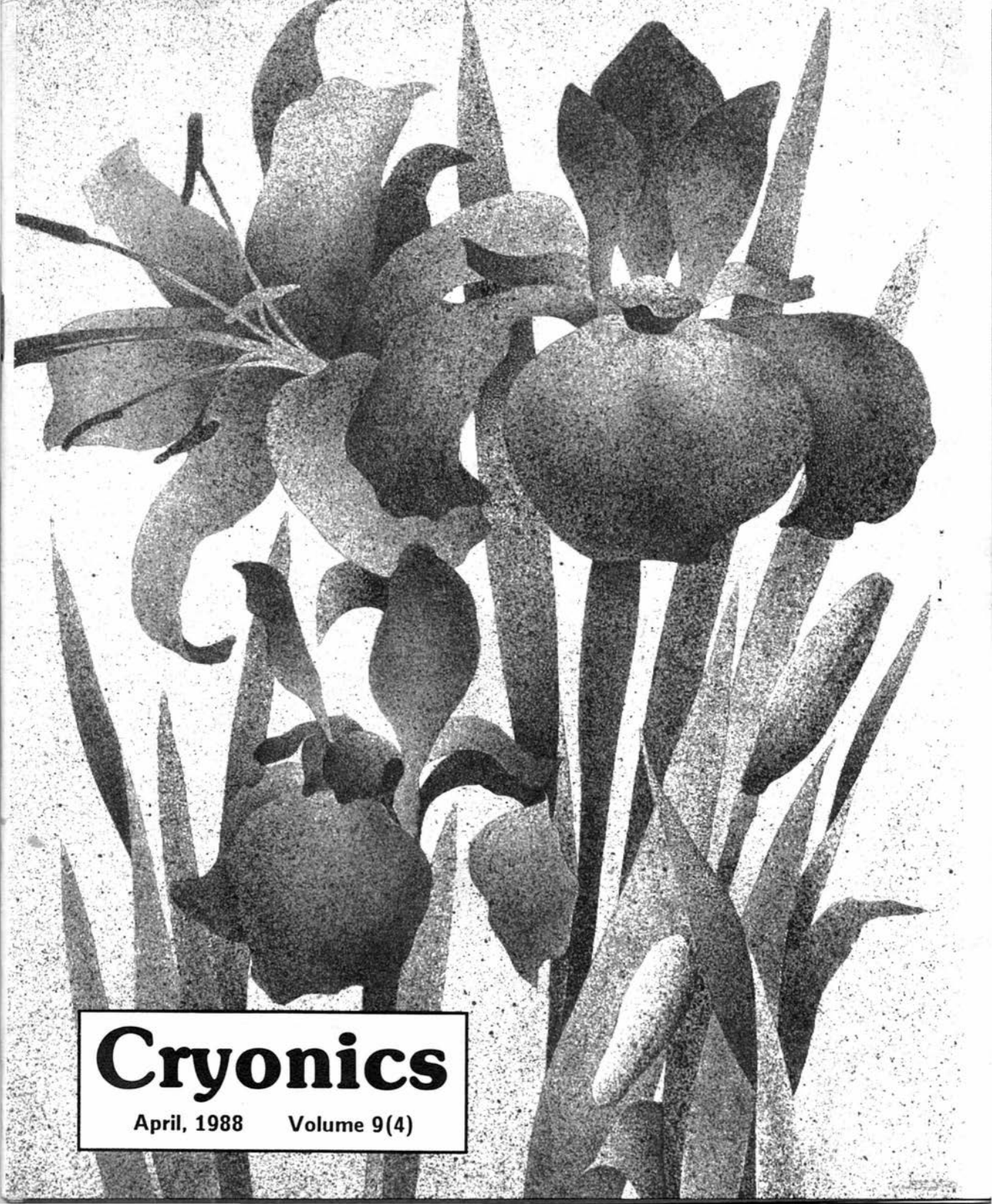

Cryonics

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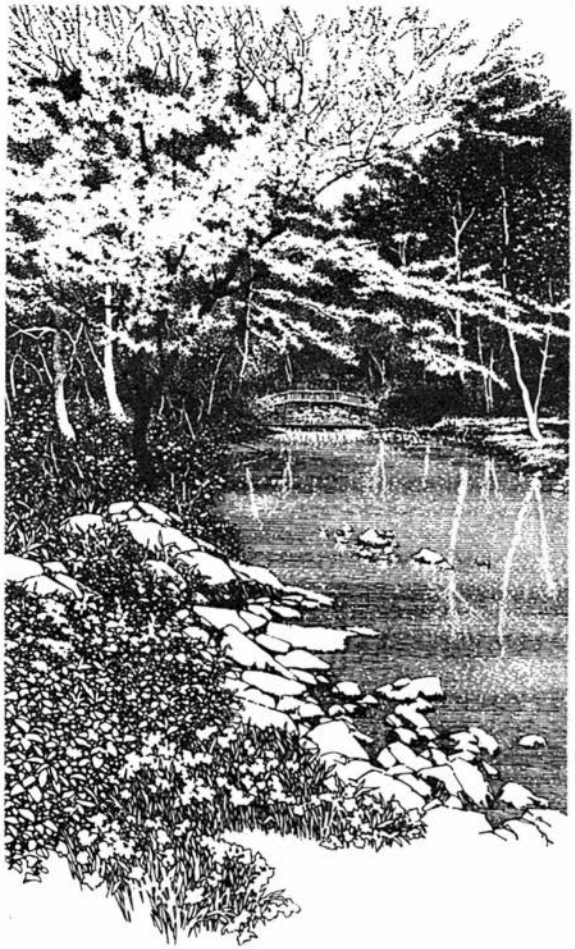

EDITORIAL MATTERS

This month's issue of *Cryonics* will not have much in the way of "timely news" since it is being produced back-to-back with the March issue (which is running nearly a month-and-a-half behind schedule). We realize that you folks are hungry for up-to-the-minute news, and we are sorry we can't do a better job of providing it. This is one time when all we can say is "watch the newspaper and TV news" if you want to know what's happening. And believe it or not, that's often how we learn what's happening!

ACS SUSPENSION

We understand that on March 12, 1988, a member of the American Cryonics Society was placed in cryonic suspension. At this time, no details of either the circumstances or the suspension procedure have been released.

THE SWITCH TO SUCROSE

When human patients are prepared for cryonic suspension they are treated with drugs to minimize the amount of damage done by cooling (i.e., the freezing process). The general class of drugs used to provide such protection are called *cryoprotectants*. Most cryoprotectants such as *glycerol*, which is used in human suspensions, and DMSO, which is often used in freezing cell cultures, work by depressing the freezing point of the cell's water and decreasing the total amount of ice formed. Indeed, such cryoprotectants typically prevent *any* ice from forming at all on the inside of treated cells. In order to be effective, such cryoprotectants must permeate the cell and displace a significant portion of the cell's water.

A second class of cryoprotectants works by a different mechanism entirely. Such agents have only recently been studied intensively, and they hold great promise for improving the quality of cryoprotection and minimizing the amount of freezing damage done.

These agents work by fitting into the cell membrane -- usually by attaching to a phosphate group at a particular site on the membrane's lipid molecules -- and preventing structural change in the membrane which normally results from freezing injury (which is technically known as the lamellar-to-hex phase transition). This transition or alteration

in the normally smooth "lamellar" arrangement of membrane materials results in a hole being created in the membrane. This in turn prevents the cell from regulating the concentration of critical ions and it thus "dies" (i.e., is rendered non-functional). Glycerol, DMSO, and other such "colligative" cryoprotectants (i.e., those which minimize ice formation) also help to prevent this transition, but must be present in very high concentration to do so.

The nice thing about this new class of cryoprotectants is that they work in very low concentrations. Two of the most effective ones are the relatively simple sugars *trehalose* and *sucrose*. Not only are trehalose and sucrose effective in minimizing freezing injury, they also work quite well to prevent injury from drying. Both of these sugars are thus used by creatures like the tardigrades (which are tiny arthropods) that can withstand desiccation.

One drawback to using sugars like sucrose and trehalose for cryoprotection in mammalian cells is that they do not penetrate cells well. Nevertheless, despite this limitation it is becoming apparent that they can provide additional cryoprotection. Human brain synaptosomes can be protected very well with low concentrations of sucrose (0.32 M) (Hardy *et al*, **J. Neurochem.**, 40, 608-614 (1983)) and a number of other papers indicate that quite a wide range of tissues can benefit from sucrose or trehalose protection (A.S. Randolph and J.H. Crowe, **Cryobiology**, 22, 367-377 (1985)).

More recently, Thomas Anchordoguy and John Crowe of the University of California at Davis have demonstrated the efficacy of sucrose and trehalose in cryoprotection of liposomes, cells, and shrimp sperm in low concentrations (Anchordoguy, personal communication).

The Alcor suspension protocol committee has had a long-standing interest in such sugars for cryoprotection. Unfortunately, significant evidence of the efficacy of these sugars in mammalian cells has largely been confined to work with trehalose, and then mostly as it affects cells tolerance to drying as opposed to freezing. This has posed two major problems. The first problem is that trehalose is *expensive*: about 25 times the cost of the mannitol which it would replace in our perfusate (the mannitol is not present for cryoprotection, but rather to prevent cell swelling during hypothermia). The cryobiologists on the protocol committee did not feel that the potential gain was worth the known "pain" (in the form of costs).

The second major problem is that in order to substitute trehalose for mannitol we would need to do animal studies to make sure that it was compatible with recovery of animals from extended bloodless perfusion. Trehalose is so expensive that even dog studies would be problematic.

However, it turns out that in Anchordoguy's studies, and with our human red cells (Mike Darwin's red cells), that sucrose and trehalose work about equally well in preventing freezing damage. We have already evaluated sucrose in the dog model: it works even better than mannitol in preventing cell swelling and is particularly effective in preventing liver injury from cell swelling (mannitol can freely penetrate liver cells and thus is not very effective).

We had already contemplated a switch from mannitol to sucrose for this reason and the recent information on sucrose's effectiveness as a cell membrane stabilizer during freezing "cinched" it.

Thus, in future Alcor human cryonic suspensions we will be using sucrose as our cell swelling inhibitor and also as a secondary cryoprotectant.

THE SEVEN STAGES IN THE EVOLUTION OF A NEW MEDICAL IDEA

With Particular Reference To The Critic (Author Unknown)

I. Idea Stage:	"Won't Work "Been Tried Before"
II. Successful Experiments In Animals:	"Won't Work In Man"
III. After One Successful Clinical Patient	"Very Lucky" "Doubt If Patient Really Needed Treatment" "Too Bad, A Tragedy Really, Because Now They'll Continue"
IV. After Four Or Five Clinical Successes:	"Highly Experimental" "Too Risky, Immoral, Unethical" "I Understand They've Had A Number Of Deaths They're Not Reporting"
V. After Ten To Fifteen Patients:	"May Succeed Occasionally In Carefully Selected Cases, But Most Patients With This Problem Don't Need This Treatment Anyway"
VI. After A Large Series Of Successes:	"So And So in Shangri-La Has Been Unable To Duplicate Their Results" "I Hear That A Number Of Their Patients Are Now Dying Late Deaths"
VII. Final Stage:	"You Know, This Is A Very Fine Contribution" "A Straightforward Solution To A Difficult Problem" "I Predicted This" "In Fact, In 1929, I Had The Same Idea" "Of Course, We Didn't Publish Anything --Nor Did We Have Penicillin, Cortisone Or Fine Anesthesia In Those Days"

AIDS AND LIFE INSURANCE

AIDS, AIDS, AIDS. It's all you hear about these days. We covered the epidemic in its early days, but have been doing so less lately because there are so many good education and information resources available in other media. However, one area of AIDS events which is of concern to cryonicists as a group is the impact AIDS is having on *life insurance*. The news is no more reassuring than the disease.

Evidence is rapidly mounting that people infected with HIV are buying insurance in amounts well over the "normal" rate for an age-matched population and then "cashing in" on their bet. Life insurance is already experiencing excess mortality: death rates for 1985, 1986 and 1987 are up significantly. Average AIDS death claims during those years were five times the death claims from other causes in one company, three and one-half times the death claims in another, and twice the average in yet another. Currently, in states that allow HIV antibody testing, the desired policy size of the average applicant *testing positive* for the presence of HIV was $1,100,000 -- ten times the average policy size! A survey conducted by the American Council Of Life Insurance and Health Insurance Associations Of America showed a substantially disproportionate share of AIDS death claims, 44% in amount, occurring within two years of the purchase of the policy!

What all this means is that with nearly 1 million people infected (almost all of whom will eventually go on to develop serious or fatal complications) the cost of health and life insurance is going to rise. If you have a Universal Life Policy, it's probably time to drag it out and look at the fine print. It may state that the value of your death benefit is tied into the rate of mortality for the population as a whole. What does this mean? It means all of us will pay for the cost of AIDS. Pay in higher premiums and pay in smaller death benefits.

What can cryonicists do? Well, supporting the ability of insurers to test for HIV infection would be a good place to start. A second step would be to keep a careful eye on the situation and begin contingency planning if an insurance crisis seems on the horizon. The small bright spot in the whole mess is that the insurance industry, the life insurance industry in particular, has been a stunningly profitable undertaking in the past and the insurance companies have an incredible amount of financial buffer. This of course is no excuse for bleeding them dry (as was done with the steel, auto, and railroad industries). But it does mean that as long as the situation doesn't turn into a catastrophe, few if any companies will go under.

The situation does merit a close watch and it would probably be advisable to contact your agent about what impact, if any, the AIDS epidemic will have on your insurance company and on your particular policy.

The source for the information used in this article was the California Department of Insurance.

* *

NANOTECH NEWS

The Atomic Force Microscope

Most long-time readers of *Cryonics* will be familiar with the Scanning Tunneling Microscope (STM), a tool developed by IBM Zurich which has allowed scientists to examine and manipulate materials on an atomic level. Such technology is the precursor to the creation of a technology capable of generating complex structures and devices built to

atomic precision.

Such a technology is of importance to cryonics because it is the kind of technology that will probably be required to revive suspended patients. At very least, the ability to examine and manipulate individual atoms or molecules will greatly accelerate our understanding of how the existing nanomachines which make up our cells work and function. For instance, the ability to examine and take apart protein molecules a bit at a time could provide powerful insights about the general principles which underlie their construction and folding. This insight has all sorts of benefits -- not just in terms of cryonics but also in terms of medical and industrial technology.

Unfortunately, the STM is somewhat limited in what it can examine due to the fact that it uses an electric current. Thus it can only look at conducting materials and use of it in an aqueous environment is problematic.

Now a new tool capable of molecular level resolution and perhaps manipulation has been developed. It is called the Atomic Force Microscope (AFM). Unlike the STM, the AFM works by maintaining an almost infinitesimal force between a diamond tip and the molecule to be examined. In other words, it's a kind of molecular braille; the tip, at the end of a tiny spring, is slowly moved over the molecule and the displacement of the tip is measured by the quantum tunneling current between it and a second, fixed, tip. The variation in current is translated into the contours of the molecule. Another way of thinking of the AFM is to use a phonograph needle as an analogy.

It's hard to say just how useful the AFM will be. It has already been used to examine monolayers of polymer molecules (*Science, 239*, 50 (1 Jan, 1988)) and shows promise for being able to image a wide range of both organic and inorganic systems. A beefed-up version of such a system might ultimately be used as a read-write tool for packaging enormous amounts of computer memory in a tiny space. Imagine a terabyte of memory per square centimeter of media surface area!

Of course, any such practical applications are probably years away. The important thing about the AFM is that it is yet another tool with which to expand the range of molecular examination and manipulation available to us. It's hard to believe that just a few years ago almost none of the "experts" would have believed such tools, able to move and image individual atoms, would ever be available!

Catalytic Antibodies

Grand ideas about the engineering of molecular computers and the like not withstanding, present chemical processing technologies are rather crude. A major driving force in the advance of biochemical knowledge has been the desire to know how living things perform their many chemical syntheses so quickly and efficiently. It has been known for a long time that the chemical reactions are facilitated by the class of *protein* molecules called *enzymes*, but unraveling how enzymes accomplish their tasks has taken many years.

Briefly, the function of an enzyme in *biological catalysis* is to contort the *substrate* molecule into a shape intermediate between that of the substrate and the *product*. This intermediate shape is called the *transition state*. When this is done, the catalyzed reaction rate is often millions of times faster that the uncatalyzed reaction rate.

When an enzyme folds itself into its characteristic shape, at some point on its

surface, called the *active site*, there is a pocket that fits the shape of the substrate molecule in its transition state. Thus, the enzyme facilitates its reaction by binding and twisting the substrate into the shape where it can most easily become the product. In real life, nature often gets a lot more involved, but this is the key concept in enzymatic catalysis.

So much for nature's way. The problem that the eager industrial chemist now faces is how to design and make a synthetic enzyme to solve *his* problem. The enzymes found in nature have evolved over billions of years, and this evolution has not taken into account that some thinking being might want to modify them for some other purpose. Eventually, it seems likely that enzyme engineering will become a major discipline in its own right, but for the present, the problem of designing enzymes with predictable effects is quite formidable. Current *genetic engineering* mostly consists of abstracting useful proteins from their native circumstances and copying them.

Recently, a way has been found to completely avoid this design barrier. It has been known for some time that the antibody molecules produced by the immune systems of living things to fight off bacteria, viruses, and other microparasites work by having pockets that conform to some surface feature of the invader. These pockets are not designed by the immune system. Rather, the immune system has a library of parts of pockets, and a system for scrambling the parts in all possible combinations. In the living animal, every conceivable pocket shape is represented by at least one living immune cell. Each cell remains quiescent until activated by the corresponding antigen that fits the antibody pocket. Once activated, the cell bearing that particular combination for its antibody pocket begins to divide and to activate the remainder of the immune system. Using genetic engineering techniques, the immune system can be manipulated to produce a stabily dividing monoclonal cell line which will produce a specific antibody molecule with its uniquely shaped pocket indefinitely.

Which leads to the obvious question: Can an antibody be made which has a pocket shaped like the transition state of a given substrate? And the answer is *yes*. Richard A. Lerner and Alfonso Tramontano report their success in the March, 1988 issue of *Scientific American*.

By substituting some of the atoms in a molecule which looks like the substrate, they made a molecule which bears a strong resemblance to the transition state of the reaction they were studying. When this molecule is exposed to an immune system, a small set of antibody-producing clones is generated, with pockets corresponding to various portions of the molecule modeling the transition state. Using simple selection techniques, the clone producing the most active active site can be identified. In the case cited in *Scientific American*, rate enhancements of up to several million were achieved.

It is difficult to guess what this development will ultimately affect. It will certainly tax the ingenuity of synthetic organic chemists in designing and synthesizing novel transition state-mimicking molecules. In the short term, it seems likely to reduce the cost of a large number of naturally produced molecules of commercial or scientific interest, including vitamins and drugs. It bids fair to revolutionize the field of organic toxic waste degradation and disposal. It may be possible to produce an "active site library" of small reaction pockets which can catalyze some reactions generically. Beyond that, human ingenuity seems to have a new and fairly extensive playground.

In its effects on forthcoming nanotechnology, immunocatalysis appears to be a quantum advance in the protein engineering route to nanotechnology outlined in Drexler's *Engines of Creation*. How this will effect the competitiveness of this route versus the route outlined by the scanning tunneling microscope and its variants remains to be seen. It may

well turn out that a hybrid approach will emerge, with nanocomponents being produced in a series of immunocatalytic reactors, and final assembly being carried out by an STM.

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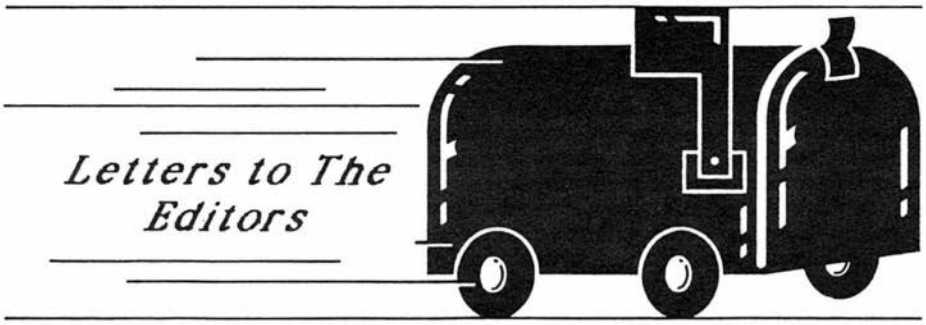


Dear Editors,

While I could scarcely disagree more with Steve Bridge's position on gun control, I do agree that such discussions really don't belong in *Cryonics*. They might make good grist for the Computer Bulletin Board once it's up and running again. Still, the discussion does raise an interesting point which might have a place in *Cryonics*:

Just what are philosophical, political, and even theological views of *Cryonics* readers in general and Suspension Members in particular? Sure, we all tend towards the Immortalism end of the spectrum, but what about other, seemingly unrelated issues? We do we fall in the political continuum (I'm a libertarian anarchist myself)? What are our religious views and what is our age and gender distribution? What are our interests and how did we first become interested in or hear about cryonics and life extension?

What I'm suggesting is a readership survey. This wouldn't just satisfy curiosity -- it could also give us a better idea of where to go recruiting. Are Libertarians and science fiction fans really good prospects, or am I biased by my own interests? Just what, besides the passage of time, causes Associate Member to "flip" and go for that Suspension Membership?

I suggest we take a few months to collect proposed questions, and then put a survey in *Cryonics* this Fall. Think of it as a snapshot of as *movement* before we become just another service in the marketplace.

Bret P. Bellmore
Capac, MI

Mike Darwin Replies:

Bret,

This is an excellent idea. In fact it is such an excellent idea that two people whose initials are Max O'Connor and Mike Perry were supposed to work up such a super-duper questionnaire during the Spring about *two years ago now*! (What happened guys? Did I quit nagging too soon?)

You are quite right in suggesting the utility of such a Questionnaire. In fact, it

was done once before in *Cryonics* and the results were published in the October, November, and December, 1982 issues. The hard part about doing such a survey is knowing which questions to ask. What I'd really like to do is sit everybody down and do a personality inventory and give them a thorough battery of psychological tests. Then I'd like to follow it up with hundreds of questions about everything from their attitudes about death to what kind of deodorant they use. Then, I'd like to load this data into a good mainframe computer and grind out all the significant correlations. There has to be something about us that makes us different, and susceptible to infection by this idea.

Of course, it may turn out that statistically speaking, only people with a certain *very* uncommon mix of traits or characteristics can be infected right now. That is always a grim possibility. Nevertheless, I think your idea is a very good one. Midwest Coordinator Steve Bridge in Indiana conducted the last survey. He *knows* how much work is involved. Perhaps if Max and Mike got to work and started the Questionnaire (as well as finished it!) Steve's help might again be enlisted for some of the detail work?

How about it guys? Wanna give it a try? Besides, it oughta be fun and it might help to take our mind of some of the grief we've been experiencing.

* *

THE QUESTION COLUMN

by Brian Wowk

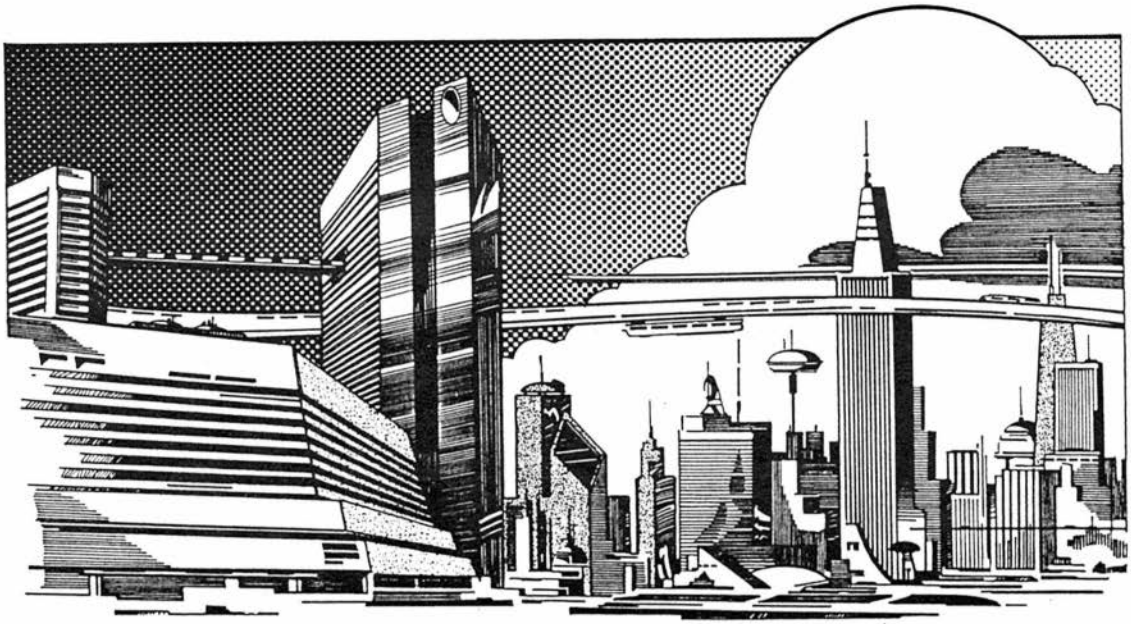
A question we cryonicists are frequently asked is, "Wouldn't indefinitely long lifespans be boring?" Here's a fairly comprehensive response to that question.

Only if one makes no effort to live it. After all, a thousand lifetimes aren't enough to even begin exploring all the interesting facets of today's world. And the world today is just the beginning. As technological progress continues, standards of living (particularly health, wealth, and free time to enjoy them) will also continue rising. The decades and centuries ahead promise to bring access to fantastic resources and technologies -- resources and technologies creating opportunities for growth and experience unimaginable today. Even the magnitude and diversity of civilization itself can be expected to grow virtually without bound as human life and its derivatives spread among the stars. In the final analysis, then, the developmental frontiers before us as individuals and as a species are *unlimited*. There is not, and never will be, a shortage of interesting new pursuits for those who seek them.

This question will not be belabored, however, for it's both tangential and specious. Life, immortal or otherwise, may at times be boring, but is being dead more exciting?

Indeed, complaints that longer lives would be boring are typical of a common tendency to not really take this issue seriously.

We live in a peculiar world. One where everyone ostensibly wants cures for cancer, heart disease, and other deadly maladies. One where people go to great lengths to feel and look younger. Yet when it is proposed that something concrete actually be *done* toward these ends -- such as bringing aging itself under biomedical control -- people often recoil in horror at the implied result: longer, healthier, and eventually unlimited youthful life spans. God forbid that curing deadly illness and improving the health of the elderly should ever actually result in people living longer (or so it might be concluded from the attitudes expressed by many people concerning this issue).



Clearly reactions of the above sort imply a dichotomy between the way people think of life span extension vs. actually saving life. If this question is to be taken seriously, however, it must be realized that life span extension is *directly* related to the defense of human health and life. If we value health and life enough to preserve them as best as nature will allow (which includes our own natural ability to develop sophisticated medicine from the tools nature has provided) the inevitable result will be unlimited healthy life spans. To ever deliberately falter in the pursuit of this goal would be to deliberately condemn millions of people to suffering and death that was within our power to prevent*.

From this perspective, the medical/ethical status of aging intervention and radical life extension is clear. If a means of treating and ultimately reversing a debilitating deadly condition is within our reach, the fact that all human beings share the condition is no excuse for not treating it. If anything, the prevalence of a deadly condition is all the more reason to aggressively pursue its treatment. In the face of this task, pausing to extol supposed virtues of aging and death -- as many people do today -- is no more productive or relevant than upholding the 25-year life expectancies of the Middle Ages as the pinnacle of human well-being. A century from now, when aging and death have been all but eliminated, and when unlimited life spans are taken as much for granted as people now take their apparent three score and ten, such praises will no doubt be looked back on as just as barbaric and inhumane as we regard ritual human sacrifice today.

Whether or not biologically unlimited life spans would finally be good for

* Indeed, without intervention in aging, all of humanity now living is doomed to destruction within decades no less certainly (and not necessarily less painfully) than if there was an all-out nuclear war. In view of this, those individuals (and there are many) who profess concern about nuclear war, but not about present life span limitations, are either hypocrites, or value human life on a chronological sliding scale that drops to zero for people past middle age. (I.e., it's bad for children to perish in a nuclear war today, but proper and OK to allow their destruction by default tomorrow.)

individuals or societies ultimately reduces to a simple question. It is fundamentally not a question of how long people should live, but rather a question of the condition in which they should live. It is a question of whether individuals should always possess personal choice and control over their health and life, or whether they should ideally be unwilling subjects of progressive infirmity and programmed destruction. Indeed, anyone who would hold that halting our present headlong rush toward disease and death (physical aging) would *not* be good, and that human beings *should* suffer and die regardless of wishes, might be asked what they mean by "good". Particularly, good for whom?

* *

CRYONICS AS RELIGION?

by Mike Darwin

It has been said that for many cryonicists cryonics occupies the same place in their lives as religion does for most people. That this should be so is easy to understand, since any close examination of cryonics as a whole (as opposed to just its technical aspects) will disclose that it shares many common elements with religion.

The obvious and central one is that both cryonics and religion offer the prospect of continued life after "death". Both offer the prospect of continued life in a world of abundance and health and well-being in a state either the same as or, more usually, better than experienced during "mortal" life. Both cryonics and religion represent attempts to deal with death.

Cryonics and Christianity share an even greater degree of overlap. Both are "melioristic" in that they see the arrival of a special era or time during which resurrection of the dead will occur and there will be a fundamental change in the nature and quality of life on earth. To Christians this end point to history is marked by the Second Coming of Christ. To cryonicists it will be marked by the achievement of a mature nanotechnology and the world of abundance and more or less indefinite longevity that it will bring. Indeed, many cryonicists foresee their "postmortem" futures as offering the opportunity of radical change in the very nature of their being.

Complete control over living systems implies the ability not only to avoid aging and death, but to change, in ways both fundamental and trivial, the essential structure and functions of our bodies. Indeed, implicit in Ettinger's original articulation of the cryonics idea was the idea of the *immortal superman.*

Another shared element between cryonics and

religion is the idea of sin and salvation. For Christians immoral behavior is determined as that which is contrary to the law of God (and as a corollary very likely to get you into serious trouble in the salvation department). For cryonicists it is any behavior or action which decreases or interferes with ones chances of continuing to live or to get frozen and revived if the need arises. Cryonicists, much like Christians, must pause occasionally and take stock of their lives and decide if their behavior is in accord with getting suspended under good conditions -- or at all, for that matter. Clearly someone who has let his insurance lapse, has a cholesterol level of 260, subsists on bacon and ice cream, and who lives alone in the woods of South Dakota is cutting away at his chances for "salvation" if "death" comes.

So, with all these shared elements, isn't it fair to classify cryonics as religion and isn't there substantial political advantage to doing so? I firmly believe the answers to both those questions are "No!" Not just "No" but "No!".

Why, you may ask? Well, before I can answer that I have to define religion. I will have recourse here to Webster's New World Dictionary which defines religion as: 1) belief in a divine or superhuman power or powers to be obeyed and worshiped as the creator(s) ruler(s) of the universe. 2) expression of the belief in conduct and ritual. 3) a) any specific system of belief, worship, conduct, etc.: as the Christian *religion*, the Buddhist *religion*, etc. b) loosely, any system of beliefs, practices, ethical values, etc., resembling, suggestive of, or likened to such a system: as humanism is his *religion*. 4) a state of mind or way of life expressing love for and trust in God, especially within a monastic order or community: as he achieved *religion*. 5) any object of conscientious regard and pursuit: as cleanliness was *religion* to him. 6) the practice of religious observances or rites.

As the reader will note from the definition above, nowhere are the words reason, doubt, educated gamble, or physical law mentioned in describing religion. The key words missing from the Webster's definition of religion are *faith* and *mysticism*. With the possible exception of humanism (which the Supreme Court has determined is *not* a religion) almost any religion you care to name has the shared elements of *revealed truth* requiring *faith* (i.e., belief in the absence of supporting rational proof) and *mysticism* (the belief in a "supernatural" power or "order" which goes beyond or is exempt from known physical law).

By contrast, cryonics does not have anything to do with revealed truth. Its premises are rooted solely in our current understanding of the real world (i.e., known physical law) and are as such susceptible to disproof. Nowhere in cryonics is there offered any certainty about the outcome. The basis for actions taken, such as cryonic suspension or not living alone in the woods in South Dakota if you are at risk of sudden death are based solely on the *real world*. Actions taken by cryonicists have nothing to do with revealed truth, higher powers, or supernatural intervention.

We undertake to freeze people at the time of legal death because we believe that: 1) Life has a physical basis -- we are a pattern of interchangeable atoms; 2) Cryonic suspension is effective at preserving that pattern of atoms with relatively little

information loss if applied reasonably soon after "death"; 3) Given our current understanding of freezing injury and the natural repair and molecular manipulation capabilities inherent in the world around us, no physical law would appear to be violated in repairing or refabricating (i.e., rearranging the pattern of atoms) damaged cells that have failed to function as a result of disease, "death", or freezing damage, and; 4) We speculate hopefully about our ultimate ability as a civilization to develop and master such technology and apply it to patients who have been treated by cryonic suspension.

There are no certainties in the outcome involved. No revealed truths. No higher orders of being and complex ethical system. Belief in the workability of cryonics, unlike religious faith in salvation, hinges completely on our understanding of and speculation about the nature of the universe (physical law) and humanity's ability and motivation to bend it to the end of resuscitating frozen "dead" people.

And it might not work. Not just for "bad people" or "immoral people" or for people who aren't members of a particular cryonics organization but for anyone. That's the breaks when you're dealing with the real world.

As to the issue of whether or not it's an "advantage" to claim that cryonics is a religion, the answer to that question is going to be a bit more complex. Obviously in some situations it may help to "end" unpleasant discussions by claiming "cryonics is my religion", because at least in this country (and most of the western world) a man's religion is his own business and it isn't polite to challenge it unless it involves smoking dope or sacrificing animals (two acts central to some religions which are illegal -- for religious purposes or otherwise -- in California and many other states).

Saying cryonics is a religion is also an easy way to articulate that it holds an important position in your life, perhaps the same one as religion does in your listener's life. But the fact remains that by any reasonable definition cryonics isn't religion and to say so is not only intellectually dishonest but damaging to cryonics as well.

It is damaging to cryonics because it undercuts the fundamental basis upon which cryonics works -- reason, trial, experiment. One of the reasons that cryonics has not "caught on" like so many irrational and crazy religious movements is because it doesn't share their common, essential elements: lack of critical evaluation of the premises involved and a complex philosophical and ethical baggage from a "higher

source". Ultimately cryonics will work not because we personally believe it will or not or because "God" says it will work, but because it will be physically, scientifically possible. In order for it to be possible, we have to work for its realization by applying reason and the scientific method to the world around us -- not by engaging in a liturgy or rituals or leading an ethical life. Even vicious, unethical people can benefit from cryonics. A blameless life has nothing to do with it.

When a cryonicist tells someone that cryonics is a religion, or when they link cryonics to religion, they are damaging cryonics badly. They are damaging it first and foremost by losing sight of cryonics as *technology* and *science* -- albeit with an element of risk or "gamble" added in -- but still fundamentally technology and science. In so doing they erode their ability to focus on the problems and work to solve them. Perhaps appropriately, it is most often people who seem to have little grasp of cryonics as a *scientific* undertaking with many uncertainties that are most attracted to cryonics as a *religion.*

Because cryonics is unorthodox, because it involves a very long timescale of action which is alien to human culture, and because it incorporates elements of "rational speculation" (such as making an investment does) which are alien to medicine, it is very hard for people to realize that it has a rational and scientific basis. When cryonics is labeled as or associated with *religion* there is necessarily a reinforcement of the belief that it is nonrational or a cult.

I think that it is very important that cryonics not become a cult. In other words, that cryonics not stray into or become associated with undertakings that tell people on a nonrational basis how to live their lives -- the very definition of a religion.

Finally, there are the very basic practical considerations. If cryonics is to work, it has to be pursued in rational and thoughtful fashion. We could probably get many, many more "adherents" if we were to claim cryonics was a divine inspiration, the instructions of supernatural aliens, or some other such nonsense. The problem with such adherents would be that they would be anathema to any possibility of success.

The notion that courts or legislatures will extend any special protection to cryonics as a religion in the absence of the key elements present in most other religions -- belief in God, revealed truth, and an ethical system which tells you how to live your life -- is not merely slim, it is nonexistent. People who delude themselves into believing otherwise are going to have a rude awakening.

We have to ask ourselves what we want for cryonics in the long run. First and foremost we want it to work if it has any possibility of doing so. It seems clear that the road to workable cryonics is going to be paved by persuading rational, competent people on the basis of the facts. What we want is for cryonics to be integrated into medicine as it rightfully should be: as a therapeutic gamble with unknown (although perhaps very long) odds which is based on a *rational* understanding of the *physical* world we live in -- not on mumbo jumbo or idle wishes or hopes.

The path to that integration is not to be found by venturing into the province of religion. To do so will only cloud the fundamental issue that cryonics will work or will fail on the basis of scientific and technical realities. Period. To confuse or associate cryonics with religion clouds the key issues, erodes our credibility as a scientific undertaking with everyone and will serve to alienate the very people we need to reach most: rational, thoughtful people.

In short, cryonics has enough problems being accepted as a reasonable, rational undertaking without having to be perceived through a veneer of mysticism or "religion" and everything that connotes.

And what about those who won't be able to appreciate cryonics without such a veneer? I think we are better off without them if the price we have to pay is to associate ourselves with irrationality. Cutting off a hand to save a finger is *never* worth the price.

* *

WHY ARE THERE SO FEW OF US?

by Max O'Connor

There are about 220 people signed up for cryonic suspension. 220 out of five billion; 0.0000044% of the population of the world, or about one in every twenty-two million. There are tens of millions of Christians, Buddhists, Hindus, and Sikhs. There are thousands or tens of thousands of adherents of even the newer or less traditional religions or "cults" (a "cult" being what the supporter of a large religion calls a smaller competitor).

Christianity, Scientology, Islam, and Marxism are clearly false and irrational doctrines -- doctrines devoid of contact with reality. Yet cryonics, we believe, is a rational pursuit, one that is not guaranteed success but for which we can produce powerful arguments based on empirical evidence and informed speculation and projection of current knowledge and technology. Why then do the false belief systems attract so many adherents while ours does so poorly?

To answer this question and to understand some other causes of the small size of the cryonics movement I want to introduce the notion of the *reality-tunnel*. A reality-tunnel is a mental model of reality, a set of general beliefs, assumptions, and ways of thinking through which our experience of the world and ourselves is filtered. I am *not* making the Kantian point (which I think is false) that we cannot know reality as it is but only as we conceive of it; we all have (and must have) reality-tunnels but this is not to say that those tunnels cannot be enlarged and made transparent enough to enable us to understand reality accurately. The problem with reality-tunnels is not an inherent one but is simply that most people's are too narrow and do not point in the right direction.

So why is that even though some reality-tunnels are so divergent from objective reality they nevertheless receive more support than rationally preferable tunnels? One reason for this was pointed out by R.A. Wilson when he said that a certain amount of arbitrary nonsense is an advantage for the survival and propagation of many reality-tunnels. Why do Christians believe that God is both one being and three? Why were the Mansonites required to believe that there was a hole in the Mojave desert which went to the center of the Earth? Why is a Roman Catholic woman required to believe that it is immoral to get divorced even if her husband is a layabout, violent drunk who beats her and makes her life hell? Why must Fundamentalists believe in the literal truth of the Bible despite its conflict with well-established science? Such obvious falsities are useful because they allow members of a belief-system to accuse their people of slipping into evil and lies, of starting on a slippery away from the truth and towards the wicked falsehoods from which they have recently been saved.

Including certain bizarre falsehoods and clearly idiotic tenets in a reality-tunnel will promote the solidarity of a group by encouraging the members to band together more tightly in the face of disagreement, opposition, or derision. These external attacks will normally reinforce their belief-systems rather than weaken them, since the bizarre dogmas will so distance the adherents from others and from reality that they will face a sharp and painful choice between an extreme change of view resulting in exile from a close-knit group, or else a little easy irrationality, a little evasion of the conflicting evidence. Some courageous individuals, despite upbringings and continual indoctrination from within a reality-tunnel, will have the intellectual integrity and honesty to break free. But for so many it is too easy to take the irrationalist escape.

Cryonics is not proof against bizarre falsities, but there do not seem to be any inherent in the activity. All the cryonicists with whom I am familiar have come to support the practice because of strong arguments for its viability -- such as the understanding that death is not an all-or-nothing event or condition, that personality depends on neural organization (whatever its exact nature), that very low temperatures halt biological degeneration, that evidence points to the essential information in the brain being preserved, and that we can reasonably expect the arrival of a technology that will make reanimation possible. This is where a problem lies for the appeal of cryonics. It is too rational, too reasonable and hard-headed, too well in tune with reality and the objective requirements of survival (and survival is an objective requirement for the pursuit of all other goals). If this is a problem, then why not introduce some irrational and blatantly false elements in order to strengthen our resolve and to appeal to other types of people?

The answer is that irrationality will not work for cryonics, because cryonics has rational goals. Denial of reality can work for religions (although too much can wipe them out -- as in the case of Jim Jones and his followers), because religions are really systems of placation and subjugation. From the point of view of the potential convert, religion offers a strategy for relieving fears about destruction at death, and it provides a means by which those who feel they have had a raw deal can get even in the next life,

since they will be rewarded and their oppressors punished (with a vengeance!). This feature is clearly important in Christianity and many of its offshoots, and in the notion of Karma in the East.

Of course, religion provides other psychological rewards (not without costs) such as relief from the responsibility of formulating an ethical code by trying to understand reality and therefore the rationally necessary requirements for the promotion of life, happiness, and well-being. Marx identified another function of religion when he wrote that "Religion is the opium of the masses". This view can be taken to express not only the point that religion is a comfort for its adherents, but also the belief that it is an instrument of control by the rulers over their subjects. While they would not agree with Marx that the relation between religion and rule is that simple, many libertarians would assent to the idea that religion co-evolved with the State and was designed and promoted as an instrument of control. In earlier times it seems that the head of State was invariably also a god or else a representative of divinity on Earth. Crimes against the State were also crimes against the gods. How convenient for the rulers!

The point of the foregoing was to identify briefly the purpose of religion. The functions of religion are not usually recognized or acknowledged, for ignorance and denial of these facts is essential to the effectiveness of the religious strategy. Now, the purpose of cryonics is quite different, and so it would be foolish to think that irrationality, though successful for the fulfillment of the functions of religion, will work for our activity. The purpose of cryonics is to provide a means, in the absence of better suspended animation techniques, for avoiding an otherwise likely permanent death and to get us to a point in the future where we can be returned to a fully functioning condition. The best means for achieving this in the face of numerous difficulties is to maintain an unyielding commitment to rationality in our affairs. Only the fullest use of our minds, the most effective employment of our intelligence, and an uncompromising self-criticism will have a chance of winning through. Only reason can tell us how to triumph over natural disasters, human errors, physical attacks, scarcity of resources, and mindless and vicious attacks by coroners. Only reason can tell us which suspension techniques to adopt, what equipment to use, and how best to organize our complex affairs given the painfully limited resources at our disposal.

It should now be clearer why religions have been so successful while we haven't, if we are talking in terms of numbers, but it still seems puzzling why more people have not joined us. Part of the reason must be simply that cryonics has only been going for just over twenty years. It takes time for a new idea to break through old misconceptions and competing well-established belief-systems. People are born and brought up with a reality tunnel that not only does not contain cryonics as an element but which contains many elements inimical to it. Apart from religion, another great mind-killer is tradition. For example, a friend of mine was considering joining Alcor. His mother, who was not at all religious, expressed horror at the idea of his being frozen, saying, "but you *must* have a decent Christian burial". Cryonics clashes violently with religious traditions, moral traditions, traditions regarding the "proper" way to die, and the "correct" way to dispose of remains, and it requires a shake-up of someone's whole world-view. One has to face the fact that *tens of millions of people are needlessly disappearing into nothingness*

face the fact that *tens of millions of people are needlessly disappearing into nothingness every year.*

Cryonics shakes up traditional but irrational moral views by making us face the fact that we are primarily responsible to and for ourselves. It is no one else's duty to look after me and it is not my duty primarily to look after others. I have a right to what I have produced or have voluntarily acquired from others and I have a right and a moral imperative to use my resources to promote my own life and well-being even if others are screaming at me that they *need* my resources for themselves. Cryonics only appeals to people who have a sense of their own self worth, of their right to keep themselves in existence, of the highest value of their own life to themselves.

Cryonics also has to overcome the barriers of lack of intelligence, foresight, and imagination, and of the pervasive sense of negativity about ourselves and our future that exists in the present culture. Many people are too intellectually lazy to think through the scientific, technical, moral, and philosophical issues necessary to sustain their lives. Many are lost in a swamp of negativity about their own ability to cope with a future world, and their fear is exacerbated by their poorly-founded, dark beliefs about how the future must be.

We need more people in order to improve our chances of long-term survival. Let us not despair: our movement is young, and there are still a huge number of people out there who have not even *heard* of cryonics, along with many more who have had so little (and often very inaccurate) exposure to the idea that we cannot blame them for not being involved. Cryonics may never be a huge enterprise, but I am convinced that there is a potential for enormous growth if we can beat the dark forces which now assail us, and if we remain loyal to ourselves and to our rationality.

* *

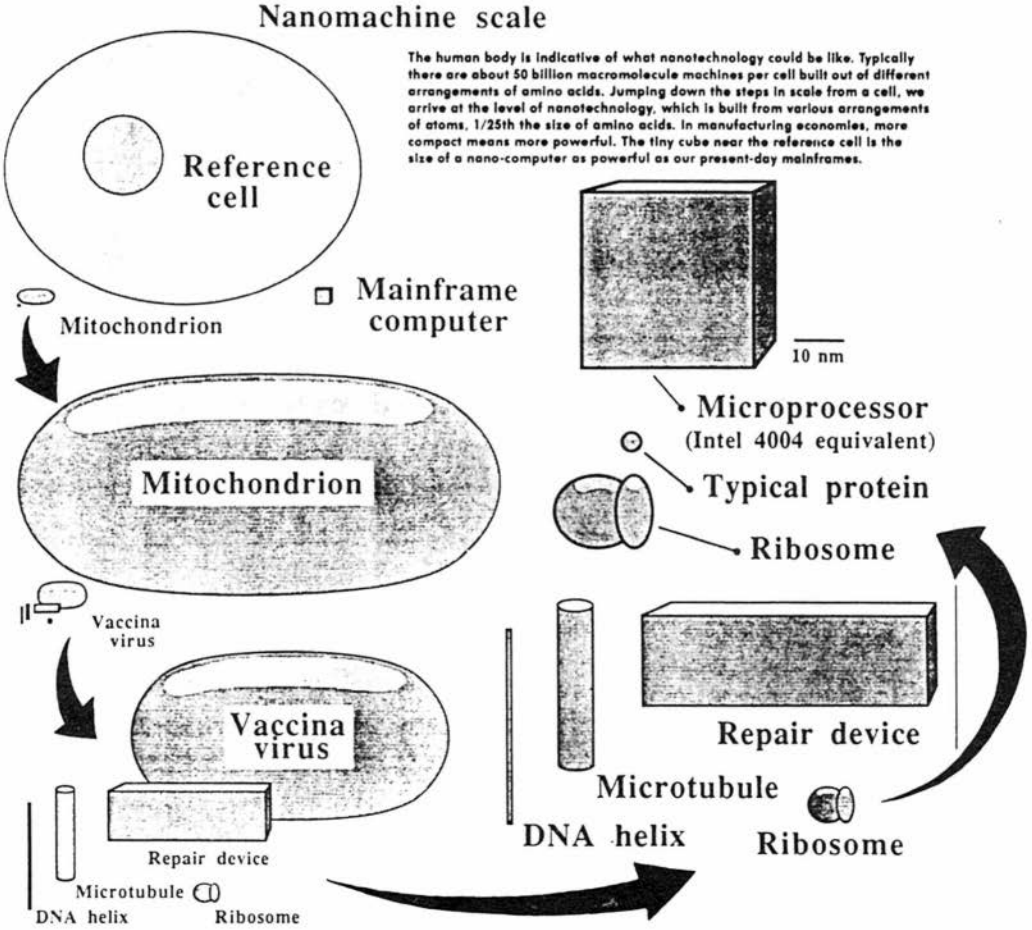
THE GLORIES OF BIOCHEMISTRY: AN APPRECIATION

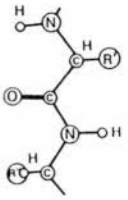
by Thomas Donaldson

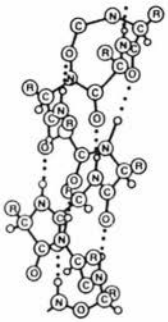
Not long ago I received a questionnaire about nanotechnology from the *Foresight Institute* (PO Box 61058, Palo Alto, CA 94306). One question asked me to estimate how long until nanomachines could be created which would, if placed in a suitable chemical mixture, replicate themselves.

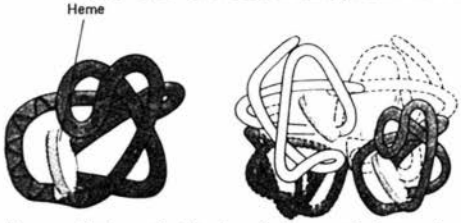
I found this an astounding question. Such machines flourish all about us. We call them bacteria, fungi, paramecia, diatoms. Our bodies, our blood, our skin are all inhabited by different species of these machines. Our bodies consist of such machines, all cooperating. I found it hard to understand the point of the question. In and of itself, by creating such machines we would not prove any new *principles*. What would it mean to create such machines if they already exist? It is as if the originator of the questionnaire had temporarily forgotten 4 billion years of history, and proposed the task of recreating *life* without ever looking at the book for hints about how to do so.

This is an article about the original "inventors" of nanotechnology, roughly four









The four levels of structural organization of a protein (hemoglobin). Left to right, peptide chain, alpha-helix, tertiary structure (folded alpha helices), and quaternary structure of two alpha- and two beta-hemoglobin molecules.

billion years ago. My aim here is to describe a little of biochemistry and how it works, draw lessons about what we can learn from it, and finally discuss what this technology can *do.*

Molecular machines

The first molecular nanomachines, of course, were probably strings of RNA. RNA consists of a sequence of nucleic acids. The backbone of RNA is a chain of sugar phosphate molecules (ribose phosphate). To this chain, in an arbitrary sequence, attach four different chemicals, adenine, guanine, cytosine, and uracil (if we were discussing DNA instead, thymine would replace uracil).

But some time after that first nanomachine, others developed. They are the most common nanomachines in the world today. We call them *enzymes.* Enzymes are protein molecules, formed out of chains of chemicals (amino acids). The probable advance of enzymes over RNA is flexability. There are many more amino acids than the four nucleotides which make up RNA. Twenty amino acids make up the vast majority of proteins. That means that enzymes can take up a much larger range of shapes.

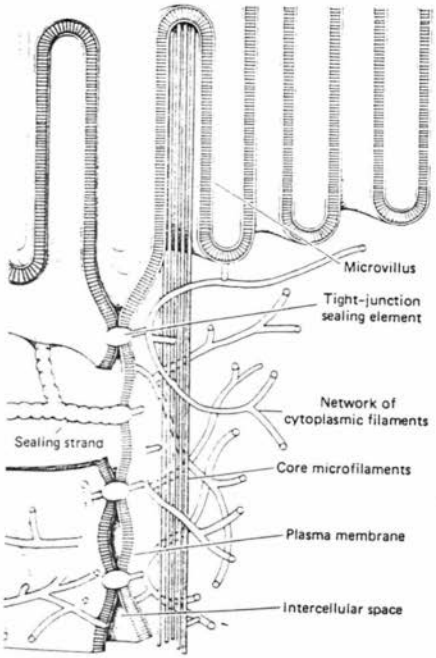
Shape is important because enzymes are true nanomachines. They act to promote many chemical reactions. They do so because their particular shapes make the molecules involved in a reaction stick to them. Once brought together, these molecules will react. The enzyme then releases the product chemical. It is all done by the peculiar shape of a particular enzyme.

But that's far from the whole story. These shapes are so specific that enzymes will promote only one particular chemical reaction and no others. For instance, one enzyme, *acetylcholinesterase* (often mentioned in discussions of brain and nerve metabolism) catalyzes the breakdown of acetylcholine (the nerve transmitter chemical). It has little effect on any other reactions.

And even that isn't all. Enzymes can be regulated by the presence or absence of other chemicals. For instance, they might have a site to which anoth-

er chemical sticks. When this happens, and only when it happens, the enzyme will act to catalyze a reaction. Otherwise it will not. An example is the enzyme *aspartate transcarbamylase* (or ATC). This enzyme catalyzes a chemical reaction which makes nucleotides (nucleic acid precursors). If another chemical, *cytidine triphospate* (CTP), attaches to a site on the ATC, ATC won't catalyze the reaction. The CTP changes the shape of ATC, exactly like throwing a switch. (The reason for this switch is to make the reaction stop as soon as it makes enough nucleotide molecules, but that's a long story).

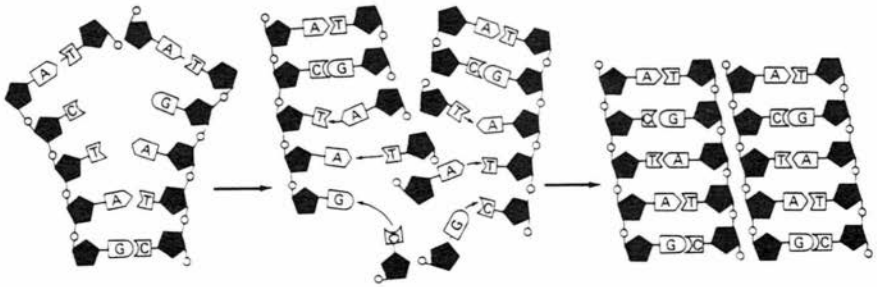
Since these nanomachines are so specific, and can control one anothers' actions by throwing switches to turn one another on or off, they can build immense and complex interacting systems. They needn't float about in a liquid, they can bind to membranes, catalyzing reactions from there. We don't just have to catalyze chemical reactions with these nanomachines either. Other protein molecules such as *hemoglobin* catch and release oxygen, again because they have a special shape which lets them do this. Interacting systems of nanomachines perform all of the steps of what we call life.



Model of a tight junction between cells

How do these machines compare to those discussed by K. Eric Drexler? Normal enzymes can consist of between 3000 and 100,000 atoms. This means they are, in linear dimensions, about 10 to 50 times the scale of Eric's machines, which may only be a few atoms wide. *On the other hand, and this is very important, these nanomachines actually exist.* I'm not talking about science fiction dreams, but about commonplace realities, so commonplace that we rarely think how strange they really are.

If we can build systems of nanomachines on the scale of enzymes and other biological nanomachinery, we can attain all the goals of cryonics. Since such nanomachines already exist, it makes more sense to learn from them rather than trying to make totally new versions on totally new principles (as yet unknown!).



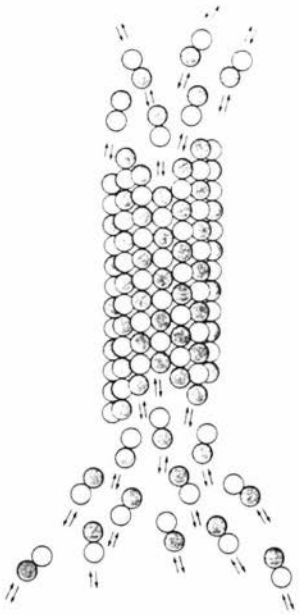
DNA Replication. G, C, A, and T are the codons, the filled pentagons are deoxyribose, and the small circles are phosphates. The chain is unzipped, and new codons take their places.

The Primacy of Chemistry

Let's see now just how much we can learn from these nanomachines in their current form.

Richard Feynman, one of the earliest writers on nanotechnology (in *There's Plenty Of Room At The Bottom*), pointed out that we'd need a new physics and engineering just to know how to operate on a molecular scale. Right now, we have only the beginning of this physics and engineering. Most of its guiding principles aren't even *formulated*.

Why are these nanomachines 10 to 50 times larger than "theoretical limits"? Of course we could simply decide that existing nanomachines are too inept, designed purely by chance. In short, we could be arrogant. That's a bad method both scientifically and personally.



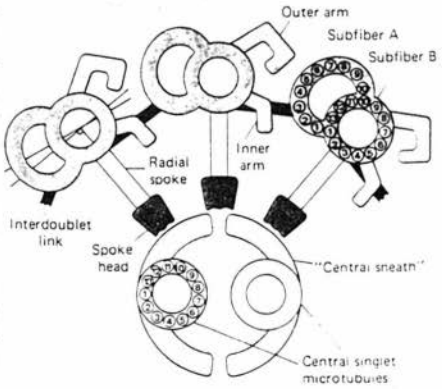
Tubulin self-assembly.

We don't really understand how and why nanomachines came to be what they are. Still, I would like to suggest one reason for just one of the differences: the fact that they're 10 times "too big". There is a problem of *chemistry*. When we design ordinary-sized machines, we can engineer a part, making it a particular shape, and expect it to stay the same shape afterwards. On a molecular scale, chemical reactions take place. Objects and molecules try to reach a minimum energy configuration. Everything wants to stick to or react with everything else. There is no such thing as an "inert" part to a nanomachine.

So far, existing attempts at designing nanomachines "from scratch" haven't really come to grips with *chemistry*. That is reasonable. Eric's estimates are penetrating and novel as first approximations. I don't believe he seriously believes that we can soon build nanomachines to such a scale. I also don't believe that his indications of how we could build nanocomputers are intended as actual working devices. We know too little.

The major constraint which the protein components of nanomachines attempt to solve is the problem of chemistry: creating a machine (an enzyme, for instance) which will respond mechanically while at the same time *remaining stable*. Dealing with quantum mechanics is only a first step. Ordinary chemical reactions are much more serious problems. Unlike quantum mechanics, chemistry doesn't involve any single problem we can slay with a single calculation. If bothered by one reaction, we can always devise some way to avoid that particular reaction. But then we have another problem, with a different reaction.

The *existence* of nanomachines shows us that ways exist to overcome the problem of chemistry. Furthermore, it's clear that we can use these chemical principles to devise special nanomachines suiting our own purposes. But we'll also have to learn how to operate in this tiny realm, where machines don't behave the same as macromachines and everything sticks to everything else.



Flagellar cross-section.

Self Repair

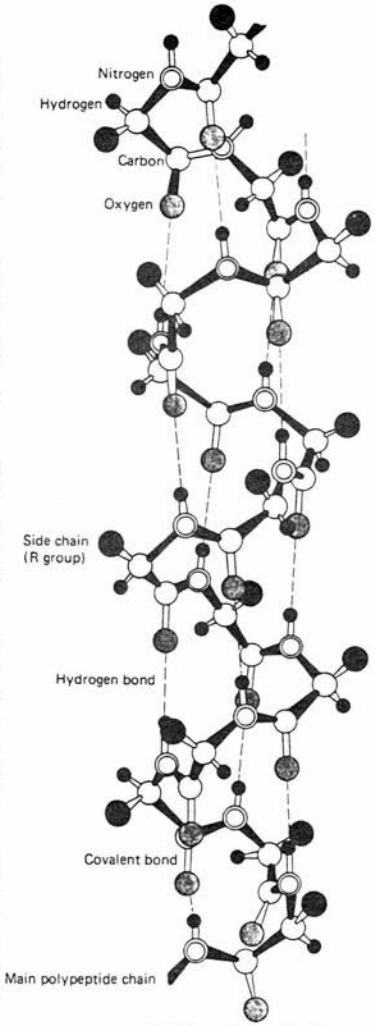
Nanomachines currently show two major differences from our constructed normal-sized machines. One of these is that they are *wet*. Everything is gooey chemistry. These are not smooth, dry, solid objects. The larger nanomachines, such as human beings, are mostly dry only on their outer skin. Inside they are all liquid. Even individual cells are bags of fluid.

Nanomachines aren't just wet. They are extremely dynamic. The fluids bubble with chemical reactions of all kinds. Individual cells don't retain their shape or even their location. They slide and move past one another over time. Their constituents are continually torn down and replaced. We are much more like Niagara than like silicon chips.

These two facts are closely related to one substantive difference between nanomachines and our current macromachines. Nanomachines are self-repairing. Not completely, true. But they show a persistence over time, and even a toughness, far beyond any existing macromachines.

It's one thing to think of an ideal machine. By definition ideal machines never suffer from any problems. Existing macromachines, though, have a ridiculous record of longevity compared to nanomachines. Our computers regularly go down after only a few weeks. We have to reboot them. Our cars, without constant external repair, wouldn't live as long as a dog. Few cars would even live as long as mice.

The fact that nanomachines are wet chemistry of course goes along with their abilities for self repair. The fluid they bathe in is a medium to bring new materials and carry away the torn-down residues of the old, on a continual basis. The fact that every cell membrane is in contact with this fluid means *access for repairs* to all the nanomachines making up the cell.



Protein coiled in alpha-helix.

Of course we'll someday make machines with as much or more longevity as nanomachines now have. Currently we attempt to do this by making them of ever more durable materials. That can't work well. If we really want *durability* in our machines, we're going to borrow the notion of wet repair and dynamic continuity from nanomachines.

Dynamic repair is particularly important for nanomachines. It *may* be very significant that current nanomachines do not form single-molecule structures behaving like whole electrical circuits or mechanical devices. Instead, they are wet mixtures of much smaller nanomachines, each one performing a simple and redundant task. The reason for this is that the larger a nanomachine becomes, the more susceptible it is to disruption. Consider Drexler's rod logic nanocomputer. Anything which disrupts one rod will disrupt the machine. A rod is only one atom wide. Unless these machines are dynamically self-

repairing, or extensively redundant, they'll soon go down due to cosmic rays, chemical attack by trace contaminants, or even external vibration.

Existing nanomachines such as enzymes or hemoglobin are usually replaced every few weeks. The need for constant replacement molds their design: cells consist of many multiple units. None of these nanomachines, individually, carries irreplaceable information or performs a unique role. We'll have to adopt this design for replacement in our own nanomachines.

Assembly

Many current nanomachines contain assemblers. These are called *ribosomes*. Ribosomes assemble protein molecules from plans brought to them from elsewhere. They can assemble any arbitrary sequence of peptides into a protein molecule. However ribosomes alone aren't enough to make most nanomachines. Ribosomes make long strings of peptides. After that, other processes combine these strings, change their shape, or add new molecules to them.

For instance, ribosomes do not make hemoglobin directly. Ribosomes make two different peptide chains, the alpha and beta chains. Two each of these combine with an iron-containing molecule, the heme group, to form hemoglobin. Hemoglobin is a nanomachine constructed out of five different parts, one of which is *not* a peptide chain. Depending on the protein, peptide chains can be welded together (one particular amino acid, cysteine, plays an important role. It can bond with others in a special bond, the sulfydryl bond. This allows assembly of these parts). Peptide chains are modified in other ways too. One modification important to the chemistry of memory involves the addition of a phosphate group. Many hormones, insulin among them, begin life as different proteins, prohormones, which are then modified to become the physiologically active hormones.

The general term for these processes is *post-translational modification.* As yet, we don't have good general principles for post-translational modification of nanomachine parts. The genetic code and ribosomes are just a beginning. Eventually though, we can expect to acquire this knowledge.

In the meantime we can state some possible lessons. Current nanomachines contain one central, very general (but not totally general) kind of assembler nanomachine (the ribosome). After this nanomachine makes a part, other devices, usually enzymes, assemble it into the final nanomachine. It seems unlikely that we'll ever have or *want* to have single universal assemblers. It's much more likely that we'll have a toolkit of devices than a Swiss army knife.

But there is another lesson here too. Some nanomachine assembly currently works by a totally different process from any assembly we currently recognize. This process differs so profoundly that it must contain very important lessons not yet formulated. *Chemistry can work for us rather than against us.* Most nanomachines adopt minimum energy shapes. Their chemical content *determines* their structure. It also determines the way they combine with other parts. For instance, the four peptide chains in hemoglobin assemble together in one unique way, not because they are placed in that form but because their chemistry itself drives them to adopt that assembly. Collagen assembles into fibers for the same reason. Cell membranes form their particular structures because they have a natural affinity for that shape.

The lesson here is that *a great variety of structures can self-assemble*, by chemistry

alone. Their chemistry guides their assembly. They need no special intelligence or plan. Even when post-translational modification happens, the final nanomachine comes together by a kind of judo, not just brute force assembly.

Some thinkers in nanotechnology believe that medical repair requires intelligence, particularly pattern recognition, from the repair machines. Pattern recognition as we do it now requires great computational power. Pattern recognition: the ability to respond only to one particular molecular shape, is exactly how enzymes work. But they don't carry computers with them to do so. *That is the point.* Great computational power is no more needed for nanomachine assembly than it's needed to assemble crystals. Not only may we not *need* molecular-scale computers to solve repair problems, it may actually be better not to use them.

Development

Development is the process by which billions of nanomachines assemble together to form a macromachine. But this macromachine is of a complexity we currently don't know how to duplicate or understand. At the same time, just like all the workings of nanomachines, development is a commonplace miracle. If it weren't for the fact that it happens every day right in front of our eyes, we'd be astounded that eggs can grow into chickens or human ova and sperm can combine and grow into human beings.

When we discuss development we've moved into realms where few hard facts are known. But we do have a broad understanding of how development works.

The crucial concept (worked out before 1940, without specific chemical understanding) is that of *morphogens.* But only recently, since discovery of homeo boxes (collections of genes controlling development in both fruit flies and human beings) have we come close to chemically characterizing these morphogens. We don't have any classification of them or anything like a complete list, even now. One reason for the long delay in understanding development is simply that morphogens are known to exist only in very dilute concentrations.

Development works like this. Even within the single egg, a chemical is produced which diffuses throughout the egg in such a way that there is a *gradient.* More of the morphogen is at one end of the egg than at the other. The concentration of morphogen controls the level of other chemical activities. Different parts of the cell therefore become very different. When this cell divides, still other morphogens form. Their concentration also has gradients. As the complete nanomachine builds itself, these morphogens control the level, form, and character of cells. Every cell has the genetic potential to develop into an entire creature. But the exact tissue which it actually forms depends on its position relative to all of these morphogenetic chemicals.

This is a very interesting idea. It involves no idea of outside intelligence or outside construction at all. Even without knowing the exact chemicals involved (and in fact we still know very little about the exact chemicals) we can see that morphogenetic control could produce arbitrarily complex forms, very finely machined. We don't have to have *just one* morphogen. Moreover, even whether a cell *makes* a particular morphogen can be controlled by other morphogens in its environment. This process can build upon itself into structures of immense complexity.

Development becomes even more complex when we realize that cells don't have to stay in one place. They not only divide, they migrate. Neurologists have seen this with transplants of brain tissue. It's certain that it happens naturally,. not just to infants

but to adults, and not just to brain cells. Our body cells respond to morphogens by actually creeping about inside us: nothing is passive or inert. On a nanoscale level, our bodies resemble much more a collection of army ants than they do a single hard structure.

We can see development as an extension of the methods by which current nanomachines assemble their own molecules. The machine comes together by direct "recognition" of molecules for one another, not by any computational recognition from the outside. The process needs no special intelligence or computational power. Very simple nanomachines all act collectively in the proper way, because each one gets the correct chemical directions telling it what to do.

What Can These Methods Do?

The most outstanding insight from design of existing nanomachines is that large computational abilities are *not* needed to carry out and actively maintain an extensive developmental and repair program. These nanomachines solve the problem of recognition the way locks recognize their keys.

As a computer problem, recognition is hard. It doesn't become easy just because we've miniaturized our computers. That problem of recognition is exactly what repair machines must solve. Enzymatic chemical recognition is superior to computational recognition.

The second lesson is much harder. It's one thing to conceive *ideal* nanomachines and quite another to make a working model. Working models never equal ideal machines. It is not efficient to recapitulate the whole history of life on Earth by rediscovering again for ourselves the design problems the original nanomachines mastered billions of years ago.

In particular, there is no obvious reason why nanomachines of this kind could not, through evolution, produce yet smaller nanomachines of pure carbon: *unless* chemical attack, radiation, or the need for self-repair made such nanomachines impractical for most uses. Carbon is not a rare element.

But this point isn't just a negative one. Hemoglobin uses a heme group, *not* a protein, to hold oxygen, its essential function. We can consider many current nanomachines as structures in which peptide chains *protect* and *control* even smaller nanomachines doing the essential work. Nanocomputer elements might consist of a peptide

matrix holding rod logic devices which would not be stable on their own.

Such nanocomputers can use a water solvent for self-repair. For instance, computer elements could form membranes, with cell sap circulating between them. Repair enzymes within this cell sap could scavenge and replace damaged elements. The macrocomputer made up of these nanocomputers would have a hard outer shell, like an insect. Inside, though, it would be gooey and cellular.

In fact, we can use the principles of *current* nanomachines to achieve virtually all the effects discussed in Drexler's book, including medical repair and manufacture. But these principles go much farther. Here are some ways we can extend current nanomachinery to new realms:

* We can use new structural materials for our nanomachines. These can include rare elements such as gold. They can also include iron, which is not cosmically rare but is normally rare where current nanomachines operate. Furthermore, iron and steel suffer chemical attack which nanomachines could constantly repair. (Current nanomachines which use iron do so in combined form. Some mollusks use teeth of FeO. We can afford the energy to keep steel free of chemical attack).

* We are not limited to the chemistries exploited by current nanomachines. Silicon chemistry, particularly when combined with carbon-hydrogen chemistry, might let us create nanomachines of new types. Resistance to high temperatures is one important possible gain. (This requires a different solvent than water: see below).

* The solvent used for repair need not be water. Some ordinary, unmodified enzymes can function in ammonia. This means that we can have nanomachines operating at below-freezing temperatures.

One function of hydrogen in current nanomachines is to create hydrophobic structures. Ammonia solvents won't need this. Nanomachines using liquid ammonia will have a very different chemistry, even though based on peptide structures just like water machines.

The basic ideas of current enzymes aren't limited to water chemistry. It's very likely that other solvents exist within which nanomachines can work. We aren't limited to any solvents normally existing in nature. It would be valuable to explore solvents such as silicone fluids or liquid nitrogen for even lower temperature operation. Chemistry at lower temperatures, of course, would require much faster reactions than water chemistry. Biochemical reactions involving rhodopsin and other visual pigments occur rapidly even in liquid helium. Chemistries suitable to very low temperatures therefore exist.

High temperature nanomachines are also likely. Thermophilic organisms thrive in deep ocean hydrothermal vents at over 100°C, and probably at over 250°C. Their enzymes are stabilized by many cross-links.

Fundamentally, when we discuss nanotechnology we discuss the potential of *chemistry* to achieve machines on a nano scale. Current nanomachines show this potential is very great. We all (collectively) need to understand much more chemistry and biochemistry if we aim to make these nanomachines.

* *

BECOMING AN EMERGENCY MEDICAL TECHNICIAN

by Steve Bridge,
ALCOR Midwest Coordinator

"Each year more than 100,000 people die needlessly in the United States because of the lack of adequate and available emergency medical services. Most of the deaths occur from heart disease, accident injury, burns, poisoning, alcohol and drug overdose, premature births, and acute psychiatric disorders."

Brent Q. Hafen and Keith J. Karren, *Prehospital Emergency Care & Crisis Intervention, 2nd Ed.*, Morton Publishing Co., 1983.

About three years ago I got a call from Mike Darwin. Calls from Mike are always interesting, but they are also usully dangerous. That's because Mike usully wants something. What he wanted in this case was for me to become the Midwest Alcor Rescue Coordinator. In other words, I was being asked to acquire basic training to carry out the initial phases of a cryonic suspension: the resusitation initial cooling and transport of the patient. Since we had three people signed up in Indianapolis at that time, it seemed like a reasonable request. Mike suggested that the best way for me to acquire the basics of the training I would need was to become certified as an Emergency Medical Technician (EMT).

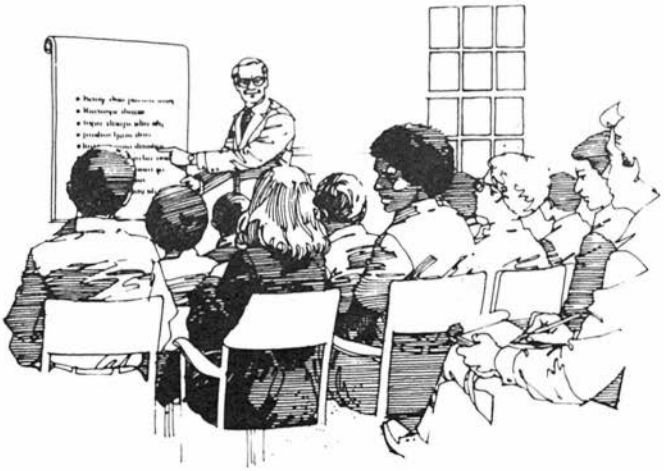
* * *

When I started taking the course to become an EMT two years ago, I didn't know what I was getting into. Professionally, I am a librarian in Indianapolis; I deal with books and knowledge more than with actions. Paper cuts are usually my most serious injury problem. But during the semester, I grew to understand how important this training is. On one of my ambulance observation evenings, we were called to the house of a woman who had drowned in a bathtub. Her husband had just arrived home and found her. She couldn't have been underwater very long, since the water was still very hot when we arrived. The paramedics with us suspected she had fainted and had slid under the water. The woman's husband did not know CPR, so all he could do was pull her from the tub and call for an ambulance. No one can be sure, of course, but there was a significant possibility that the woman could have been saved if her husband had taken at least a CPR class. All the way to the hospital, as I pumped oxygen into this woman, I thought, "This could be my lover or relative or friend. This is why I am taking this course."

Many of our members ask us how they can be more involved with Alcor or, if they live far away from Riverside, they may ask how they can improve the survival chances for themselves and their families. One of the most important ways you can increase the odds on staying alive is by improving your ability to deal with emergencies. One of the many ways Southern California residents could help Alcor is by gaining basic medical training to make you useful for suspensions and research. While we would be delighted if several of you rushed out and became physicians or nurses, we recognize that such a career change would take years, would be beyond the abilities of most of you (and us), and would be impractical for many other reasons.

However, there is a way in which any healthy, reasonably intelligent adult can receive basic emergency training which would be useful in many circumstances, both

receive basic emergency training which would be useful in many circumstances, both personal and for cryonics: take an *Emergency Medical Technician* class. EMT's are most well-known to you as the people who ride on ambulances and give emergency care in case of accidents, heart attacks, etc. Many cities are also fortunate enough to have a number of *paramedics* (much more highly trained emergency care-givers) to work from ambulances; but most primary care will be provided by EMT's. Many EMT's are not full-time ambulance workers but are volunteers who respond via radios and in their own vehicles. And many people take EMT classes without planning to participate as a professional or volunteer. They may just want to know how to recognize medical emergencies and how to do emergency procedures in case they are confronted with such an emergency at home or work.



Typically, an EMT class is two nights a week, three hours per class, for approximately one semester. Federal regulations require a minimum of 120 training hours for EMT certification; most states require far more. The course I took included 166 hours of class and observation. Some of your hours will be on non-class time as an observer in a hospital emergency room and on an ambulance. I would not classify it as a difficult class to understand, certainly not as difficult as most college science classes. Most of the class members had only high school diplomas. The class does require a lot of reading, memorization, and thought, however. And it is treated as a regular class -- you are graded both on your written tests and on your practical skills. In many ways, it was more work than almost any course I had ever taken; but then I was in the class to *learn*, not just to pass, and I took it very seriously.

EMT courses may be offered in a number of places in your community. I took my class through a local fire department, in cooperation with a nearby hospital. Large hospitals may offer their own programs, frequently as prerequisite for paramedic training. Vocational schools and community colleges may also give such classes. Every state is required to have an Office or Department of Emergency Medical Services, which can give you a list of accredited programs in your area. I also recommend you talk with EMT's, paramedics, and emergency room nurses to compare the different programs. Ask them which programs seem to turn out the most competent EMT's. You want a course with plenty of equipment on which to practice; but, as in any other class, the capabilities of the instructor are paramount. You want an instructor who not only knows the book requirements (so you can pass the state certification exam), but who also knows the practicalities of "the street." It is good to know the accepted way to splint a broken limb with professional equipment; but in an emergency a rolled-up phone book and a broom handle may be all you have to work with. And you can imagine that learning to save lives in a classroom is a far cry from actually having that responsibility on a three-car pileup at 2:00 AM during a rainstorm, surrounded by screams, sirens, and your own emotions.

What You Will Learn

It is amazing how many things can go wrong with the human body. You will learn hundreds, and those are only the immediate emergencies. Of course you must start with the basic anatomy and physiology of the human body, especially organs and bones. You will learn how to assess a patient's condition quickly, looking for situations requiring urgent attention. One of the first rescue techniques you will be taught is cardiopulmonary resuscitation (CPR), along with the Heimlich maneuver for choking victims. Next you might learn how to control bleeding and treat "shock." That does not mean "electrical shock." **Shock** is a state of circulatory deficiency, when blood is not being distributed to all parts of the body (like the brain). As a secondary result of many injuries and conditions, it kills a lot of people. You will learn about the truly amazing "shock pants," which can save many of those victims.

As you might expect, you will learn to deal with fractures, trauma, poisoning (including drugs and alcohol), and diabetic emergencies. You will learn to treat burns, heat stroke, and hypothermia (low body temperature). You will learn how to extricate, move, and stabilize patients. If you are fortunate, you may get to use power tools to tear cars apart (the "jaws of life", as the press has dubbed them). And you will be taught how to deliver a baby.

What You Will <u>Not</u> Learn

An Emergency Medical Technician is not a physician or a nurse. EMT's just treat the emergency conditions; they do not diagnose disease or prescribe future treatment. Basic EMT's are not allowed to start IV lines or to give injections or medications, although a few states have an Advanced EMT certification which may allow limited use of such treatment.

Keeping Up To Date

Your training does not stop with your basic class. For you to keep your certification current, you will be required to take a few hours of "in-service training" each year (Indiana currently requires 24 hours per year). Typically this is done by attending special lectures or by dropping in on regular classes for an evening here and there.

Should You Tell?

When your instructor goes around the room and asks each class member to tell why he or she is taking the course, should you announce "Because I want to learn to be a more useful cryonicist." I think not (especially if you live in Southern California right now). While I am an advocate of openness about one's cryonics involvement, when dealing with new groups of people I prefer to let them get to know me as a reas-

onable, competent individual for a few weeks. Then I can pick out the more open-minded people in the class to discuss cryonics with. Why start out the class fighting against mindless prejudice against cryonics? You'll have enough prejudice with being Black, Jewish, female, gay, overweight, underweight, red-headed, intelligent, or whatever characteristics that make you "different" anyway.

Using Your Certification

Many people taking your EMT class will be planning to use their certification as a professional full-time or part-time EMT. They will seek employment with an ambulance service, hospital, or other emergency care provider. Many people will become volunteer EMT's, typically becoming associated with a volunteer fire department. Some of the class members already will be employed as fire fighters or police officers and are taking the class to increase their emergency skills (many communities require their fire fighters to be EMT's also). A few people will find they like emergency care so well that they go on to become paramedics (several thousand hours of training) or nurses.

You may be taking the class just to learn emergency care for your family or yourself; but don't be surprised if you become so interested in it that you become a volunteer, too. In my case, my work schedule does not allow me regular hours to be a formal volunteer; but as often as possible I help with the EMT instruction course that I took. Usually I play a "victim" for the class members to treat; but I have helped with grading also, when it was in my range of competency. In any event, it never hurts to have other fields of knowledge in case you need a career change someday (although you should realize that a basic EMT is not a highly paid employee).

Other Possible Classes

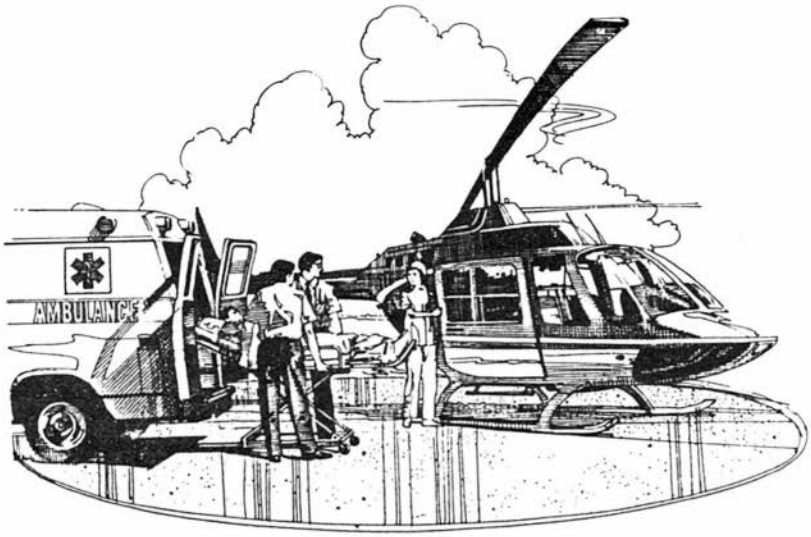
At a minimum, *every* healthy, physically able adult should know cardio-pulmonary resuscitation. CPR classes are offered by the American Heart Association and by the American Red Cross at many places in every community. The cost is never high, and frequently the class is free. There is no reasonable excuse for most of you not to take such a class.

Many communities also offer a "First Responder" class, a combination of CPR and emergency first aid. It typically runs 6-12 weeks and is good for the average citizen who wants to have basic knowledge. I would suggest that if your are serious about cryonics,
you may want to skip this class and go ahead for the full EMT certificate, which gives you more status, as well as more knowledge.

Being Useful

From Alcor's point of view, a member with emergency training is much more valuable. While little of your training will come into play directly in a suspension, the knowledge you gain will be a valuable basis for further training. You will know how the human body works, you will be used to speaking in technical terms, and you will know CPR. Since you will have made friends and acquaintances in hospitals and with ambulance companies, you may be of more use in negotiations with hospital personnel. And you will have seen and handled sick, injured, and dead people already, so you can be expected to stay calm in an emergency or during a suspension.

Even if you are not close enough to Riverside to help with suspensions, you will know



how to react if a family member or other person has an emergency. At the very least, you can give them a better chance for an effective suspension. At the most, your emergency knowledge may actually save their lives (or even your own life!) Another important consideration is that knowing emergency medical care makes you a more valuable member of your community. While it is important for cryonicists to look out for their own survival, it is also true that people helping other people make this a better world in which to live.

As an EMT, you will also gain a new perspective on cryonics. In a typical hospital, no matter how concerned and respectful the personnel are, once a patient is declared dead, he or she becomes an "it." The remains (no longer a "person") are placed in a body bag and put on a cart to be taken to the morgue (the door never says "Morgue," of course). The cart has a system of shelves to cover the patient so sensitive individuals in the hallway never know a dead body is being transported. When I was first asked to convey a body to the morgue, I was shocked at how "non-dead" this person looked and felt. It gave me a new appreciation of what a small difference exists between "legally dead" and "fully alive."

With cryonics, the patient never becomes an "it." Once the physician gives up, the suspension team takes over and the patient, at least in the eyes of Alcor, retains full status as a human and an individual. If I had gained nothing else from my semester of hard work, this insight alone would have made it worthwhile.

* *

MAPPING THE HUMAN GENOME

by Thomas Donaldson

About a year ago, sequencing the human genome became the latest project in Big Science. It's led to much discussion and commercial interest. Not long ago, at Stanford, *Intelligenetics*, a company selling software for genetic analysis, hosted a symposium on advances toward sequencing the human genome. Unlike other discussions of the issue, this symposium focused on the technologies involved.

These technologies are important to us because they affect just how fast we can expect our understanding of human genetics to move. The sequencing project with *current* technology is out of the question because of cost. The principal advances required are

advances in sequencing technology. The project isn't a simple one. They are also important to us because of the limits of what is done: we need to know what to expect from the project, and especially what not to expect.

Many cryonicists may feel that these problems are trivial. After all, these issues are only engineering details. Someday we'll handle life like clay. I believe this is wrong. Not because we won't have far greater control over life, but because we'll never have *arbitrary* control. We already result from many "design compromises". We don't understand our own current design and how it works. "Design compromises" are fundamental to engineering. Some of these simply will not go away, even if we learn how to completely rebuild ourselves. In obscure ways yet unknown, these compromises are inevitable.

That is, we need to understand our own operation so that we can see the limits of what is possible and just what we might become.

Just like maps of the United States, maps of the human genome can take many forms (we'll need them all). A *physical map* is a database of strands of DNA, each one overlapping its neighbors by a known amount, and including the whole of the human genome. Which human? That is important, especially since in practice each chromosome (or even sections of a chromosome) will be done in different countries, and probably not even to the same individual of any one country. But for now, we don't even have a physical map sufficient to cover the genome of one imaginary composite person.

Just how large an effort would this be? A DNA molecule consists of a long string of four chemicals, in arbitrary order. The exact sequence codes for a proptein molecule. These chemicals are the nucleotide bases: deoxy*adenosine* phosphate, deoxy*guanosine* phosphate, deoxy*cytidine* phosphate, and deoxy*thymidine* phosphate (A, G, C, T for short). The exact sequence codes for a protein molecule. It turns out that the human genome contains 40 billion nucleotide bases. The NIH database currently contains about 11 million nucleotide bases. We have a factor of 4000 to go.

But that isn't the only kind of map. We can have a physical map of the human genome without even knowing what the sequences are in each of the fragments of DNA which make it up. The ideal physical map would produce fragments of manageable size, about 40,000 bases long each one. This would mean that we would have about 1 million different fragments, each of which would need sequencing. The reason why 40,000 bases is a good size relates closely to our current technology. We want to use cloning techniques to make more of a given sequence. We need many copies just to find out the sequence, but more than that we need to understand how it works. *But* if we try to clone a sequence longer than about 40,000 bases the genes of the bacterium we're using will automatically cut it off. It won't clone. Of course this creates a very severe problem. Dr. Roland Davis, who spoke at the Symposium, among others, is working on methods which may let us clone base sequences as long as 1 million. That would obviously help the cloning and sequencing problem a good deal.

The third map is actually the most important and the hardest. Let's suppose we actually *had* a complete sequencing for a composite human being. This would be exactly like having a complete encyclopedia of the 30th Century, unfortunately written in a language we did not know and for which we had no key. What we *need* is knowledge of how the sequences of DNA relate to the characteristics of the human they will produce. A map which tells us this, specifying which sequences of genes at which locations relate to particular inherited traits, is called a *linkage map*. Lloyd Smith, who spoke at the Symposium about his methods of automating the sequencing of a genome, showed a slide

illustrating this issue quite well. It predicted 2 years for a physical map, 5 years for sequencing, and 10,000 years to understand the human genome (laughter). I don't believe we'll need 10,000 years. But this primary problem won't be solved for many years after we have a physical map and sequencing.

At the symposium, Helen Donis-Keller explained how we currently construct a linkage map. This study is the sort which recently located the gene for Alzheimer's disease, for instance. It has also uncovered the gene for cystic fibrosis, for a variety of manic depression, and for Duchenne muscular dystrophy. A large base of stored human cells from all over the world already exists. To locate a gene for a disease condition, we need cell samples from a *kindred* with the disease: grandparents, mother, father, and preferably a large number of children.

The second tool needed is an RFLP, a *restriction fragment length polymorphism.* Some genes on our DNA will easily cause it to break into two different pieces when attacked by suitable enzymes. These sites are inherited, and most important, they can tend to accompany other genes (such as a gene for Alzheimer's disease). If we have a large enough kindred showing inheritance of a gene (say for Alzheimer's disease) we can then break up their DNA, looking for RFLP sites. Since some of these correlate with the Alzheimer's gene, we have a good way of finding out approximately where it lies. It won't be the RFLP site itself, but it will be close by.

This technique of course requires that we have kindreds for the particular genes. This isn't an easy problem, especially if the gene is rare.

Paul Berg, who is at Stanford and led the panel discussion about the project of sequencing the genome, has been very much in favor for as long as the project has existed. The panel led to the sharpest discussion of the Symposium. One man got up and pointed out that sequencing the human genome wouldn't tell us about "anything" important: it wouldn't tell us about aging, development, or and other profound medical condition. Another member of the audience pointed out that if we sequenced mice instead of human beings, we could experiment on mice. We'd therefore come much closer to actually understanding how the human genome works, rather than just getting an encyclopedia in an unknown language.

Berg was very much a smoothie: he agreed with everything but in the end it became clear that the sequencing project was going to go forward his way. The objections will probably all come back once this big Federal project is done. On the plus side, the cost estimates for sequencing have fallen a lot. Participants were quoting total costs no more than $100 million. For biologists this is big money, but it only pays for a few jet fighters and comes nowhere near the NASA budget.

The greed with which some biologists contemplated these amounts of Federal money seemed apparent to me.

There will be a sequencing project. All the signs from all the relevant Federal committees point in favor. A DOE Committee, the Health and Environmental Research Advisory Committee, has voted unanimously in favor. It's also true that it will probably lead to some benefits, among which are understanding of a large number of inherited diseases, the kind with a simple heredity. Finally, this won't give us immortality (aging is not a condition with a simple heredity!). The sum of knowledge produced, though, will probably help out indirectly even to understand aging.

This story isn't over. We'll report more on it as news becomes available.

* *

Science Updates

by Thomas Donaldson

Are These People Mad?

Not long ago a Media Event occurred. A large scale medical test of aspirin to prevent heart attacks showed such a markedly lower rate of heart attacks in those taking aspirin that its authors decided that they must, ethically, reveal their results to the participants. The participants were all doctors, 22,000 male doctors. And so, since out of 22,000 male doctors at least one would talk, the authors of this study decided to make it public.

The news that aspirin would help prevent heart attacks swept the United States. Even Gary Trudeau of Doonesbury got involved, with a cartoon sequence in which one of his characters starts taking aspirin. The announcement, together with an editorial, appeared in the 28 January issue of the *New England Journal Of Medicine*, the most prestigious medical journal in the United States (*Physicians Health Study*, **NEJM, 318(4)** 262 (1988); editorial, pp 245-246).

Since I always check primary sources I read the announcement and the editorial in NEJM myself. Herein are some interesting figures that didn't find their way into the newspapers.

The study involved male doctors between 40 and 84 years old. None had had previous heart attacks, cancer, stroke, liver disease, or any current use of aspirin. After a shakedown period to find out how many could and would participate, the study started with 22,071 subjects.

The authors summarize their results in a table on the bottom of page 263 of their study. They break up all cardiovascular deaths into 6 different categories, including heart attacks, strokes, ischemic heart disease, sudden death, and "other". The total cardiovascular deaths in the aspirin group were: 44. The total cardiovascular deaths in the control group were (WAIT FOR THIS!): 44. They did also keep records of deaths from other causes than cardiovascular, for which their results were: 66 deaths in the aspirin group, 71 deaths in the control group. This difference is not statistically significant.

Looking at these figures in more detail, we find out that doctors taking aspirin were having strokes rather than heart attacks. Several different kinds of event were involved and the statistical significance for each one is not large. Even if these figures are preliminary, they are spectacular. Those taking aspirin showed a 5 times greater risk of moderate, severe, or fatal hemorrhagic stroke. A "severe" stroke is one in which the patient undergoes what these authors euphemistically describe as a "major change of lifestyle or dependency".

And so, the entire reading public in the United States has just learned that regular doses of aspirin will cause a death rate equal to that of people not taking aspirin at all. This news caused great public excitement.

The authors of this study are continuing a study of beta carotene and cancer. There is evidence that beta carotene, a less toxic chemical from which our bodies can make Vitamin A, will help protect against cancer. We can hope that these authors won't terminate their study after finding out that beta carotene does decrease cancer rates, announce it loudly in the press, and *then* let us discover that it raised kidney disease to new levels and left mortality unchanged.

What is positive in this study? Not an awful lot. But it does show that some funding agencies will support a very large study of a common chemical for its effect on health. That is a step in the right direction. Of course, we need work on a better selection of chemicals. We also need a less imbecile choice of objective for the study.

Gene Therapy Moves Closer

We've all dreamed of the day when we can cure our inherited genetic defects by injecting viruses (nanomachines) which spread throughout our bodies, transforming our genes and removing our problem.

It is only a few years ago that a researcher, Nathan Cline, got himself into trouble by trying to cure thalassemia (an inherited blood disease) with genetic therapy. His attempt didn't work. He's now forgotten. Scientists interested in genetic therapy turned their attention to other diseases, which they felt would be easier to cure. Among these were diseases such as Lesch-Nyhan disease, an inherited idiocy depending on a single gene and a well characterized metabolic fault.

It's therefore very ironic that quite recently, in *Nature* (*331*, 34-41 (1988)), three researchers at Cambridge, Massachusetts have just reported experiments which strongly suggest that blood diseases like thalassemia are actually very good candidates for gene therapy.

Elaine Dzierzak and her coworkers report in their article that they have successfully created a virus vector which inserts the human beta-globin gene into the bloodforming cells of mice. But the most important fact about this isn't that we can make such vectors but that the only tissues affected by them were the blood-forming tissues of the mice. One major problem with gene therapy is exactly that the inserted genes make their products not just inside the right cells but inside many other cells as well. Of course that's a disaster (and a new form of disease).

Dzierzak and her coworkers didn't have this success by pure chance. The difference between their work and others is that they didn't just insert the single gene for the proper kind of hemoglobin. They also inserted other sections of DNA which control the production of this hemoglobin. Previous attempts to transfer hemoglobin genes fell down on precisely this problem: the genes proceeded to not express themselves at all. Or even worse, they caused the brain cells, muscle cells, and others to make hemoglobin! By including not just the DNA sections describing the hemoglobin, but also regulatory sections, Dzierzak and her coworkers made mice which continued to make human hemoglobin for 4 to 9 months, and only in their blood-cells.

In all other respects, their techniques resembled those involved in other attempts to transfer genes. In particular, they irradiated the mice to kill off all their bloodforming tissue, and then transplanted new bloodforming cells which they had infected with the virus vector for their (human) hemoglobin DNA.

In the accompanying commentary published in *Nature*, D.J. Weatherall, who has worked in this area, points out that these experiments might alter the genetic makeup of later generations and *therefore* ought not to be applied (!!!!). He also presents several much more practical objections: these techniques don't yet make mice which make a high proportion of their hemoglobin as human hemoglobin. There's also a problem making enough modified bone marrow for a patient. Finally, he raises the usual absurd fears about

cancers caused by genetic therapy (no cancer has yet been caused by genetic modifications in animals).

Inherited faults in our hemoglobin are one of the most common inherited diseases in human beings. These new results take us much closer to a cure and alleviation of significant human misery. Thalassemia, in particular, may soon become curable, just as early visions suggested.

New Cryoprotectants For Vitrification

Since the work of Gregory Fahy, the idea of *vitrification* rather than freezing for cryopreservation has become more and more practical. When water freezes, it causes mechanical damage to blood vessels and organ structures. One way to avoid this damage is simply to prevent water from crystalizing. We can do this by vitrifying it, which is to make it form a glass rather than a crystal. Fahy believes, in fact, that we are very close to preserving kidneys through vitrification (cf. G.M. Fahy, in D.E. Pegg, I.A. Jacobsen, and N.A. Halasz (Eds), *Organ Preservation, Basic And Applied Aspects*, 1982).

However, even vitrification has problems. To cause water to form glass when cooled, we mix it with glycerol, ethylene glycol, or another substance which causes it to form a glass. But current glasses are quite unstable. They can crystallize either when cooled to too low a temperature or during warming.

Recently in *Cryobiology* (24, 355-367 (1987)) Pierre Boutron and P. Mehl at the *Laboratoire Louis Neel* and the *Laboratoire de Hematologie* in Grenoble France presented further work on special cryoprotectant solutions. Boutron is a physicist and immortalist who has actually written a book about the potential of suspension (although he is not a cryonicist, since he does not accept the possibility of reversing "death"). He has carried out a long research into possible new cryoprotectants, concentrating on their physical properties.

In this latest paper, Boutron and Mehl discuss water solutions of two different cryoprotectants. They are specifically searching for special solutions which will be more stable than any known before. That is, solutions which vitrify and at the same time show less tendency to spontaneously crystallize on cooling or rewarming. All solutions they studied were different alcohols.

Their solutions, this time, were mixtures of water, 1,2-propanediol, and 2,3-butanediol or water, 1,3-butanediol and 2,3-butanediol. They found the highest tendency to form glasses at fixed level of cryoprotectant (35%) in solutions with 2,3-butanediol. This tendency exceeds that of previously known cryoprotectant mixtures. The same chemicals would also show significant stability of the glass against crystallization. Although 2,3-butanediol is toxic, small amounts will improve glassforming tendency and stability without a corresponding increase in toxicity.

For any practical vitrification, we need solutions which form glasses at lower concentrations. We need more stability also. These researches are therefore very much to the point. In fact, short of a more fundamental biological understanding of freezing damage and its repair, search for a better cryoprotectant IS search for drugs more prone to form stable glasses than are the current cryoprotectants such as glycerol.

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Meeting Schedules

Alcor business meetings are usually held on the first Sunday of the month. Guests are welcome. Unless otherwise noted, meetings start at 1 PM. For meeting directions, or if you get lost, call Alcor at (714) 736-1703 and page the technician on call.

ALCOR

The MAY meeting will be held at the home of:

(SUNDAY, 8 MAY 1988) Bill Seidel and Candy Nash
10627 Youngworth
Culver City, CA

The JUNE meeting will be held at the home of:

(SUNDAY, 12 JUN 1988) Paul Genteman
535 S. Alexandria, #325
Los Angeles, CA

The JULY meeting will be held at the home of:

(SUN, 10 JUL 1988) Brenda Peters Combest
8150 Rhea
Reseda, CA

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The Alcor Cryonics Supper Club is an informal dinner get-together. These meetings are for newcomers and old-timers alike -- just an opportunity to get together and talk over what's happening in cryonics -- and the world!

If you've wanted an opportunity to ask lots of questions about cryonics, or if you just want a chance to spend some time with some interesting and nice people, pick a date and come! All dinners are scheduled for Sundays at 6:00PM.

SUNDAY, APRIL 24

The Breakers (seafood)
400 Fisherman's Wharf*
Redondo Beach, CA
(213) 376-0428

*Take Torrance Blvd. all the way down to the ocean.

DUE TO THE LIFE AGAINST DEATH WEEKEND MAY 27-30,
NO SUPPER CLUB MEETING IS SCHEDULED FOR MAY

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