Evidence-Based Cryonics

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UK Cryonics and Cryopreservation Research Network

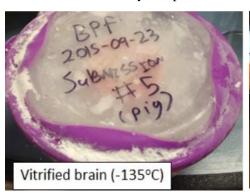
www.cryonics-research.org.uk João Pedro de Magalhães, Chair +44 151 7954517 aging@liverpool.ac.uk

Groundbreaking Scientific Results Show that the Proposition of Human Medical Biostasis has Potential and Needs to Be Brought into Mainstream Scientific and Medical Focus

Recently we have seen evidence that long-term memory is not modified by cryopreservation in simple animal models (C. elegans nematode worms, see appendix). Other small animals can also be healthily revived after storage in liquid nitrogen at -196° C (O. jantseanus leech).

It was previously known that in mammalian brain slices, viability, ultrastructure, and the electrical responsiveness of the neurobiological molecular machinery that elicits long-term potentiation, a mechanism of memory, can be preserved without significant damage following cryopreservation. Published transmission and scanning electron microscopic images from a whole brain cryopreserved through vitrification also indicate structural integrity.

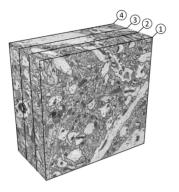
And now, a new cryobiological and neurobiological technique, aldehyde-stabilized cryopreservation (ASC) today won the large mammal <u>Brain Preservation Prize</u>, announced in 2010 by the <u>Brain Preservation Foundation</u> (BFP). This provides strong evidence that large mammalian brains can be preserved well enough at low temperature for hundreds of years for neural connectivity and the connectome to be completely visualized. The connectome is believed to be an important encoding mechanism for memory and personal identity (i.e., where the mind lives) within the brain.

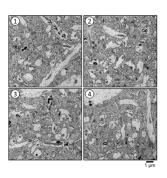




Left Picture: Vitrified pig brain at -135° Celsius (-211° Fahrenheit) - a temperature at which chemical and biological actively virtually stopped and storage without any change or degradation is possible for not centuries if millennia. Right Picture: Previously vitrified brain after rewarming later subjected to extensive electron microscopic examination, showing that near perfect ultrastructure was preserved. Source: 21st Century Medicine / can also be accesses at BPF here.

This is a truly groundbreaking result. It puts the proposition of human medical biostasis as a way to save humans who otherwise would die squarely within the realm of what may be possible.





Frames from a FIB-SEM stack of mammalian neuropil near the CA1 band of the hippocampus. "Overall structural preservation is excellent: processes are clearly defined and organelles are intact. When observing slices of this volume in sequence, it is easy to track the progression of any process through the stack, demonstrating that connectivity in this region was not impaired by our preservation method (see full video available in online supplemental materials)". "KR8H washout solution. Vitrified; CPA removed by diffusion. Experiment date: 2015-04-15." Source: R.L. McIntyre, G.M. Fahy / Cryobiology 71 (2015).

This technology and these results were recently <u>published</u> by Robert McIntyre and Dr. Gregory Fahy in the journal *Cryobiology* of the Society for Cryobiology. Dr Fahy is the inventor of large tissue vitrification (<u>Cryobiology 21, 407-426 (1984)</u> and <u>Nature 313, 573 - 575 (1985)</u>), and the Chief Science Officer of organ banking R&D firm, 21st Century Medicine, Inc. Robert McIntyre is an MIT graduate and neuroscientist who recently cofounded the company Nectome.

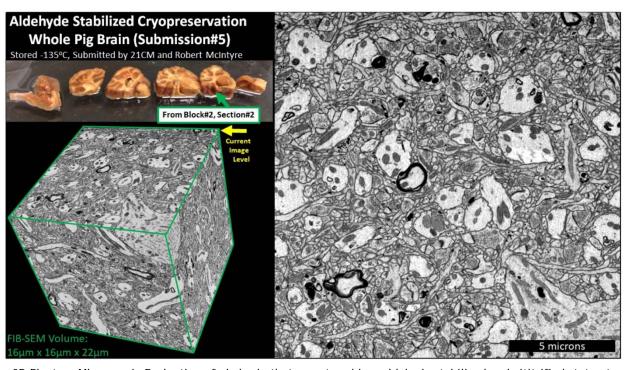
<u>First demonstration that long-term structural preservation of a large intact mammalian brain</u> is achievable wins the Brain Preservation Prize

"This result directly answers what has been the main scientific criticism against cryonics - that it does not provably preserve the delicate synaptic circuitry of the brain - and sets the stage for renewed interest, research, and debate within the mainstream scientific and medical communities"

Brain Preservation Foundation press release when the small mammalian prize was won

These results come nearly 8 years after the Brain Preservation Foundation (BPF) launched the Brain Preservation Prize. According to the BPF, in the small mammalian brain preservation prize, 21st Century Medicine narrowly beat a team led by Dr. Shawn Mikula at the Max Planck Institute of Neurobiology, which focused on chemical preservation and plastic embedding without cryopreservation (published recently in *Nature Methods*).

In addition to the accomplishment and the full "Aldehyde-Stabilized Cryopreservation" protocol for larger pig brains recently being published in the peer-reviewed journal *Cryobiology* by 21CM, it has now been independently verified by the BPF through <u>extensive electron microscopic examination</u> (link also includes videos). The prize was independently judged by neuroscientists Dr. Sebastian Seung, Professor at Princeton University and Dr. Kenneth Hayworth, President of the BPF and former Harvard scientist.



3D Electron Microscopic Evaluation of pig brain that was stored in a aldehyde stabilized and vititrified state at -135° Celsius (-211° Fahrenheit) (see first and second figures above on page 1) figure above after Source: The Brain Preservation Foundation, click here for further images and also videos.

"Imagine being able to save, and at low temperatures, indefinitely preserve people who can no longer be sustained by contemporary medicine so that future medicine can both revive them and restore their health – these results provide strong support of that being possible"

Dr. JP de Magalhães, Chair, UK Cryonics and Cryopreservation Research Network "In the winning of the Brain Presevation Prize, one of the most important scientific results in the history of medical biostasis and cryonics has been accomplished"

> Aschwin de Wolf, Cofounder, Evidence-Based Cryonics

What Does This Breakthrough Mean (and NOT Mean) for Cryonics - Our Perspectives

(Any of the below can be attributed as quotes from Aschwin or João Pedro)

- Aldehyde Stabilized Cryopreservation (ASC) is a proof-of-concept that brains can be preserved cryogenic temperatures without ice formation for neural connectivity (the connectome) to be completely visualized using current technology. The connectome is believed to be an important encoding mechanism for memory and personal identity (sense of self/where the mind lives) within the brain.
- This is a truly groundbreaking result. It puts the proposition of human medical biostasis as a way to save humans who otherwise would die squarely within the realms of the possible. Medical biostasis now clearly warrants mainstream scientific discussion, evaluation and focus
- The avoidance of freezing damage in ASC is based on vitrification, a technology from mainstream organ banking research that was introduced in cryonics in 2001 by Alcor Life Extension Foundation.
- The implementation of ASC that won the first Brain Preservation Prize also utilized a blood-brain barrier opening technology first studied for cryonics use by cryobiologist Dr. Yuri Pichugin at the Cryonics Institute ten years ago.
- The idea of ASC (even including specific use of the chemical glutaraldehyde) originated with Dr. Eric Drexler's book <u>Engines of Creation</u> in 1986 under the name "fixation and vitrification" where it was specifically suggested for use in cryonics
- At the same time it is crucial to note that we primarily see this accomplishment as <u>an important stepping stone</u> towards true reversible human biostasis through cryopreservation/vitrification without the destructive nature of fixation and cross-linkages. Such approaches better meet precautionary/conservative principles about ensuring that everything that is needed in order to preserve a human's entire self has actually been preserved.
 - In fact, even though the general idea of ASC has existed since 1986, the field of cryonics has preferred to avoid use of chemical fixation because the resulting chemical changes (the same as embalming) are extreme and difficult to evaluate in the absence of at least residual viability.
 - Fixation is also known to increase freezing damage if cryoprotectant penetration is inadequate, further adding to the risk of using fixation under non-ideal conditions that are common in cryonics.
 - If future research shows that ASC can indeed preserve enough information to permit computer emulation of animal brains, this will have to be reevaluated.
 - Currently, our view is that ASC is more an important stepping stone towards a repair-free form of human suspended animation than a final solution itself.
- The first proposed revival method for ASC was actually reversal of chemical cross-links and repair by
 molecular nanotechnology resulting in revival of a biologically natural human, not mind uploading (see
 Engines of Creation).
 - Therefore, while the combination of ASC, destructive scanning, and mainstream brain emulation research may provide a route to cryonics revival, ASC is also compatible with revival in natural biological form by using foreseeable molecular nanotechnology¹.

For more information, references and suggestions on scientists to talk with contact:

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¹ Drexler, K. E., "Molecular Engineering: An Approach to the Development of General Capabilities for Molecular Manipulation," Proc. Natl. Acad. Sci. U.S.A. 78(1981):5275-5278. Ralph C. Merkle, "The Technical Feasibility of Cryonics," Medical Hypotheses 39(1992):6-16. Robert A. Freitas Jr., "Comprehensive Nanorobotic Control of Human Morbidity and Aging," in Gregory M. Fahy, Michael D. West, L. Stephen Coles, and Steven B. Harris, eds, The Future of Aging: Pathways to Human Life Extension, Springer, New York, 2010, pp. 685-805.

Appendix – Context in which You May Want to Cover This

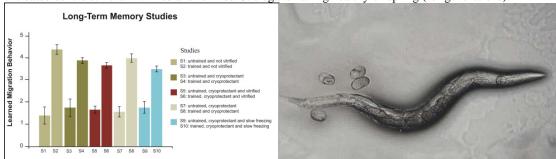
- Ever more leading people believe that it may be possible to arrest aging within a generation. Just a few examples of significant efforts towards this end include:
 - Google starting a new company called Calico with at least \$1.5 billions in "seed funding" that has the aim defeating death and that has recruited world class scientific and business talent, including former Genentech CEO and Apple Chairman Dr. Art Levinson.
 - o Meanwhile, Dr. Craig Venter, who famously tied the US government to sequence the first human genome and then created the first organism with a synthetic genome, has formed <u>Human Longevity</u>, Inc to work on ending aging.
 - o And Peter Thiel, who co-founded PayPal and is a successful biotech investor is making big investments in life and health extension via his investment firms and the SENS Foundation.
- But without a path towards medical biostasis enabling "<u>medical time travel</u>" or <u>human cryopreservation</u>, millions, if not billions, of humans will die before achieving "longevity escape velocity".
- The "Scientists' Open Letter on Cryonics" that is administrated by Evidence-Based Cryonics, with
 - Signatories encompassing all disciplines relevant to cryonics, including Biology, Cryobiology, Neuroscience, Physical Science, Nanotechnology and Computing, Ethics and Theology.
 - o Signatories including leading scientists from institutes such as MIT, Harvard, NASA and Cambridge University to name a few.
- Just recently scientists began to come together in the UK and founded <u>The UK Cryonics and Cryopreservation Network.</u>
- The definition of what constitutes death continues to evolve and there now is a consensus that it is a process and not an event that occurs at a given moment:
 - o More and more cases are reported and document in leading journals like the Lancet of people who in accidents in the cold enter a state of suspended animation for hours without heart beat or brain activity and are then resuscitated after being considered clinically dead.
 - And more and more surgical procedures rely on this phenomenon, <u>intentionally arresting brain activity</u> with the help of hypothermia and drugs.
 - Recently the FDA even approved <u>Defense Department funded clinical trials</u> to induce profound hypothermia (<10°C) in critically injured trauma victims, effectively shutting the brain down and restarting it later to buy time to save the patient's life.
 - o And <u>DARPA</u> just announced a human biostasis program while <u>NASA</u> has is funding human torpor research.
- The public's interest has increased after for instance
 - o The New York Time's Cover on <u>"A Dying 23 Year Young Woman's Hope in Cryonics and a Future"</u>.
 - o Media from all over the world featured <u>the youngest person to be cryogenically preserved</u> a two year old baby.
 - o A <u>14-year-old girl dying of cancer was allowed by the high court in UK to have her body cryogenically preserved</u> in the hope that she can be brought back to life at a later time.

Each of these recent stories generated perhaps the largest amount of public discussion of cryonics since Ted Williams was cryopreserved.

 Leading to mainstream scientists and physicians entering the debate in support of the concept of cryonics – see for instance the recent piece: <u>The Science Surrounding Cryonics in the MIT Technology</u> <u>Review</u>

- And "More than 1/5th of Germans Imagining Doing Cryonics" as published in a recent peer-reviewed article
- There is a growing momentum towards organ cryobanking among the world's scientists and government agencies where the remaining sub-challenges were codified at a global scientific summit at Stanford (Note: The high level and main sub-challenges in the cryobanking of a hearts, kidneys or livers are almost identical to those of banking a brain). And a recent consensus article by 42 leading scientists, transplant surgeons, Noble Prize and Breakthrough Prize Laureates, etc, on solving the remaining sub-problems of organ cryobanking was published (www.nature.com/articles/nbt.3889.pdf) and a second global summit on oran cryobvanking was convened at Harvard Medical School and covered in the Proceedings of the National Academy of Sciences (PNAS) and again in Nature Biotech.
- Just within the last year or so we have seen we have seen scientific evidence and publication on
 - That <u>long-term memory is not modified by the process of whole organism cryopreservation through vitrification and revival</u> in simple animal models:
 - For decades, C. elegans roundworms have been cryopreserved at liquid nitrogen temperatures and later <u>revived successfully</u>. And in October 2015 it was <u>published</u>, that using well-established assays for assessing recall of long-term memories practically 100% of C. elegans can survive cryopreservation through vitrification, and <u>retain learned behaviors acquired before cryopreservation</u>.

Right: Regardless of cryopreservation method (vitrification / slow freezing) or cryoprotectant use, memory scores of trained C. elegans after cryopreservation and warming do not differ significantly from trained but untreated controls. Left: Vitrified and revived C. elegans having healthy offspring (for generations).



Adapted from Vita-More, N. & Barranco, D. "Persistence of Long-Term Memory in Vitrified and Revived C. elegans."

- o that other animals can be healthily revived <u>after storage in liquid nitrogen at a temperature of </u>
 -196°C (ozobranchid leech)
- o [and less relevant, the recent publication and story in new news this month about healthily revival after 30 years of high-subzero cryopreservation (water bears)]
- Perhaps this means that we are closing in on the vision of US Founding Father (and polymath) Benjamin Franklin, who in 1773 wrote to Jacques Dubourg (French physician and inventor):

"It appears that the doctrine of life and death in general is yet but little understood...

I wish it were possible... to invent a method of embalming drowned persons, in such a manner that they might be recalled to life at any period, however distant; for having a very ardent desire to see and observe the state of America a hundred years hence, I should prefer to an ordinary death, being immersed with a few friends in a cask of Madeira, until that time, then to be recalled to life by the solar warmth of my dear country!

But... in all probability, we live in a century too little advanced, and too near the infancy of science, to see such an art brought in our time to its perfection..."