makes his implicit decision on the value of avoiding risk to life or limb.

And of course, entertainment is a huge industry, with very specific dollar value placed

on certain types of enjoyment

— with sometimes surprising and disturbing revelations as to what people value. Ah well

— we're not so far removed from bear baiting, and in some places, there are still cock fights, and as far as I know, Spain and Mexico still have bull fights. On a more reasonable level, Hawaii and California have high priced land because of pleasant climate, and scenery has its price tag.

Yet, even though we do frequently, indirectly, measure subjective pleasures and pains in dollars, there has been no general solution to the apples/ oranges problem—either in society or in individuals. So—can we find a common denominator of *fruit*, or must each variety be handled separately?

Does the brain have a single, underlying internal definition of pleasure or satisfaction? If so, how do we get it in conscious focus? If there is more than one hierarchy, how do we discriminate between parallels?

One clue may lie in the analogy with econom-

ics. Material goods are typically priced on very clear and solid criteria based on supply and demand. The price is said to be more "elastic" if it is more sensitive to changes in supply or demand. If an item is unique, such as the original Mona Lisa, then there is no price elasticity of supply because the supply is fixed. (But the fraud and substitute questions are significant here.) If something is very cheap in context, such as tap water in a restaurant, then it is usually provided without charge, and there is no price elasticity of demand—although of course the guest does pay for it in the same way he pays for other items of overhead.

Our needs or wants are highly context sensitive, varying with the situation and from moment to moment. As I have frequently noted, "basic" drives such as hunger, sex and even self preservation will often take a back seat to more urgently perceived needs stemming from habit, duty, or coercion—and in some cases, this is exactly as it should be. If you forgo a present pleasure, or resist a temptation, to save money and improve your future, that is usually the right choice. But if you volunteer to be a "martyr" by hijacking an airplane, that is usually a rather serious mistake.

So for the time being, we must remain in the cut-and-try/common-sense mode of goal setting or value assessment, which is not ideal but far from worthless.

Higher Values in Lower Animals: It isn't only humans who sometimes choose "higher" over more "basic" ends. In Gazzaniga's *Human* (Harper Collins 2008), we are told of observations of primates and birds revealing aesthetic drives. Some chimps like to draw and will ignore food in order to continue painting, or throw a tantrum if compelled to stop. The "artistic temperament" goes back a long way!

Studies in this area are still in early stages, but hints are emerging that could be applied to humans as well. It is impossible to doubt that eventually we will understand the biology of motivation.

"It Feels So Good When I Stop" & "Hunger is the Best Sauce": In the old joke, the village idiot is beating his head against a wall, and when asked why he would do such a thing, he says, "Because it feels so good when I stop."

There is a widely held and deeply entrenched view that most good things, if not all, attain that status only by contrast. Pain (or at least its possibility) is necessary for pleasure, the existence of disease is necessary for appreciation of health, and death is necessary to validate life. Even such an elemental pleasure as eating, although it may not actually require initial hunger for its appreciation, is greatly benefited thereby. "Hunger is the best sauce."

Once more, we find a degree of realism in some of these ideas. Contrast may sometimes heighten appreciation. Also we know that many pleasures tend to pall over time, and some are intrinsically transient. For example, the exultation of a moment of triumph or ovation is necessarily brief, and orgasms don't last long. Further, even if we could somehow stretch out pleasurable moments indefinitely, that would be stasis or paralysis, and it isn't physiologically possible anyway with our present construction. But it is easy to be misled by these partial truths, and we are just at the beginning of our investigation into the actual physiological details of pleasure and pain.

The main thing to remember here is that the Yin-Yang or contrast thesis just isn't universal by any means. If anyone doubts that it is

possible to be happy or enthusiastic without the goad or specter or remembrance of pain, you need only remind yourself (among many other examples) of the colts and kids and puppies and kittens. They gambol and cavort for the sheer joy of it, with the distress potential nowhere in their thoughts. For that matter, adult human game players feel much the same way. If you object here that the element of competition provides something akin to the goad of pain, then think instead of such non-competitive activities as strolling or paddling a canoe, or even admiring the sunset. If any contrast is involved, it is just the contrast of absence, not of countervailing sorrow.

As still another example, think of eating a meal of several courses. Why soup to nuts? Why not just one course? Many dishes can each provide plenty of nutriment and good taste. The answer is that we enjoy variety, and the point is that the change need not be from pain or distress, but merely from a different kind of pleasure.

"It Hurts So Good": Another murky area is related to masochism and kindred phenomena, the close association of pleasure and pain, the pain being necessary for the pleasure. More in the mainstream, the pleasure of achievement may be intimately related to the difficulty or pain involved in the accomplishment. But again, it is too facile by far to draw any conclusions before we learn more about the biology. There seems to be no reason in principle why we cannot have pleasure without pain.

Bad Ways to Feel Good —Zealotry: At this point, just one nod to a dramatic example of what in one sense might be called delusional feel-goodzealotry, or what Konrad Lorenz called "militant enthusiasm". He said it is a true instinct or endogenous drive, and writes that, like the triumph ceremony of the greylag goose, militant enthusiasm in man is a true autonomous instinct, with its own appetitive behavior, its own releasing mechanisms. Like the sexual urge or any other strong instinct, it engenders a specific feeling of intense satisfaction. The strength of its lure explains why intelligent men may behave as irrationally and immorally in their political as in their sexual lives. [*On Aggression*, Harcourt, 1966]

Most of us have not observed greylag geese, but we have observed babies, and seen babies carried around with pacifiers in their mouths. Lorenz reminds us that babies have an instinct or "hunger" to suck, distinct from the hunger for food. If the need for food is satisfied too soon, the baby still wants and needs to suck, deriving satisfaction from sucking, and feeling deprivation if not given something to suck. Obviously the sucking instinct is related in its evolution to the need for food, but nevertheless the desire to suck has become at least partly autonomous. Again, it may give us pause to reflect on what is "natural" and whether the "natural" is necessarily desirable.

Not all of Lorenz' ideas are universally accepted, but anyone with the least experience of the world can see he has illuminated something here. A striking recent example is related to the Iraq war of 2003. Before the fall of Baghdad, crowds would chant, "We will give our blood and our souls for Saddam!" On one day of April 2003, in at least some cases, the chant changed to: "We will give our blood and our souls for Iraq!"

Different names, same games. Interchangeable symbols = meaningless symbols. What was truly important to these people was neither Saddam nor Iraq nor anything else outside of

their own heads. The important thing was the feeling of militant enthusiasm.

The Zealot's Little Brother: Akin to zealotry in some ways is what Karl Popper has called *commitment* or *incorrigibility of belief*. This covers a whole lot of territory, and in fact most of us suffer from this disease at least to some extent, some of the time. The "committed" are just those who are unwilling, or less willing, to face reality and adjust their beliefs and actions when facts demand it.

The problem is partly of education, partly of laziness or habit, and partly of pride or of perceived loyalties. It is *unpleasant* even to review your beliefs, let alone change them when those all around you, and also those within you (your younger selves) clamor protest or look askance.

But pride and honor offer spurs and rewards too. There is satisfaction—if sometimes a grim satisfaction—in doing your duty to yourself and maintaining your integrity.

The Devil's Disciple: Perhaps zealotry is an outgrowth or branch of a broader and more basic drive, akin to what Nietzsche and others called will, the urge to prevail or to have one's way, especially against opposition. This in turn may be a branch or outgrowth of a still broader and more basic drive, namely, to exercise one's capabilities, related to what Abraham Maslow called self-actualization, at the top of his hierarchy of drives.

In George Bernard Shaw's *Man and Superman*, the author says in his preface that what attracts and impresses us is the heroism of daring to be the enemy of God. He also says that from Prometheus to his own *Devil's Disciple*, such enemies have always been popular.

Also, in the dream scene of *Man and Superman*, Don Juan says:

> "... to be in Hell is to drift; to be in Heaven is to steer." Again, it's about control, and the evolutionary connections are obvious.

Sense of Purpose: Going at it from a slightly different angle, and again asking ourselves how near the mark— or how far off—Lorenz was—it seems plausible that we can gather a family of motivations under the rubric of *sense of purpose*.

Primitive drives are sometimes said to include the four Fs—feed, flee, fight and fornicate. These are obviously often useful or necessary. But at a slightly higher level of abstraction, we might add a fifth—to find, or perhaps to seek. After all, if the object of desire or fear isn't right at hand, we have to find it. And if we are to be successful very often in our quest, we need to have a built-in tendency to persist, to persevere, to be stubborn, to keep our eye on the ball and hang on through thick and thin.

Well, once we have established a quest or goal in consciousness —and perhaps in unconsciousness too—then we have motivation at a higher level. We no longer seek food or a mate or a sign of danger only for its own sake, but also for the sake of our need to triumph, or at least to avoid capitulation.

And there, perhaps, we have the root of such notions as "honor" and integrity.

The Highest Ideal? Many believe—and insist, loudly and often—that human nature demands a lofty sense of purpose, a high ideal, because without that, we become mired in anomie and alienation. There is a bit of merit in this claim, but as far as I can see, there is only one valid candidate for that ideal, and its

name is *integrity*.

The commitment you (probably) need is to be totally honest with yourself. With qualifications to be noted, don't flinch at facts and don't kid yourself. Face reality, as best you can judge it.

Yes, there are qualifications even here, some obvious and others not. For example, you don't deny that the world is full of misery, but you protect yourself by deliberately ignoring most of it, most of the time. You might even reasonably decide that the questions are too hard and the answers too unclear, and that your best shot at psychic comfort is to (continue to) embrace one of the traditional value systems, such as a religion or an ideology. Yet again, we have no surety, no guarantees, no fully reliable map or compass. For myself, integrity is a basic.

No Mama, No Papa: Most people of my generation are already orphans in the literal sense, both parents deceased. Yet even most of the elderly cling to their milk-tooth need for parental comfort and guidance and sanction. Instead of literal parents, of course, they look for Big Daddy or Big Mama in institutions or ideals or traditions or simple habit.

To say it in the most offensive way, they are immature and cowardly. Maturity and courage require acceptance of total responsibility, refusal to be a rubber stamp on even the most impressive documents. (Yes, to characterize this maturity in the most offensive way, you could also call it hubris or vain-glory.) Insults aside, we are dealing with practical matters and should face the lessons of life.

As the communists used to say, we have thesis and antithesis. On the one hand, a plain and simple lesson is that you—a single individual of extremely limited experience—cannot personally validate even a tiny fraction of the accumulated wisdom of the ages, and disregard tradition or authority at your peril. Yet, we also know that the received wisdom has proven, time after time and often with lethal result, to be hollow or skewed or outmoded or even just plain wrong from the start.

So courage and judgment must be tempered by caution, yet not smothered by it.

The most common error today is not in over-reaching, except in the minor instances of aiming for stardom in sports or entertainment. The more important problem is mindless conformity. This may seem odd to those who look at body-pierced teenagers and listen to their rap noises and think of them as rebels. They aren't rebels, except in the most superficial sense; they are merely testing the limits of what is allowed and achievable in instant gratification. Maybe some of them will be smart enough to become genuine rebels against genuinely oppressive traditions.

Testosterone Poisoning & the Milk of Human Kindness: Evolution assures that individual propensities, on average, have in the past tended to benefit individuals or/and their offspring in the sense of survival and proliferation. This is elementary arithmetic.

Evolution likewise assures that societal propensities have tended to benefit the societies in the sense of survival, growth, and proliferation. Societies that develop self-destructive traits tend to self-destruct.

Two vital points must be reiterated and emphasized. The second point is that times and conditions change, and what was useful in the past may be less useful now, or useless, or even counterproductive.

The first point is that benefit to society does not automatically mean benefit to you, although there is usually a correlation.

Examples of the second point are in the nearly universal disease of boys and young men, "testosterone poisoning". "The male idea of group therapy is WWII." Males are hard-wired for aggression (compared to females, on average), and most boys and young men feel enormous pressure to be brave and tough, to accept challenges, to fight if insulted and take revenge if wronged. Many cultures cause this tendency to be exaggerated by their traditions of "honor". This also has obvious psychological connections to the zealotry phenomenon, although it is not the same.

Conclusion? Your testosterone is part of you, but not all of you, and not the most important part. If your cojones say, "Stand

and die!" but your brain says, "Live to fight another day," you are usually better off listening to the higher authority, if you can't find a way to finesse it. (When it comes to love, I won't repeat the old jokes about the big head and the little head.)

Another example of the second point is the mothering or nurturing or empathic tendencies that usually seem to be more pronounced in women than in men. In *Rosemary's Baby*, the protagonist is raped by Satan and bears His child, and even though she sees with horror that she has borne a monster, she can't resist mothering the little devil. I realize that the behavior of a fictional character is not exactly scientific anthropological evidence, but this has a plausible ring to it. And even though lower animals aren't people, it is suggestive that females with milk will sometimes suckle the young of other species, even a goat suckling a lion cub, we are told. Lions lying down with lambs is apparently already a fact, in the world of mamas and babies.

Examples of the first point—that what is good for society isn't necessarily good for you—are to be seen in abundance. But even before specific examples, it is important to realize that "society" is not only not you, but it is not even the *collective* us.

A society, considered as an "organism" from an evolutionary perspective, is not the sum of its individuals, but something distinct, with no necessary loyalty to or benefit for its individuals.

In Orwell's *1984*, there was one dominant society on earth, divided into three regions or nations. The society was very successful, but not one person in it was happy—not even the dominant oligarchs. Of course, *1984* was fiction, but not such a far stretch from the fascist and communist regimes of the loth Century. For the hive or society to survive and prevail or proliferate, there is nothing whatever that requires you to enjoy life. In fact, your enjoyment might even be counterproductive or inconsistent, most obviously in connection with your work output. To make individuals work hard and die young could easily be the best way for a society to flourish, and that has been a frequent occurrence in history.

People People: Abraham Maslow is well known for his hierarchical view of motivations.

He also separated motivations into those based on "deficiency" and those based on "growth". Hunger is the lowest or most primitive in the hierarchy, and it is one of the deficiency motivations. Self-actualization (fulfillment of creative potential) is the highest in the hierarchy,

and it is in the growth category.

Most people today are "people people." We love to love, we love to be loved, and we need to be needed. Maybe we even need to need. Again, there are obvious evolutionary implications, and again these are impulses we may decide to jettison, although not entirely and not all at once.

I Feel with You—More on the Sharing Problem:

Through the usual combination of heredity and environment, we have a propensity to enjoy the company of others and the approbation of others, and to feel their pain. The various aspects of this need to be examined, reviewed, and in some cases, possibly modified.

We recall first that all predators are naturally disposed to ignore, if not to enjoy, the suffering of prey. By extension, most of us in earlier times were disposed to regard everyone except immediate family as "other" and not entitled to consideration except as property or tools or prey. In the softer circumstances of relatively advanced countries in recent times, many urge the community of man, and some even

the community of life. Some of these will regard the thesis of *Youniverse* to be a horrid throwback to primitive egocentricity and hedonism, an affront to the higher values so slowly and painfully achieved over the ages of human prehistory and history—but that would be a hasty and superficial judgment.

We must constantly remind ourselves that in many cases the apparent anomalies are just language traps. If I treat you well not "for yourself alone" nor as a "higher duty" but simply because I find you useful or your company pleasant, there is no rational reason why that should offend you. There is certainly a practical reason why you might prefer "unqualified" affection

or empathy, since you might find more safety or profit in that situation, but then you would prefer my delusion rather than a rational reciprocation.

Remember too that cold calculation and fuzzy feelings are not always mutually exclusive. If a shopkeeper is friendly and polite, as many are, the main reason is that he profits financially from this behavior. But he still may, and often does, derive social satisfaction from the interaction, and wishes you well, and might on occasion go above and beyond the call of mercantile duty just to be nice, because it feels nice to be nice.

Yet we must bite the bullet and resolve never to forget the bottom line—that when everything has been properly computed, you must come out ahead—not ahead of the other guy, but ahead of the alternatives. Otherwise, you have been suckered.

The Ann Landers Syndrome: Can a psychiatrist change a light bulb? Only if it wants to change.

This old joke helps underscore the extreme difficulty that may be encountered in attempting to change one's values or motivations. I once knew a drunk who said, "I don't have a drinking problem. I have a drinking solution." And then there is the

woman who wrote Ann Landers, complaining that her husband kept pestering her for sex, which she didn't want. The point is that her problem, as she saw it, was not how to cure her frigidity, but just how to make her husband leave her in peace.

Excising a counterproductive drive or urge or habit is generally painful. You are cutting out part of yourself—a diseased part, to be sure, but still it hurts. You make your choice, and—either way—you pay the price.

Misguided Objections to Self-Centrism: Which desires should we follow, and which should we try to suppress or re-educate?

Maclntyre writes that since we have numerous actual or potential desires, many of them conflicting and mutually

incompatible, we have to decide between the rival claims. We have to decide in what direction to educate our desires, how to order our impulses, felt needs, emotions and purposes. Hence the rules of choice, he says, including the rules of morality, cannot themselves be derived from or justified by reference to the desires among which they have to arbitrate.

Aside from the mistake of including "rules of morality" among the "desires", we see here the essential blunder of almost all philosophers. They fall into the error, I presume to surmise, because they are not scientists and tend to allow words to be their masters rather than their tools. In this instance, part of the mistake is in the implicit assumption that all "desires" are on the same footing—an egregious error indeed.

We are not simply pots holding a stew of more or less random ingredients that someone happened to throw in. And even in a chowder, some ingredients are healthier or more nourishing than others. The sprig of parsley, the slice of carrot, and the chunk of fish are very different, and if Mrs. Murphy accidentally threw in her husband's overalls, that would be something else again.

There is a long, hard road ahead in sorting out the types of feel-good or feel-bad, their hierarchies and interconnections, their dependence or independence. But it is "just" a technical (biophysical) project, not the logical impossibility that Maclntyre and others make it out to be, and we can easily see specific instances that eviscerate Maclntvre's assertion here.

For example, surely some of the more basic drives or impulses (sometimes conscious and sometimes not) include those related on the positive or attraction side to hunger, sex, soothing noises, favorable differentials of temperature,

and challenge or the successful exercise of initiative; and on the negative or avoidance side to damaged tissues, falling, loud noises, suffocation, excessive heat or cold or light, fear, and physical coercion. They are not all on an equal footing with regard either to evolutionary precedence or to individual long-term benefit when they give rise to actions. It is not circular reasoning to say that we are driven toward pleasure or satisfaction and away from pain or dissatisfaction. It is not a hopeless project to sort out the varieties of impulses, drives and motivations, and then to calculate maximization of long-term satisfaction.

I don't claim our project is guaranteed to succeed, or that no "philosophical" problems will be found. In particular, as I discuss in considerable detail later, there are unanswered questions about the criteria of survival and indeed about the nature of space and time. But no sophistry can deny that there are such things as pleasure and pain, satisfaction and dissatisfaction, and that some strategies are better suited than others to achieving a clearly desirable outcome (from the individual's point of view).

Guided Objections—Orgasmic Rats & Authenticity: Expanding a bit on the last paragraph above, one can indeed see troubling suggestions in the view that pleasure is our guiding principle and that the pathways of pleasure are built into us.

Greg Egan is one of the science fiction writers who have been bothered by the apparent implications of remaking yourself, e.g., in his story, "Reasons for Being Cheerful". His characters develop ways to provide happiness through chemicals and gadgets that make you feel good almost without regard to external circumstances. We are also reminded of the rats provided with access to a pleasure button, allowing them at will to activate electrodes in the sexual pleasure nodes of their brains and have orgasms any time. According to report, such rats will keep pushing the button until exhausted.

In Egan's story, the main problem is that of authenticity. Who is the "real" you and what do you "really" want? Egan's protagonist feels, at least at one point in the story, that if he can arbitrarily decide which elements of the internal and external environment shall give him pleasure, and which (if any) shall cause him grief, then he has no roots, no authenticity and nothing matters. Will an ethics committee decide who you become?

It seems to me that this type of question, along with the "authenticity" problems of many of the "bioethicists", simply shows a failure to think the thing through.

First, whether explicitly or not, one of the main worries is that we will be tempted to place too much value on "crude" sensory pleasures, or just aesthetics, and not enough on "higher" satisfactions of the "spirit" including not just ordinary aesthetics (visual and auditory etc.) but "moral" or "ethical" as well as intellectual interests. This worry seems misplaced, except perhaps in the case of rats. Even monkeys don't masturbate all the time. For one thing, we have a built-in tendency to limit our attention; just about anything becomes boring if it goes on and on without interruption. Of course, this tendency may depend in part on the fatigue factor, which conceivably could be eliminated; but there are other factors as well. We have-built-in subconscious governors that tend to remind us when we are going off the deep end; even the pure focus of genius has to come up for air once in a while.

Second, even if in some ways, some of the time, we can and do choose or revise our own values, that does not really say much about the "authenticity" issue. If a patient is clinically depressed for either environmental or genetic reasons, and can be relieved of that depression by a drug, does he thereby lose his authenticity? Even if you say yes, would you rather be happily a "different" person or miserably the "original" person? It certainly is not true that the mere knowledge of "inauthenticity" would automatically make and keep you miserable.

It especially needs to be emphasized that precedence or tradition need not and should not be given priority in deciding what is authentic. If precedence were the criterion, every improvement—whether by new species or new abilities in an individual—would entail a loss of authenticity. The word itself —authentic—should probably not even be used in discussions of value. What counts is results, not lineage.

Remember, too, that our choices are not necessarily irreversible, and that the "lower" drives do not by any means always take precedence over the higher. If "martyrs" can do crazy things to satisfy "higher" values, the rest of us ought to

be able to maintain a balance. It's "just" a matter of keeping your eyes open and your head clear and your calculations up to date.

Finally, it helps to remember that "loss of self' happens all the time, in the sense that your maturing and developing self always modifies the values of your earlier selves, and sometimes betrays them. Within each of us, in varying degree, are shades

or remnants of former selves, quick to reproach or accuse or resent. Sometimes you change for the worse, and the reproachful former self is in the right. But you have the watch now, and the helm, and you steer the best you can.

Pratfalls & Ignobility: In attempting to systematize our values as they are and as they ought to be, a slightly different perspective is in the phenomenon of ignoble tendencies, one of which is illuminated by the nearly universal humor of the pratfall.

The reader, or any thoughtful person, will at first be hard put to agree, on the one hand, that our basic values are built on the bedrock of biological need or want—yet, on the other hand, that we can be mean in our genes, in a sense, born to be bad.

The fact is that we were not designed; we just grew, and the parts are not all fully compatible. For example, as social creatures resulting from success in proliferation, we want the esteem and applause or even the servility of others, as well as our own self esteem. This inevitably means that some of us to some extent, and especially children or the ignorant, tend to take pleasure in the misfortunes of others. We can't help this initial propensity; it's hard-wired into us. I very well remember from my childhood, taking secret pleasure in the failures or boggles of other children. (The\pleasure was secret because I already knew this was a "bad" or guilty feeling and was trying to grow out of it.)

Anyone who has ever watched *Funniest Home Videos* knows the overwhelming dominance of the pratfall. There are countless variations, but the essence is that people and animals fall down, and are chagrined. Of course, among civilized people, the funny pratfalls don't do any serious damage, and we can even laugh at our own mishaps, but the underlying ignobility is still there. When the young or ignorant mock and taunt the crippled or deformed or victims of misfortune, we see the full face of the ignobility.

A naive opponent of self-centrism might say this is a fatal flaw in our thesis—that if we insist on the validity of self service, then we should disallow the -ignoble" label. Our logical position, they might say, is that nobility is just in hewing closer to the line of self service despite difficulties or obstacles, and if our nature gives us pleasure in the discomfiture of others, then we should work for the discomfiture of others. If we naturally enjoy the fear and obedience of others, then we should make them subordinates or servants or slaves if we can.

This naive objection, in its various forms, has already been answered repeatedly. The wants or needs that we should promote are those which are most basic and which will hold up best in context and in the long term. This does not yet allow a logically or mathematically exact conclusion or strategy, but I believe it offers the best guidelines available.

Decision Theory—Optimizing the Future: Clearly (well, fairly clearly; we'll note some problem areas later) all our choices and values refer to thefitture. We know of no way to change the past or present (although there are

hints of possibilities!), so our only motivation can be in attempting to shape the future to our preferences. "Long term self-interest" implies that we must always try to calculate or estimate the effects of present choices on future feelings.

As perhaps the simplest possible example, if we decide our future lifetime is likely to have a preponderance of satisfaction over dissatisfaction, then our most basic choice is always to live rather than die. We should then never sacrifice life for anyone or anything.

...And, already we have an example of the inevitable complexities and practical difficulties. If saving your life requires that you sacrifice someone or something you hold dear, you may simply be unable to implement the logical choice. In fact, the "logical" choice may really be *illogical* in the sense that, realistically speaking, your betrayal of love would result in the shattering of your personality and your early death in misery. Yet again, *in extremis* you might grasp at straws, such as reincarnation, and try to balance this slim possibility against the horror of betrayal.

In every case, what counts is a realistic and accurate assessment of the future con-

sequences of present choices—consequences on several different levels.

It should be **emphasized**, before going further, that the question of sacrificing one's life hardly ever arises in practice. Even the question of *risking* one's life occurs rarely in modern circumstances. Usually, the question is vvho will sacrifice certain kinds of convenience or pleasure, who will do the chores and pay the bills, who will carry what share of the load.

So we have arrived at a formulation many people will consider very strange. Trying to decide what we "ought" to do, trying to solve the "normative" problem in personal behavior, we have no hard rules at all about choices—except always to choose to live, and even that with the implicit premise that future life will on balance be pleasant. Instead of fixed rules of conduct, we find ourselves compelled at each stage to make a kind of calculation of probability, trying to estimate the future effects of the proposed action on each of many levels of the consciousness and personality.

Hey, as they say, nobody promised you a rose garden. Later on we'll work through some specific examples, and also look at some difficulties so far only hinted.

Reprise—Basics in the First Approximation: What is it that you want, in the most basic and necessary sense? Clearly, you want to feel good. (We leave until later the study of the various ways of feeling good, their interactions and possible inconsistencies, and their time horizons. We also ignore some of the more esoteric possibilities, restricting ourselves mainly to the likely and feasible.)

Your most basic value is feel-good.

"Want" implies a goal for the future. Clearly, we can expand a bit on the previous statement and say that your most basic value is to *maximize your feel-good over future time.*

Since "you" are localized in your personal skull, your ultimate concern is what goes on inside that skull (in particular, as much feel-good as possible, appropriately evaluated over time). Despite the pretensions of social conventions and standard conditioning, there is no such thing as altruism in any proper sense; your ultimate concern is *always* and *only* for yourself. Hence, *feel-good* also implies *me-first*.

Thus our bedrock of value becomes *me-first and feel-good.*

We next inquire whether it is possible and useful to divide values into the categories of ends and means. We will

conclude that, in general, it is not, since almost all values fall into both categories. However, there is one "means" value, or enabling value, that is unique, since it is the condition precedent for all types of feel-good: survival.

Survival is not quite an unconditional value. As repeatedly noted, if you reasonably conclude that your future life is likely to see a preponderance of pain over pleasure, or dissatisfaction over satisfaction, then you may not want to survive. But I think we can show that such a conclusion would not be reasonable in almost any currently imaginable circumstance. Hence, in most circumstances generally, and probably in all circumstances presently, we can say: *Our most basic single, specific value is self- preservation.*

Survival Fantasies: As remarked elsewhere, the "survival instinct" is highly overrated. In most circumstances of modern life, and especially in the case of older people, the fear of death does not loom large. Old people near death are apt to be matter-of-fact about it, and even welcome surcease. (Admittedly, the evidence either way is not exactly scientific. Physicians attending dying people, and their relatives, and the dying people themselves, are mostly very reluctant to probe or be probed or raise uncomfortable questions. They mostly do "go gentle into that good night.")

Young and healthy people, and especially those given to wonder, may sometimes feel a horror at the incomprehensibility of oblivion. For this and other reasons, people have always concocted metaphors and locutions to talk death to death.

In *The Tempest*, Shakespeare's character says:

Full fathom five thy father lies;
Of his bones are coral made;
Those are pearls that were his eyes:
Nothing of him that doth fade
But doth suffer a sea-change
Into something rich and strange.

There is a saying in Japanese to the effect that Life and death are the same." I am offering a cash prize of $io to anyone who can explain what that means.

There are many devices for suggesting that dead people aren't really, completely, finally dead. A few of them are rational, if extremely speculative, discussed elsewhere in this book. Most of them are merely rhetorical, as above, and as in the notions of reincarnation and the like.

Weakness and stupidity are not crimes in themselves, but self deception—on the part of those who ought to know better —is at the least a breach of integrity. Those who seek comfort at the price of dishonor may lose everything.

A Soft Word turneth away wrath, sayeth the psalmist (or one of those fellows), and those who bridle at an ideal of avoiding pain and gaining pleasure may just possibly reconsider if we change the language a bit.

After all, don't the beneficent gurus routinely tell us we should "make the most" of our lives? Does anyone bristle at that? No. But what does it *mean* to "make the most" of your life? The slightly obscure message is that our greatest potential satisfactions are those of the "spirit", and, in particular, in *achievement*. Even a saint gains his satisfaction through achievement,

which in his case means doing his saintly duty despite all obstacles and discomforts. Need I say more?

Self-Interest by Iteration: I'll not spend much time here on the more elementary aspects of me-first and feel-good; it just amounts to another look at enlightened self-interest, which has had many distinguished defenders. But I will very briefly recapitulate a couple of points.

The main point is that the primacy of self-interest cannot be denied; claims of altruism are always language traps. To the extent that behavior is motivated (rather than accidental or random or a hard-wired habit pattern), no one ever makes a "sacrifice" for someone else or something else. The only sacrifice anyone chooses, ever, is that of one value or one facet of his psyche in favor of another, the momentarily dominant value or personality aspect. In other words, your only motivation is to please yourself—the currently dominant aspect of your psyche —or to avoid a worse alternative. There are no exceptions.

In slightly different words: It is not possible to sacrifice oneself for another person or for a principle. It is only possible to set one value, or one presently perceived good, above another. In the extreme case, you value your prospect of survival less than your desire for virtue or guilt avoidance.

Or: Values are goods like any other, bid and offered in the marketplace of the soul, so to speak. You buy and you sell, you pay and you collect, in coin of your own choosing. How

to avoid cheating yourself, or how to avoid being cheated by your conditioning—that is the problem.

Although there are some fairly subtle pseudo-counterarguments to be cut down, and very formidable barriers of conditioning to be surmounted, the argument for enlightened self-interest is mainly rather simple. But the procedure for ascertaining where self-interest lies, and the strategy for securing it, are not simple.

Part of the problem, of course, is just prior conditioning. Evolution has ingrained in us the tendency toward self-preservation; but also (through evolution of groups and memes) it has inculcated the tendency to self-sacrifice, which in the era of potential immortality needs to be cut back. This part of the problem is imposing in practice, but rather trivial in principle. The non-trivial problem is in the strateu for self-directed evolution of values.

In broadest outline, the problem can be stated in deceptively simple terms—to maximize your personal feel-good over future time. But there are monumental difficulties.

First, of course—once again—there are many ways of feeling good, some of them mutually inconsistent or even ultimately self-destructive. That is why certain classic approaches never gained much favor—hedonism, epicureanism, utilitarianism —even though each of them embodied important elements of truth. Some aspects of this problem still require much study.

Second, it is hard, even conceptually, to accept that values are malleable and transient. It is a bit like a computer program that must not only seek its current objective, but also continually review and reevaluate its own master plan. We have certain present wants —feel-good objectives—but it is not enough to try to satisfy those. At each stage we must ask not only what we "really" want, and which of our wants are most important, but also what we ought to want—what the developed future self is likely

to want as a consequence of the current game plan and possible developments. We attempt to grow by successive iteration.

The new values will have some things in common with the old values—including the need to sacrifice immediate wants for long-term gain. But most people will find it a shocking and staggering concept that, instead of a few rules graven in stone, what we "ought" to do can often only be estimated by a sophisticated mathematical calculation, the maximization of (a certain kind of) expected utility over time, with constant feedback. People or societies or institutions that are too ignorant or too stupid will not only often do the wrong thing—they will not even have a clue how to decide what to do.

Well, once more, nobody said it would be simple. But the task is not really beyond the understanding or capacities of ordinary people, if they are willing to work. One can do "sophisticated mathematical calculations" without a Ph.D. and without making funny marks on paper: it is "only" a matter of developing your intuition, a feel for the texture of reality.

It is certainly difficult to do brain surgery on yourself with a mirror and a hacksaw. Or, if you hammer your psyche too hard, it may shatter. Values can only be changed, and the psyche restructured, slowly and cautiously. Even so, with attention and effort we can gradually modify the bad habits of previous millennia and acquire the traits suitable for immortalists. But now let's look a bit more at some associated questions.

Who Wants Warts? Suppose you are revived after cryonic suspension, but contemporary technology could improve you in the process. It could also revive you as you were and improve you later. "Improvement" in this context we understand to mean replacing some of your habits and attitudes with better ones.

It is difficult for me to imagine that I would not choose to be improved, if I were revived as my old self. But having said that, it is also difficult to see any strong reason for deferring the improvement; why not do it during the revival?

A possible why-not concerns the problems of continuity. If "you" occupy a non-zero volume of space and time, and overlap your predecessors and continuers, then lack of any overlap might just might—imply lack of identity, hence lack of any valid concern for the future version.

Accidental You: We start out shaped by a set of genes—which we did not choose. Our bodies and minds grow and change, partly in response to environmental influences—also initially imposed and not chosen. If the environment is suboptimal, the best potentialities of our genes cannot be realized. As an extreme example, someone raised by wolves will be an idiot; as a slightly less extreme example, someone abused or neglected as a child will be psychologically warped.

Suppose you had an unfortunate background—child abuse or neglect and all that, on top of genetically limited intelligence. (And don't most of us have both of those, in some degree?) You made a lot of bad choices. What is the "real" you? Is it the guilt-wracked wreck with the wretched memories and inferior capabilities? Is it the better and happier person you might have been, or could become after technological intervention? Even if you decide the "real" you is the historical one, is that the one you want revived and perpetuated?

Some would say yes: I want the truth. I want to change and improve—but not retroactively, not

unconsciously, not without my knowledge and consent, and not suddenly. I don't want to keep on licking my wounds, but I want to remember them, or be able to remember them—otherwise there is no validity.

Again, this has a plausible ring, but little if anything more than that. Personally, I would just as soon be rid of my bad memories and traits and habits instantly, and "know" the history only as an archive that I can look up if I wish. At the same time, I want sufficient physical and psychological overlap to justify identification.

You've Got to Know the Territory. You can't go home—unless "home" is just the current place you tie your goat.

There may be said to be two basic questions: (i) what is the self? (2) How can it best be satisfied?

These questions are basically biological/physical. They do not necessarily have answers that we will like, or any unequivocal answers at all. The universe is not necessarily user-friendly. Time may separate successive "selves" as decisively (or indecisively) as space separates twins or duplicates.

But unless we opt for the cow or ostrich "solutions" (stupid contentment or refusal to face unpleasant facts), we can only push on. We must mostly ignore Level Two at first, e.g., the "philosophical" questions involving paradoxes of continuity and so on, relating to time and quantum reality and similar matters presently beyond our reach. On Level One, we ignore some of the subtleties and take first things first.

Questions for the Laboratory: Can amateur philosophers help the experimentalists? To get the right answers, it helps to ask the right questions, and conceivably, we can contribute a little here.

First, we are *not* likely to find localized brain regions identifiable with the self by any of the currently known experiments. For example, we know that stimulation of certain points in the brain produces sensations —but so does stimulation of points on the skin and elsewhere. Those known points in the brain are more likely way- stations or switching points than parts of the central self.

Second, once we have located and identified the self circuit or aspects of it, we have to learn what constitutes pleasure/ satisfaction and the opposite.

Is it a single condition, state, or sequence of events? Or is there more than one kind? Can more than one kind coexist? If more than one kind can coexist, with different strategies favoring each, then life becomes even more complicated.

Who's in Charge? Short Circuits & Overrides: One of the most remarkable of all facts is the dominance of presumptively secondary or derivative satisfactions in practical motivation. Most of us, most of the time, would rather finish a game of tennis than go home early because of hunger. Much more bizarre, many of us will stake life itself on a fine point of politics or theology. Is this appropriate, or in some sense a tragic accident of development?

To hammer the point, it seems clear that the most primitive organisms with feeling and LAWKI had only "physical" pleasures and pains, not intellectual or "spiritual" ones. Intellectual satisfactions are of course ultimately just as physical as the primitive pleasures; but are they variations, intermediaries, or something new or different?

Not only can people choose "spiritual" values despite physical pain, but physical pain may even be unnoticed by people caught up in battle, sports, religious martyrdom, or even just intense intellectual concentration. This suggests that the self circuit is not a mere register for physical sensations, even though it may have evolved for that purpose.

If "spiritual" values (perhaps including such things as music appreciation) can be imprinted onto or attached to the basic self circuit, becoming a physical part of your (current) biological nature, that would seem to imply that you are basically infinitely malleable. Then values—even the most "basic" of biological imperatives—are not permanent givens.

If we can want whatever we choose to want—if what we *ought* to want is a complex feedback function of current wants and calculations of the future probabilities associated with various strategies—then almost all current worldviews are by the board. The philosophical and political implications are beyond present reckoning.

Rationally Irrational? This is repetitious, but important. Many have pointed out implicitly, and some such as Cornell's Robert Frank explicitly, that "calculative rationality" is not always such a neat idea, if approached without great care. We have evolved tendencies to reflect this—for example, the notions of fairness and social approval. We tend to dislike people who don't play fair, and we will often sacrifice short term self interest rather than allow a cheater or villain to prevail. A display of anger, even if immediately counterproductive, may help check the evil-doer's impulses. Displays of gratitude or affection likewise may help reinforce behavior we approve, and we may offer such rewards in ways that are disproportionate in the short term.

Such patterns can also be overdone, obvious examples being vendettas or an inability ever to relinquish a grudge.

On the level of society, these considerations are sometimes reflected in the philosophy of jurisprudence and criminal justice. Many "progressives" think punishment of almost any kind is just revenge, barbaric and fruitless. But revenge—personal or societal, within bounds—is a perfectly legitimate object, which tends to help maintain morale and stability.

A Tentative View of Survival—The Overlap: "You" consist essentially of your brain, or some parts and functions of it.

You cannot exist at a geometrical point in space, if there is such a thing. You necessarily enclose a non-zero volume—you have spatial extension or you "bind space". In particular, your "self circuit" has spatial extension.

Since presumably nothing can happen in zero time, and it takes time for signals to move around in the brain, or for a self circuit to perform an oscillation, any subjective experience you have probably requires non-zero time. You can't feel anything at an "instant" of time, if there is such a thing. Thus, an indivisible you has temporal extension or duration. You "bind time".

This means that you overlap your predecessors, as well as your successors or continuers, in space and time. You are at least in part the *same physical person* as your recent and near-future selves, as well as the same psychological person. Thus "your" interests are to at least a considerable extent the same as those of your near-future self. It is therefore logical, as well as an inevitable result of evolution and an almost inescapable intuition, that we "identify" with our future selves, and more strongly, with our

nearer future selves.

A Deeper Look—Changing Your Biology: A main aim of this book has been to debunk the two most common views of value—that it is externally given, or that it is arbitrary. The second is much the more slippery.

In the context of today's knowledge and capabilities, it is difficult enough to expound the view that our basic biology —the anatomy and physiology of the brain, including the "self circuit"—allows and mandates a unique rational approach to a value system. You are what you are, and that determines what is good or bad for you. To be sure, you can change what you are at some level and in some degree, but the basics are difficult, if not impossible, to alter. Some brain events feel good and some don't.

But at some point, we may be able to change our own biology even at the most basic level. If the uploaders are right (which I doubt), then it may become possible in less than a century, within the lifetimes of most people now living, to transform or transfer ourselves into electrolife, which would permit the equivalent of millennia of biological change in years or even minutes, and remove most design constraints.

This is not terribly interesting as a practical problem at present. It's just not a suitable conduit for our energies; many other problems are more pressing. As a purely philosophical problem, it has a certain interest, but let's stop here for now.

Guilt: Although I have many arrows in my quiver, my main aim is a nitty-gritty practical one—to help ourselves solve our problems of planning and conduct. One of the chief impediments—and also one of the chief motivators—is guilt.

Countless wretches allow large segments of their lives to be dominated by feelings of guilt, unworthiness and emotional debt. Countless others delude themselves that they have jettisoned guilt, when they have only swept it under the rug. Hordes also feel guilt for the wrong reasons, often 180 degrees wrong.

As motivation, guilt serves us, the consciously self-interested, just as it serves or seems to serve anyone, by nudging conscience when we fail, or threaten to fail, in our duty to ourselves. Nothing very complicated here, except that we hope, over time, to eliminate the negative emotion and instead rely on intelligence and habit. Yes, this means a "colder" persona, if you choose that language, but "calmer" would be more appropriate. You can be alert and quick and still be calm.

Perhaps the most obvious cases of guilt as impediment arise in connection with violation of societal norms or previously inculcated "normal" habits. If your best and broadest analysis clearly shows a need to betray a former allegiance or habit, then you will almost inevitably tend to feel some guilt.

The only cure I know is the traditional one, in cases where one loyalty is pitted against another. You hold fast to your primary conviction, and rely on growing habit and the passage of time to subordinate and erode the guilt, which will finally retreat snarling into its cave. There are also many little tricks that may be adapted here, such as slogans or ditties and reinforcement by the like-minded.

But there is also the opposite case, where you obey societal norms and thereby fail in your duty to yourself. If you are consciously self-interested you will, in effect, have two partly separate sets of norms vying for influence, and

some decisions will necessarily make you guilty from one point of view or the other. If you have failed yourself, then you may need the feeling of guilt to help you make corrections and firm up your new habits. Again, reinforcement by the like-minded can help.

More subtly, there are interesting and important questions in management of one's own persona. My wife Mae used to say that, faced with unhappy situations, we can still choose whether to be gloomy or cheerful. As the old song has it, you've got to accentuate the positive, eliminate the negative, and don't mess with Mr. In-Between. Of course, Mae was often unable to benefit from that attitude, but there is still potential help in it. Few of us can choose by an act of will to turn on a dime in the face of adversity and accentuate the positive, but we can often make some moves in that direction.

Part of the reason for the difficulty we find in overcoming guilt or sorrow is the notion of payment. We have a built-in implicit notion that, by feeling guilt or sorrow, we are atoning for our faults or/and reaffirming our loyalty to whatever or whomever was lost.

Evolution has given most of us a medium-sized "conscience" in this area. For example, bereavement (say of a spouse or sibling) usually results in intense feeling and change of habits for a year or two, with a gradual easing. Those who rebound from bereavement too soon or too late, too much or too little, are regarded as abnormal. In logic, if psychological health would permit, rebounds ought to be virtually instantaneous —maybe a big wake and then 100% back to the land of the living. Once more, the only ways I know to approach this would involve tricks such as slogans and songs, along with networks.

Taken to the extreme, Jack Erfurt's slogan of "fuck guilt" would lead us in the direction of Pearce's "hedonistic imperative" so that we always find a way to do what is best without any taint at all of pain or even discomfort. Whether such a thing is possible, even in principle, is still unknown—but we do know that at best it is far in the future. For now we have to live with guilt to some extent, but we can surely cut it back and pare it down.

More on the Hedonistic Imperative: I have previously mentioned David Pearce's work (hedweb.com), and have recently found a development of that. See www.bltc.com/

Some excerpts from that site:

"BLTC RESEARCH was founded in 1995 to promote paradise-engineering. We are dedicated to an ambitious global technology project. BLTC seek to abolish the biological substrates of suffering. Not just in humans, but in all sentient life.

"Absurdly fanciful? No. The blueprint for a Post-Darwinian Transition to a cruelty-free world is conceptually simple, technically feasible and morally urgent.

"The ethical importance of the decisions we take can scarcely be exaggerated. For soon we'll be forced to choose how much suffering in the living world we want to conserve and create. Or we can choose instead to abolish suffering completely.

"Life on earth can be animated by gradients of ecstatic wellbeing beyond the bounds of normal human experience.

"In the end, the greatest obstacles to lifelong superhealth and a cruelty-free world may prove ideological, not technical. BLTC RESEARCH campaign to promote paradise-engineering as

a rigorous academic discipline and a mature applied science."

This is a stunning and admirable vision, but almost certainly close to hopeless in terms of any significant impact in the foreseeable future.

The Trouble with Psychotherapy: Most of us have been influenced in some degree by the spate of psychological and pseudopsychological chatter by professionals and semipros. Much of the jabber has a degree of merit, in context; but it can also be seriously or even fatally misleading.

Here's the nub: From the psychologist's viewpoint, the key goal is mental health—even though there is no agreement on the meaning of this term. Presumably it includes stability of the psyche. But stability and comfort do not rank first among ends. In many situations, for example, stress is essential to success, if not to survival. Worry is not a good in itself, but sometimes only worry will expose the perils and the opportunities. With this red flag waving high, let's look next at a few of the useful hints from professionals.

A Mirror and a Hacksaw: As remarked elsewhere, it's not easy to do brain surgery on yourself using a mirror and a hacksaw. Changing the metaphor, you may consider yourself both the sculptor and the marble, and you must use bold strokes and make the chips fly, which could be painful. But a number of writers and practitioners have given us encouragement in the possibility of improving and even "changing" yourself—even though their standards of "improvement" are often different from mine.

George Weinberg (Ph.D. psychotherapist) has written several books—one of them three times, so to speak. *The Action Approach, Self Creation* and *The Pliant Animal* all had more or less the same theme, that by analyzing your problems and deliberately modifying your behavior, you can also change and improve your inner life.

Weinberg teaches in thw school of William James, the nineteenth century American philosopher and psychologist, who wrote:

> *"Action seems to follow feeling, but really action and feeling go together, and by regulating the action, which is under the more direct control of the will, we can indirectly regulate the feeling, which is not."*

We also remember "Whistle a Happy Tune" from *The King and I*, and the admonishment of Blaise Pascal, who said that by following religious observances and rituals, we could gradually gain faith, even if we lacked it beforehand. And of course, many rabble-rousers have exploited this device with the leverage of zealotry. So the principle can be used or misused, another warning.

Happy self-creation.

And Finally, An Extreme Example of a Warped Sense of Duty: *Casabianca* is a poem by Felicia Dorothea Hemans, first published in the *Monthly Magazine* for August 1826. The poem opens:

The boy stood on the burning deck
Whence all but he had fled;
The flame that lit the battle's wreck
Shone round him o'er the dead.

He stands his post until he goes down with the ship, because he has no orders or permission to leave. The poem was taught to generations of British and American children as an example of heroism—even though (if the story was true) the young boy's sacrifice served no useful purpose, other than his irrational sense of honor.

This is the mindset I ask you to reject.

Next Issue: *Chapter Six: Ethics 1—Interpersonal Morality*

10 Worst Mistakes in Cryonics

Don't ruin your chance for a succesful suspension

1) Not signing up ahead of time

Becoming a member, having contracts in place, and having paperwork in order should not be a last minute decision. Waiting until the last minute or after death results in an unnecessary delay of care or worse- No suspension at all! Don't wait. Sign up here and be prepared. **https://www.cryonics.org/membership/**

2) Not providing proof of funding

Some people believe that they can worry about funding later or if they have funding, they have put off providing proof of funding to CI. This should be done annually. Failing to provide this can result in a delay of care while the funding clears, which can take weeks. Send your proof of funding to CI now to be prepared.

3) Not telling anyone your plans

Being reclusive or not telling family or friends your wishes is not recommended. You should not be afraid to tell those around you what your wishes are, especially your next of kin. Wearing a bracelet, necklace or having identification or other items in view can speak to your wishes. This is all you have when you can't speak for yourself. Disasters have resulted in the past from not sharing. Talk with your family, close friends and your estate attorney, so you can be prepared.

4) Not planning

Many think cryonics is a turnkey service where you can just sign up and let fate take over. No matter how much you pay for cryonics, you are the only one who can make sure that you will have the best chance by planning. CI has provided a lot of information on our website and in our standby manuals. Those who plan succeed those who don't fail.

For more information visit: https://www.cryonics.org/resources/ci-standby-kits-and-instructions

5) Not notifying CI of Emergencies

There is no way that your cryonics provider can help you if they do not know of your emergency. Your family, friends, standby group or next of kin must immediately contact CI when you are having health issues or worse. It is also important for CI to know if you have up and coming surgeries or procedures, including terminal illness. Patients with a diagnosed terminal illness could enter hospice care, which might help your cryonics situation vastly. Any delay in notifying us directly could result in a poor suspension. Those helping you must have simple and clear instructions.

Here are some tips... https://www.cryonics.org/resources/category/C57/57

6) Committing suicide

Anyone who commits suicide who is not terminally ill or breaks a local law in doing so is potentially putting both themselves and our organization at great risk. CI will not risk itself for people who engage in behavior that goes against our mission to preserve life. Such activity will likely lead to an autopsy and long delays, rendering the suspension process substandard or impossible to carry out.

Do not consider cryonics as a way out of your problems. You are likely to not get suspended under those circumstances. If you do not have a terminal illness and are considering suicide, you should seek mental health advice and treatment as soon as possible. https://www.mentalhelp.net/articles/depression-hotline/

7) Engaging in Risky or illegal activities

Risky behaviors or associations that lead to the patient dying around suspicious circumstances will also likely lead to mandated autopsies that will also stand in the way of your cryonics wishes. It is best to use common sense and not put yourself in harm's way. Not only could your

10 Worst Mistakes in Cryonics

life be ended, so too could your chances of cryonics suspension or future reanimation. Use common sense and stay safe.

8) Providing financial or legal incentives that encourage your **not** being suspended.

Leaving all of your insurance or cryonics money to family if you are not suspended is certainly an option at CI, but ironically it does provide financial incentive for hostile family members to block your suspension. As often is the case, people will make sure you are not suspended to get a hold of your money.

One suggestion is to leave family and next of kin some separate money from cryonics funding while suggesting that Cryonics funding go to cryonics as a donation no matter if you are buried or suspended. In addition, family or next of kin can be further compelled to cooperate if they will actually lose the money that is allocated to them for not cooperating. It is also suggested that your family be made fully aware of your wishes and stipulations, so they know what the results of their actions will be. You want to make sure you put incentives and disincentives in the correct place, so that your wishes are honored. It is suggested that your will and cryonics documentation reflect this and get reviewed by an attorney. See https://www.cryonics.org/resources/protect-yourself-from-legal-threats

9) Not removing a hostile next of kin from rights to your remains and finances

In many states and areas you can legally remove a hostile family member or next of kin from your estate. You can reassign someone who is sympathetic to cryonics and who has the legal authority to disposition of your remains, as well as your assets. In some states and locations there are disposition of remains reassignment documents, as well as powers of attorney, both in regards to financial as well as medical decisions. The executor of your will or anyone involved with making decisions should be sympathetic to your cryonics wishes. It is your responsibility to make your wishes very clear and to remove any doubt or potential legal resistance from family or next of kin.

We suggest seeking legal advice to help you in this regard. Some members have even made a video statement of their wishes and given it to both their cryonics organization as well as their attorneys. Not being careful could mean that you don't get suspended, despite your wishes. Many are surprised to learn that they lose their rights upon legal death. See an attorney and prepare.

10) Dying under less then favorable conditions

This seems harder to control then the other situations, but there are some things you can do to make your situation more favorable. You can diet, exercise and follow the latest official medical advice to stay healthy longer. The longer you are alive, the better the technology will probably be for suspending you and the closer we will be to a future that may be able to reverse your condition.

You can also avoid travel to remote or hostile places where such travel is risky. Some overseas travel can result in long delays both logistically and bureaucratically. In general, dying near your cryonics provider or cryonics standby group helps your chances. Living a healthy lifestyle and staying sociable, while surrounding yourself with people who will act on your behalf is paramount. Building solid, positive relationships with good people is probably one of the most important things you can do to have your wishes honored. Take care of yourself and maintain social connectivity.

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Bulletin Board

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Got something to say?

The CI Newsletter is looking for submissions from our readers!

If you've got a great idea for a story, please forward it to:

dg@cryonics.org

CRYONICS QUESTIONS?

Need some help with your membership?

Want to understand your suspension options?

Need to fill out important cryonics paperwork?

CONTACT US!

Our team is here to help.

1-(586) 791-5961

FREE Memberships?!!

Did you know the Cryonics Institute offers FREE LIFETIME Memberships for minor children of paid Lifetime Members? Any minor children (under the age of 18) of fully-paid Lifetime Members are eligible for a permanent Lifetime Membership of their own. If you'd like to give your children the priceless gift of a second chance of life with you in the future, please contact us at 1 (586) 791-5961 and ask about Lifetime Membership Benefits.

Show the world you support cryonics with CI gear from our **Cafe Press store**.


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