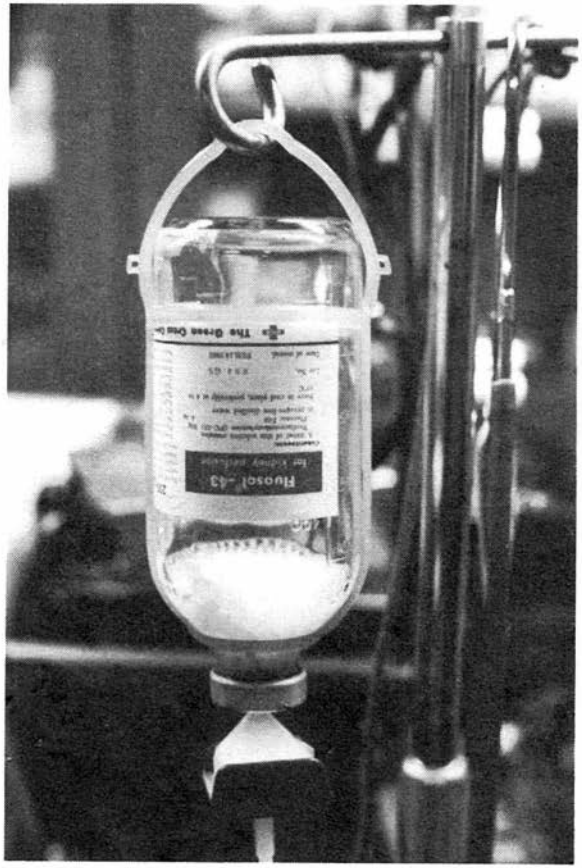
CRYONICS

VOLUME 6(5) MAY, 1985 ISSUE # 58



FLUOSOL 43 TO THE RESCUE

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VOLUME 6(5) MAY 1985 ISSUE #58

Contents:

CRYONICS is the newsletter of the ALCOR Life Extension Foundation, Inc. Mike Darwin (Federowicz) and Hugh Hixon, Editors. Published monthly. Individual subscriptions: $15.00 per year in the U.S., Canada, and Mexico.; $30.00 per year all others. Group rates available upon request. Please address all editorial correspondence to ALCOR, 4030 N. Palm St., #304, Fullerton, CA 92635 or phone (714) 738-5569. The price of back issues is $2.00 each in the U.S., Canada, and Mexico, and $2.50 for all others.

EDITORIAL MATTERS

No sooner had a copy of CRYONICS gotten to Dick Marsh, our correspondent in the Bay Area and an instructor in Communications, than he turned to his letter that was printed in the April CRYONICS. Then he called us to give us our grade. On page 7, second paragraph, first sentence should read "..., stop worrying the question, hyphen (-) should be a dash (--). As Dick points out, it changes the meaning. Sorry, Dick.

As it happens, we have also achieved some sort of a final solution to communications with Dick. We now have a piece of computer software (UniForm), which allows us to read text files off disks from Dick's word processor, an IBM PC running WORDSTAR.

With UniForm and the MFDISK that came with our Kaypro computer, we are now in a position to read a rather large number of 5-1/4" disk formats. The notable exceptions are the APPLE II, and unfortunately, the Teletek S-100 machine sitting here on the desk with the Kaypro. We have also read Fred and Linda Chamberlain's **Compaq**, running the **Volkswriter** word processor in MS-DOS. The Volkswriter file had to be worked over a bit to get it to cooperate with WORDSTAR, but the amount of effort required to do so was **much** less than if the same text were re-entered by hand. Thanks to Steve Bridge for sending an article from the Kaypro user's magazine that gave useful hints for the transformation.

Apologies to Paul and Jerry

We also need to apologize to Paul Genteman and Jerry Leaf for failing to credit the picture of them which appeared on the cover of the April issue of CRYONICS. Paul and Jerry generously consented to allow their photographs to appear in the magazine so that we could better tell the story of the recent suspension of an ALCOR member. Our apologies and our thanks.

A Word About This Month's Technical Paper

In this issue, and for the next two issues we will be presenting a paper on nanoengineering entitled "Prospects and Applications for Genesis and Ultra Mass Production of Submillimeter Machines, Devices, and Replicating Systems". Quite a mouthful, we know. Some readers may question the relevance of such a technical paper to cryonics. We want to point out that the advances of nanoengineering and full-scale molecular engineering are critical to the success of cryonics. Certainly they are critical to the development of repair techniques which will be necessary to recover patients currently in suspension

as well as those placed into suspension for the forseeable future.

But beyond the issue of repairing suspension patients looms the issue of saving the world, or at least of reshaping the world into one which cryonics becomes practical. Melodramatic? Not really. If civilization is to survive and grow it will need nanotechnology; it will need the resources, capabilities, wealth and change of lifestyles and attitude microtechnology and nanotechnology will bring. Conrad Schneiker's paper is an excellent technical overview of the prospects for micro and nanoengineering. Hopefully it will help to acquaint our more technically oriented readers with the possibilities this emerging area has to offer. As a minimum it will provide those with a nascent or established interest in this area with a rich source of reference materials which should provide much food for thought and act as a resource for the evolution of their own thinking. The bibliography of Schneiker's paper alone justifies its publication.

We hope to publish more papers in the future on micro- and nano-engineering, particularly those which deal with prospects for repair and reversal of freezing and other types of biological injury. We believe Schneiker's paper serves as an excellent base for those which are to follow and we are pleased to present it. At a later date, we will also be offering it as a separate reprint.

LAKE TAHOE

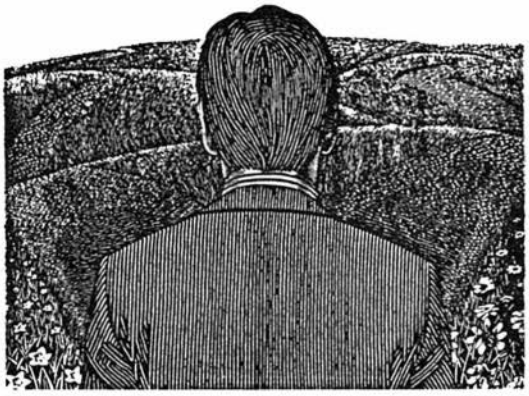
This issue of CRYONICS should reach most of the California subscribers sometime before the Tahoe Life Extension Festival, at least we hope it will! Why? Because some of us Southern California people have expressed interest in a Monday afternoon/evening horseback ride similar to the one offered last year. We're not sure how much interest there would be primarily because a lot of people will heading back home on Monday. However, if you're one of the lucky ones who plan to hang around for a while, and you're willing to brave the rocky slopes and dusty trails, give Fred and Linda a call at (916)542-1329 and let them know. DO IT NOW, 'cause by the time you get this magazine there will be **very** little time left to make the arrangements.

SUMS BOOKLET READY

For the past six months or so, Steve Bridge and Mike Darwin have been slaving away (in spare moments) on writing "documentation" for ALCOR's new suspension forms. From the very beginning of this effort (even before the paperwork was drafted), Mike Darwin had a "vision" of what "sign-up" instructions should be like. Mike had been exposed to cryonics legal forms practically since DAY ONE when he first signed up for suspension membership with the Cryonics Society of New York (CSNY) at the age of 15 (nearly 15 years ago). The old CSNY paperwork, while much simpler than today's forms, was overwhelming. There were five or six documents to fill out and have witnessed, and nowhere, but nowhere, was there anything or anyone to answer the hundreds of questions which naturally arise when someone is confronted with a task with which they are totally unfamiliar. Who can witness the forms (what about relatives)? How many

Signing Up Made Simple

A guide to making Cryonics arrangements with ALCOR



copies are needed? What is the correct procedure for executing a Will? What is the difference between whole life insurance and term life insurance? How do you handle hostile or uncooperative relatives? Question after question and no easy answers.

When ALCOR completed its latest legal update, the need to answer these kinds of questions and to provide simple, concise instructions on how to make cryonics arrangements became even **more** pressing because, for the first time in cryonics history we were signing up an average of **three** new members a month—month after month. For every member we were able to get signed up, we probably lost two or three who had purchased a set of paperwork, but due to distance or other problems were simply not able to fill it out. Additionally, those who **did** persevere and fill the paperwork out, required immense investments of time--answering hundreds of questions which could be answered more simply and effectively in print.

Mike spent a great deal of time buying and reading "self help" legal books such as those produced for use in California by Nolo Press, and in reading over the better computer software documentation packages which ALCOR had acquired (in supporting its three computers). The idea was to produce a lavishly illustrated, highly readable and even mildly entertaining guide to making cryonic suspension arrangements using the ALCOR suspension forms.

It wasn't easy. More than once Mike threw up his arms and shouted abusive invective at any nearby man, woman, or machine. (Fortunately, children rarely visit ALCOR. Even the resident dogs, Slinky and Dixie, suffered a tongue lashing or two) Finally, after completing about three-fourths of the writing, Mike turned the work over to Steve Bridge to finish up and to edit. The edited and completed work came back and Mike once again set to work: illustrating and doing a final layout and edit with the crucial assistance of Hugh Hixon.

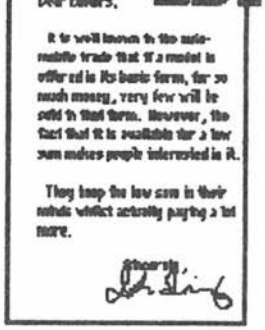
What resulted is a 98-page-long booklet entitled **Signing Up Made Simple: A Guide to Making Cryonics Arrangements With ALCOR** (SUMS). We think it's the best tool ever produced to "get people signed up." We realize we probably aren't the most objective judges, but we can't help but be excited about it because it turned out to be exactly what we expected—and more.

SUMS is readable, visually attractive, and it addresses most of the major issues people have concerns about. We realize that our first edition has some bugs in it (we've already started a test market with 1Ø people who have recently

requested suspension paperwork from ALCOR) and we hope that subsequent editions will cover more issues in greater detail, and even better meet the needs of people trying to sign up who live some distance away from ALCOR.

So, if you've tried to sign up in the past and the paperwork is still just sitting there (if you have a set of paperwork already, SUMS is available for $12.00), now's the time to think again. SUMS is available from ALCOR with a complete set of paperwork for $22.00. If you've thought about trying to get friends or relatives signed up, then you should also consider buying a copy of SUMS. Or, if you just want an attractive book which covers the legal and financial aspects of cryonics in an easy to understand way, then SUMS is something you'll definitely want.

LETTERS TO THE EDITORS


Dear Editors,

It is well known in the automobile trade that if a model is offered in its basic form, for so much money, very few will be sold in that form. However, the fact that it is available for a low sum makes people interested in it.

They keep the low sum in their minds whilst actually paying a lot more.

Sincerely

Dear Sirs,

As a mere subscriber to CRYONICS may I offer a word or two about your low cost option?

1. It is well known in the automobile trade that if a model is offered in a basic form for so much money, very few will be sold in that form. However, the fact that it is available for a low sum makes people interested in it. They keep the low sum in their minds whilst actually paying a lot more for various factory-fitted embellishments.

2. The high prices that need to be charged for cryonics can make people close their minds entirely. I agree wholeheartedly with the point made by both your correspondents in the April issue that trying to see to the needs of the many at the expense of the few often results in a dilution to destruction of resources, so no one benefits. This isn't the whole effect of offering reduced cost services. If you can offer a $17,000 option a person may feel that he can consider that, and then as his circumstances improve he can upgrade his membership. If he has to offer $35,000 to start with, he may reject the idea entirely, never to return to it.

It is possible that the appeal of cryonics is reduced the older a person gets, because of some form of sanity protection mechanism in the brain as death approaches. Such a mechanism could evolve because those that go mad with horror at the thought of their own demise would fail to reproduce. (Remember that throughout most of history, few people lived beyond the age of reproduction.)

If this is true, then the time at which recruitment is most easy is also the time when providing money is most difficult. I know that life insurance is cheap at young ages, but there are so many other financial demands. A young mind closed to cryonics is unlikely to open again at a future date.

3. Another point that is valid is that which was raised in **The Immortalist.** This is that we don't know for certain what we need to send to the future for reanimation to be possible. **The Immortalist** hints that organizations may form

that offer morphostasis in glutaraldehyde, and I understand that interment in the Arctic is also being considered for commercial exploitation at around $7,000.

Molecular machines may be able to retrieve program and data from the remains of brains that could never be made to work again themselves. If this is the case, they will also be able to retrieve data from the rest of the remains to build a new body that can be "loaded" with the program and data recovered from the old brain.

Denying people who can't make the best possible cryonics arrangements this level of hope is to fall into the same train of thought that tries to deny people the hope of cryonic suspension because it is not an FDA and professionally approved process.

4. If a person can only afford a full suspension for himself, and then have to leave behind his wife, girlfriend, parents, or children, then he may decide that none of them will go.

If he feels bitter about this he may even attack the concept of cryonics. After all, consider how the socialist organizations in Mr. Anzis' letter actually thrive by recruiting people to destroy something because they can't have it. It is well known in the UK when the Labour Party imposes punitive taxation on the rich that the actual revenue raised by the operation is minute compared to the take from ordinary taxation.

5. Through the Life Extension Foundation in Florida, ALCOR is probably going to get the biggest exposure to preselected interested people in the history of cryonics. It would be a great pity if this causes a turning-off of interest for financial reasons.

I can see the point of some of the arguments raised against the reduced cost options from the point of view of fully paid up ALCOR members. If ALCOR is not going to offer the reduced cost options, then I do feel that when the Life Extension Foundation decides to emphasize cryonics it should tell its members about lower cost options elsewhere.

Sincerely,
John de Rivaz
Cornwall, United Kingdom

Recently, we have referred a number of times to a forthcoming book by Eric Drexler. With the permission of Ed Tandy and Eric Drexler, we quote a portion of a letter from Mr. Drexler to Mr. Tandy concerning the forthcoming publication of Mr. Drexler's book.

> You wrote to ask how you can help with the matters outlined in Engines of Creation (formerly The Future by Design). At present, the problem is to get the book printed, distributed, and sold. The editor who purchased the book for Doubleday has left, and the new editors are still unknown quantities. Will they see the book as important and likely to do well? Will they be able to convince the decision-making

committees at Doubleday of this? If not, then the first printing will be small (only 7,000 copies or so). Then, if the book does do well, the bookstores will soon be sold out--and will stay that way for months, during which many people will look for the book, fail to find it, and give up.

People who want copies of the book--whether to have, give, or sell--should order them now. By doing so, they will not only guarantee copies for themselves, but may encourage Doubleday to decide to print more copies for everyone else, to meet a greater anticipated demand. Thus, one way to help is to order the book now and to encourage other people to do the same. To do this, write to Dave Barbor (my editor), state how many copies of Engines of Creation you will want, and ask him to forward your request to the mail-order sales department sometime before publication. They will contact you near the publication date (next March) to tell you the price and request a credit-card number or check. The address is:

Dave Barbor
Doubleday
245 Park Avenue
New York, NY 10167

Additional block-orders (or notice of planned orders) by groups and organizations would also be an excellent stimulus to the Doubleday bureaucracy.

In general, we need to make Doubleday see this as something more than "just another non-fiction book by a non-famous author." This means presenting the editors with concrete evidence that this is an unusual book that will generate strong word-of-mouth sales by a large, enthusiastic audience.

If they were to get several letters asking "How can I help promote this book?" this would probably shock them considerably. Ideally, these letters would come from different parts of the country, from capable-sounding people with diverse reasons for their interest in the book. If it were clear that these people are not a bunch of my old personal friends, but people independently attracted to by the ideas in the book, so much the better. So far, this is even true: you contacted me, not vice-versa. Again, the person to write is Dave Barbor, but with a suggestion that he forward your letter to the publicity department.

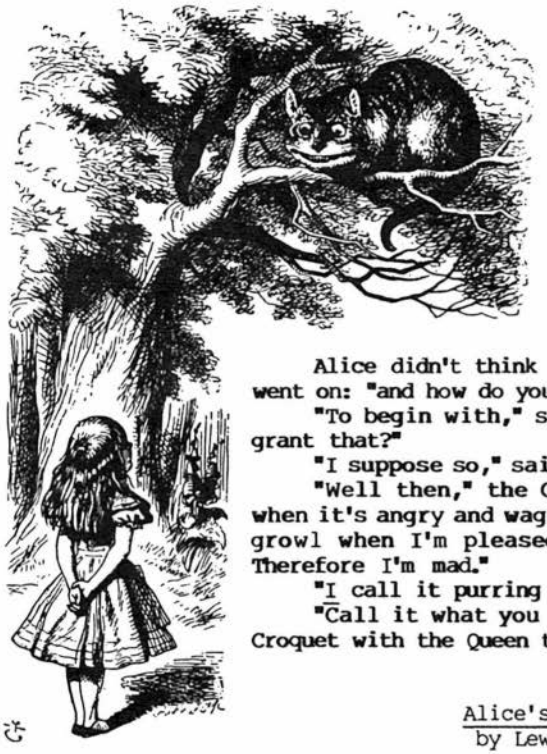
Please feel free to copy this page and pass it on.

Sincerely,
Eric Drexler
Cambridge, MA

[Ed. note: the date of this letter is 5 March, 1985. Therefore, publication of Engines of Creation should be in March, 1986]

An Invitation From The Rabbit Hole?

by Mike Darwin



"In that direction," the Cat said, waving its right paw round, "lives a Hatter: and in that direction," waving the other paw, "lives a March Hare. Visit either you like: they're both mad."

"But I don't want to go among mad people," Alice remarked.

"Oh you can't help that," said the Cat: "we're all mad here. I'm mad. You're mad."

"How do you know I'm mad?" said Alice.

"You must be" said the Cat, "or you wouldn't have come here."

Alice didn't think that proved it at all; however, she went on: "and how do you know that you're mad?"

"To begin with," said the Cat, "a dog's not mad. You grant that?"

"I suppose so," said Alice.

"Well then," the Cat went on, "you see a dog growls when it's angry and wags its tail when its pleased. Now I growl when I'm pleased and wag my tail when I'm angry. Therefore I'm mad."

"I call it purring not growling," said Alice.

"Call it what you like," said the Cat. "Do you play Croquet with the Queen today?"

Alice's Adventures In Wonderland
by Lewis Carrol

As a good number of our readers and members no doubt know, THE IMMORTALIST is the publication of the Cryonics Association (and Cryonics Institute) located in suburban Detroit, Michigan. CA/CI is headed by Robert Ettinger, the man who was profoundly influential in starting the cryonics movement a little over 20 years ago with the publication of his book "THE PROSPECT OF IMMORTALITY".

In the twenty years that have come and gone since publication of "THE PROSPECT...", great differences in philosophy and approach have developed between the various cryonics groups. To some extent these differences are legitimate and even laudable: they provide for a range of options and services that would not be available otherwise. In any event, they are not going to go away, not easily, not without a lot of hard work and sweat to resolve the questions they hinge on.

We offer this background because the February, 1985 issue of THE

IMMORTALIST contains an article which we find more than a little surprizing. It's entitled "An Immortalist Association?" and it's authored by Robert Ettinger. In this article, Ettinger proposes the creation of an amalgamation of existing cryonics and other life extension groups into an "Immortalist Association," a kind of super promotional entity which would publish a newsletter and get trendsetters to lend their names in its support.

On the surface, this might not seem like such a bad idea. After all, as Ettinger points out, consolidation of resources and the ability to attract more mainstream figures to "the cause" would be a plus. But, a look deeper in leaves us feeling a little like Alice after she took her tumble down the rabbit hole.

First of all, there is the very way we found out about this proposal: we read about it in the pages of THE IMMORTALIST. This seems a bit peculiar to us because in Ettinger's article ALCOR is mentioned. In fact, to quote: "It (the Immortalist Association) would publish a monthly called THE IMMORTALIST (Perhaps CA would relinquish the name and Alan Harrington who published a book of that name, might not object.) This magazine would allow the individual cryonics organizations to publish reasonable amounts of reasonable copy therein. Initially, if funding and labor were problems, perhaps publication could be worked out between the present IMMORTALIST (Cryonics Association) and CRYONICS (ALCOR)."

We find this peculiar because for the past several years we have barely been on speaking terms with the Michigan group (<u>they</u> sometimes refusing to speak to us—we have never refused to speak to them) and they have been anything but open about their facilities and capabilities. (In April, 1983 they refused to allow Jerry Leaf to visit their perfusion/storage facility <u>after</u> he had made an appointment with them and flown to Detroit expressly to do so). Relations, to put it mildly, have not been warm.

In part, CA/CI has been responding to disapproval from the leadership of ALCOR (and other cryonics and life extension organizations). In the past, ALCOR has published articles critical of some of CI's practices and we still have serious doubts about the way in which they are pursuing some aspects of their suspension program. These doubts have <u>not</u> gone away over the past few years.

Ettinger opens his proposal with a bit of rhetoric which can hardly be construed as an invitation to cooperation. He comments: "Newer (cryonics and life extension organizations) have generally had nothing to offer beyond another ego trying to round up the sparse herds under his own brand." But what really amazes us about THE IMMORTALIST article is that such a sensitive and potentially interesting proposal was handled in such a strange and unthinking way. Anyone with even slight savvy would have realized from the start that such a proposal would require a tremendous amount of careful groundlaying. Critical questions would have to be addressed and answered: Who would be involved? What kinds of cooperation would be expected from groups or individuals involved in the Immortalist Association? Does everyone fully understand what the organization would consist of and what its goals and objectives would be?

As a minimum, we would expect such a public proposal to come only after many letters had been exchanged and many phone calls made. This is not just a matter of soothing egos. It's a matter of addressing real issues and preventing the kind of misunderstanding and hostilities which have invariably cropped up in

the past due to lack of good, or even of any, communication.

It's instructive to realize that Ettinger has not travelled to California in years and that he has consistently turned down invitations to attend and to speak at the Lake Tahoe Life Extension Festival, which is THE meeting for every American cryonics group outside of CA/CI. Over the past several years the phones of ALCOR, BACS and Trans Time have seldom (if ever) rung with a call from either Ettinger or any other officer or director of the Michigan group. Indeed, all the communications received from Ettinger over the past decade by all the cryonics groups combined would probably not fill the average 14-page issue of THE IMMORTALIST. We mention this because it points up the hopelessness of Ettinger's proposal: it was made in a vacuum by a man who, whatever his past accomplishments may be, seems to understand little of what is happening today in cryonics outside of CA/CI.

The message from ALCOR is clear: cooperation is a two way street. Public proposals involving sensitive areas such as publications (and thus resources) must come long after and as a consequence of good, working communication and cooperation between organizations. Furthermore, as Ettinger himself points out, "There have also been several attempts to link up existing cryonics organizations under a single umbrella of one kind or another; these have all foundered on the rocks of strongly differing views." Well, what's changed in 20 years?

ALCOR stands ready and willing to both communicate and cooperate, but we will not compromise on the core issues: good patient care, honesty and integrity, and a commitment to action and research. The past few years have seen a tremendous growth in ALCOR, we believe largely as a result of these commitments. Before we can deal constructively with others we must be able to respect them. An Immortalist Association, or any other kind of association for that matter, is going to have to be something we can believe in and which we feel will materially help us to better reach our goals.

Until and if such a situation materializes we will echo Alice and avoid (as much as possible) the rabbit hole of internecine politics.

STANDBY IN FLORIDA : ALCOR EAST GETS A WORKOUT

The East Coast Branch of the ALCOR suspension team got their first chance at some real action—a recent standby for an elderly ALCOR member hospitalized for some orthopedic surgery. Since the member was 82 years old and the surgery

was for a fractured hip, it was decided to have the rescue team standing by in case there were any unexpected complications.

As it turned out, the standby went smoothly and the team, led by Glen Tupler and consisting of Dana Dye, oug Platte, and Saul Kent performed well. There was the usual anxiety that the hospital would not cooperate, but things turned out well.

According to Team Leader Glen Tupler, the member's son (also an ALCOR suspension member) had spoken with the member's physician and floor nurses and secured hospital cooperation. However, Glen, quite wisely, decided to go to the hospital administration and make sure that **they** understood and agreed to what was going on. Glen said they left him sitting in an office for about an hour until finally he had to inform the secretary that his place was with his team upstairs and that if they needed him they could come and get him.

Glen said that he decided to proceed as if they had the right to be there, and even asked for and got access to an empty room to practice set up of the heart-lung resuscitator and drill the team in its application and in deploying the other equipment and administering medications.

Finally, after the patient made it through the surgery without incident (as it turned out the physicians elected to use a local rather than a general anesthetic) Glen returned to the administration office.

The hospital administrator Glen had spoken with finally emerged from the office and, with a little amazement, asked Glen if he had been waiting there the whole time (a period of hours). Apparently the higher ups never reached any firm decision on cooperating, but the bottom line was: they didn't say no, and they didn't ask that the patient not return to their facility for further treatment.

Glen reported that the floor staff and physicians were very cooperative and that there were no problems in showing up and standing by.

Naturally, a number of problem areas were identified with the team's readiness, as is always the case with this kind of operation. We need better drug dosage sheets (a problem we **think** we have already better addressed: new sheets are winging their way to Florida even as this is being written), and the team needs more practice drawing up and administering medication. As Thomas Donaldson so graphically described in the March, 1985 issue of CRYONICS, learning to handle syringes and needles and withdraw medications from bottles is a far more difficult thing than one might think. It requires repeated practice and the development of manual dexterity. This is difficult for team members who do not work in a medical environment (such as most of the Florida team). We are taking steps to try to remedy this shortcoming by providing practice bottles and equipment.

On a related note, the first training session without California people present was conducted by Glen Tupler late in March, and the second session for Team B is scheduled for late April. Glen will keep us posted on East Coast progress.

TOTAL BODY WASHOUT #7: WRAPPING UP

On the weekend of March 22, we carried out the final experiment in our preliminary series of total body washouts. These experiments were designed to verify the compatibility of our "synthetic" perfusate with survival and recovery of dogs after four hours of perfusion at 4°C. As regular readers who have been following this work will know, we have had success in five out of six previous experiments in achieving long term recovery of animals. Five of the six previous TBWs involved four hours of recirculation at 4°C with one of these experiments terminating in the death of the animal 12 hours following the conclusion of the perfusion. That animal died as a result of intestinal and pancreatic bleeding (probably secondary to an undetected viral infection present before the experiment started).

It was hoped that this final experiment would allow us to apply insights gained from the previous six in a way that would allow for even more rapid recovery of this animal, with fewer of the complications and less tissue injury than had been observed in some of the earlier experiments.

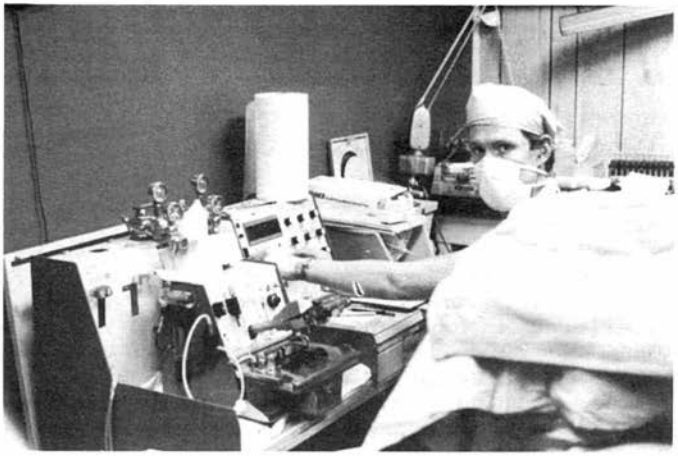
Unfortunately, our expectations were thwarted, and what we thought was going to be a flawless, routine experiment turned out to be a case study in an unusual complication.

The animal we selected for the experiment was a Huskie mix whom Mike christened "Nanook". The blood donor animal was a dog which had been previously transfused. Previously, we had not found it necessary to use dogs with a history of transfusions and we had been unaware until recently that they can be the source of hemolytic (red cell destroying) antibodies. Due to the extremely short supply of research animals on the West Coast (largely as a result of the animal rights activists) we were faced with no choice but to use this previously transfused animal as a blood donor.

The experiment, which got underway early on Saturday morning, proceeded so smoothly at the start that we completely forgot our anxieties about the donor dog. Usually, if you're going to have a transfusion reaction you see it right away, as soon as the test dose of blood is given or the animal first goes on bypass. Bypass, cooling, and washout proceeded smoothly. We were especially pleased with the smooth progress since we had a visitor from the Bay Area, Dr. Hal Sternberg, a Ph.D. biochemist working with Paul Segall and Harry Waitz of Biophysical Research and Development on the BACS hamster perfusion project (see Bay Area Update elsewhere in this issue for details).

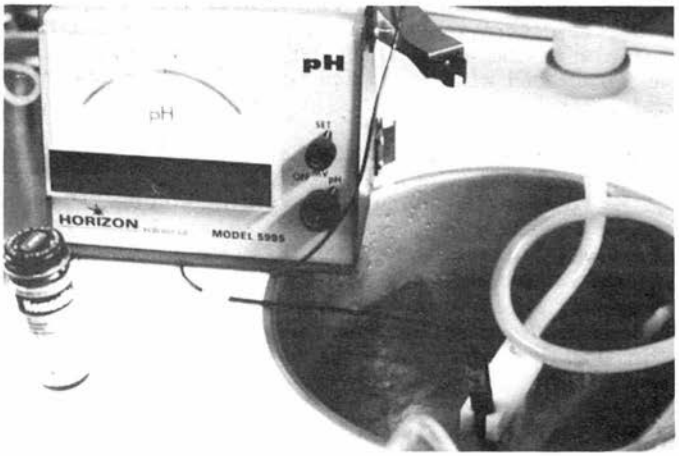
We tried, with a fair amount of success, to control the low pH which had plagued us pretty consistently up until the previous experiment. Al Lopp suggested continuously monitoring pH during the perfusion, and then volunteered for the job himself. Essentially what Al did was to sit at the blood gas console more or less continuously for about six hours and do perfusate and blood pH and gas determinations over and over again, constantly monitoring the progress of the animal and insuring that the pH didn't take a nosedive while no

one was watching (which it can do **very** quickly). During the previous experiment, about half way through dialysis we hit on the idea of continuously monitoring the pH of the dialysate (which quickly alters the blood pH to the same value) by immersing a pH electrode directly in the dialysate. We repeated this procedure during this experiment and found it very useful in providing for more or less dynamic control of pH during rewarming. Throughout the rewarming and blood reperfusion phase of the experiment everything seemed to be going smoothly.



Al Lopp at the blood gas machine doing one pH determination after another.

Our problems began to surface when the animal failed to regain consciousness when expected. (Fortunately or unfortunately, depending on your point of view, Dr. Sternberg was unable to stay for the "revival phase" of the experiment).. This was disturbing enough but was soon overshadowed by developing cardiovascular collapse. The animal began experiencing a variety of cardiac arrythmias and developing shock as evidenced by a climbing heart rate—at times well over 240 beats per minute. Despite fluid support and vasoconstricting medication, the heart rate stayed up and the animal continued to deteriorate. At 5:54 AM on Sunday Mike Darwin administered some Verapamil (a slow calcium channel blocker) in a last ditch attempt to short circuit the tachycardia (high heart rate). Shortly afterward the heart rate declined a little and stabilized. Mike went home to get some sleep (so he could relieve Jerry and the rest of the crew later in the day) and Jerry Leaf took over. Shortly after Mike left, the mystery of the tachycardia was solved. The dog voided



pH was continuously monitored in the dialysate by placing the pH meter electrode in the dialysate bath.

Sherry Cosgrove charts Nanook's re-warming.

several hundred cc's of black urine. A hematocrit was immediately done and it was discovered that the animal had lost slightly less than 2/3rds of his red cells to hemolysis! The hematocrit had dropped from a post-pump value of 26%, to 11%! Despite the fact that this is normally a lethal hematocrit for a stressed, post-surgical animal, Nanook slowly woke up and by 12:30 PM he was sitting up briefly and lapping water.

Nevertheless, the prognosis was not good. His heart rate was still higher than could probably be sustained for long, and he would need more oxygen-carrying cells to effect convalescence and recovery. Unfortunately, on a Sunday afternoon a couple units of dog blood is not something one can run down to the grocery store and buy. With time, it might be possible to round up a unit via one of the animal emergency clinics (since they maintain bleeder animals), but the problem was where to get blood now.

Finally, it was decided to expend some of a very precious commodity which we had been holding in reserve: a unit of Fluosol-43, a Japanese fluorocarbon blood substitute which is tremendously expensive and even more tremendously difficult to come by (the two units Cryovita had were a gift from a Japanese investigator friend of Jerry Leaf's). With a mixture of wistfulness and anticipation we administered the Fluosol-43. Within minutes of beginning the infusion of oxygen-carrying fluorocarbon micelles, Nanook's heart rate began to drop. His energy and alertness improved immediately thereafter.

Nanook awakens and takes his first sip of water following perfusion, as Jerry Leaf looks on.

Meanwhile, Mike Darwin began some energetic searching and managed to locate a pet clinic which could spare

a unit of blood (it was a busy weekend for the emergency pet clinics too!). At 7:30 PM, a transfusion of a unit of Doberman blood was started. Nanook promptly proceeded to hemolyze about 1/3rd of the transfused cells, but following vigorous treatment with steroids and benadryl the hemolysis stopped and his hematocrit stabilized at 21%, a survivable value (and more than adequate when the contribution of the Fluosol was added in).

Nanook's convalescence was delayed a little (though not as much as we expected) by his severe transfusion reaction. However, his recovery was complete and we are glad to report that he went home with his new "companion" today, April 8th! Nanook was fortunate enough to be adopted by Al Lopp, whose efforts no doubt in large measure contributed to his survival and reasonably prompt recovery.

A Special Thank You To Cryovita

The recent suspension of an ALCOR member and the recent completion of the TBW series, whose success has outdistanced our wildest expectations, bring powerfully home the need to point up the role of our "quieter" partner and to offer thanks.

Jerry Leaf, and Cryovita Laboratories of which he is president, has contributed at least as much, and being honest, maybe more, to the success we've experienced than our own efforts have. Frankly, we've been negligent by not acknowledging the role Cryovita has played in ALCOR's development and growth. By allowing us to occupy space at Cryovita at a ridiculously low rent, and by providing, free of charge, his expertise and equipment, Jerry Leaf, more than any other man, past or present, has contributed to the growth and success of ALCOR. His faith in us and his support is genuine and motivated only by a desire to see cryonics succeed and to see the research move forward. We can't thank Jerry and Cryovita enough.

In this series of TBW experiments Cryovita has shared with us, as an equal (and sometimes unequally **burdened**) partner. Credit for our success needs to be redefined: the "our" here is ALCOR **and** Cryovita.

In the suspension we recently completed it was Cryovita's generosity which to a large extent allowed us to facilitate growth of our donor fund by keeping marginal costs and outside charges for perfusion to a bare minimum. While it is true that the ALCOR staff provides services and benefits (by their presence) to Cryovita, they also inflict real liabilities (you should see the utility bills these days!). In the two-way street of cooperation it has clearly been Cryovita who has been logging the heaviest mileage.

Direct ways of repaying Cryovita are hard to come by in these early days. Mostly, what we have to offer is our thanks and our promise to keep up the pace of progress and to concentrate our resources, as we have in the past, on expanding our understanding of cryonics/cryobiology. We hope to have Cryovita with us every step of the way, hopefully as a less abused partner in the future! In the

meantime: THANKS! WHAT WOULD WE DO WITHOUT YOU?!

P.S. Please don't answer that question.

Cryovita Laboratories

Bay Area Update

by Dick Marsh

This issue of BAY AREA UPDATE is devoted almost entirely to a summary of a long phone conversation I had recently with Paul Segall. I found it so interesting and informative that I decided to omit from this edition of UPDATE all chitchat about who has been appointed to which committee and what we had for lunch after the last Board meeting. Instead, I have tried to present the meat of Paul's remarks with only minimal editorial alteration and embellishment.

In the conversation, Paul summarized the thrust of the research recently conducted by BACS and Trans Time researchers. More importantly, he evaluated its significance.

What follows is a mix of paraphrase and unattributed direct quotation mingled with explanatory comments and connective links supplied by me. Any incoherencies or inaccuracies are mine, not Paul's.

A Model T Research Model

What we have done (Paul explained to me) is to create a kind of "Model T" version of a research procedure useful for investigating the effects of low temperatures on small animals.

("We" refers primarily to Dr. Paul Segall, Dr. Harry Waitz, Dr. Harold Sternberg, and University of California senior Sandra Gan.)

The term 'Model T' is not meant to imply that there is anything dinky or rickety about the techniques perfected. Rather, it implies that they are simple, economic, easily available, and dependable. Low budget jewels within the grasp of everyone, not crown jewels limited to royalty.

And, although the techniques have been used only for research with small animals such as hamsters, they give promise of eventually enriching our knowledge of appropriate freezing techniques for use with large mammals such as dogs and humans.

Audrey Smith and the Beginnings of Cryobiology

To understand the achievements of BACS and Trans Time researchers, according to Paul, we would do well to go back to 1956, when cryobiology was a fledgling science and when Audrey Smith, an early founder of the field, published a series of three papers in the Proceedings of the Royal Society of London.

These three papers were collectively titled "Studies on Golden Hamsters During Cooling to Rewarming From Body Temperatures Below 0° C." They presented her observations of golden hamsters during chilling, freezing, and supercooling as well as during and after resuscitation.

They explain that Dr. Smith was able to freeze hamsters at a level substantially below the ice point. . . and then successfully resuscitate them. But they also lament the fact that there were frustrating limits to the time that the animals could be kept in the subzero state and to their survival time after resuscitation.

Therefore, towards the end of the third paper, entitled "Biophysical Aspects and General Discussion," Dr. Smith writes:

"Some means of permeating the whole animal with glycerol or some other neutral solute so that 10% or more of its body water is replaced thereby will doubtless be devised. Before this is done there is little prospect of preserving whole animals in a state of suspended animation for long periods in the frozen state at very low temperatures."

Drs. Segall, Waitz, and Sternberg, Ms. Gan, et al -- have now presented the scientific community with a model of a method for doing precisely that in the very animal which Dr. Smith wrote about — the golden hamster (mesocrycetus auratus).

Further, Paul explains, this model is based on an experiment which, unlike those using large animals, can be done very inexpensively in any university research lab, a well-equipped high school lab, or even an enterprising individual's garage.

This is truly a Model T approach as opposed to a Cadillac approach.

Work Shared With Scientific Community At Large

Moreover, the work being done by Drs. Segall, Waitz, and Sternberg, together with their associates, has been reported in the scientific journals and consequently is available for replication and elaboration by the international scientific community. It was done in the laboratories of the University of California at Berkeley and those of Biophysical Research and Development (BPRD), a small Berkeley-based company headed by Dr. Waitz.

What Have We Learned?

We now know, Paul told me, the following:

1. Hamsters can survive cooling to the ice point up to one day after

extensive replacement of blood with a simple balanced-electrolyte blood substitute.

2. Hamsters have been kept at the ice point for up to 1.5 hours, then revived.

3. Further experimentation, including the historic work on dogs at Cryovita, shows that mammals can in fact withstand long periods — up to four hours — of a similar blood-substituted state and then be revived and survive for long periods of time — six months or more.

4. The recent discovery of frogs whose bodies produce and use various cryoprotective agents such as glycerol and glucose suggests that the vertebrate body can withstand months of partial freezing at temperatures between -5° and -9° C.

5. Although Audrey Smith was able to revive hamsters frozen to well below the ice point, her success in resuscitating them and their subsequent survival periods were severely limited. This is why, as noted above, she called for 'some means of permeating the whole animal with glycerol or some other neutral solute.' Paul and his colleagues have perfected the means for doing this.

It involves the introduction into the body of the hamster of blood substitutes containing these substances. These are the substances which are naturally produced by the frog, which is therefore able to withstand freezing so spectacularly, but which are not naturally present in the body of the hamster.

Making available to the scientific community-at-large, as Segall, Waitz, and Sternberg have done, information about these blood substitutes and the techniques for introducing them into the body of the hamster adds up to an important contribution to the cryobiological world.

Why 'Model T'?

To summarize the reasons for the label 'Model T':

1. This bloodless hypothermic model is readily available to all.

2. It is inexpensive, simple, and convenient.

3. It provides a means of doing whole-organism cryoprotection research in pursuit of techniques for long-term solid-state suspended animation.

4. It can be used with small animals and thus eliminates the complex and expensive necessity of working with large animals.

5. It eliminates the need for a surgeon.

6. It permits experimentation with freezing at sub-zero temperatures. To date there are no reports of the successful revival of dogs or other large animals frozen at sub-zero temperatures.

7. It may give us an "edge" in developing techniques which, when

perfected, could be applied to larger animals such as dogs and humans. Hamsters are hibernators and thus may have a little extra resilience in the face of the techniques necessary for freezing and reviving them before these techniques are fully developed. The edge provided by this toughness may be important in allowing us to perfect techniques which could be applied to the larger animals.

8. It makes feasible the large number of experimental freezings, near-freezings, and sub-zero freezings which may be necessary before dependable methods for freezing and thawing large animals are perfected. Reversible solid-state suspension may be the culmination of numerous preliminary experiments. In our labs (especially Biophysical Research and Development), Paul explains, we have done more than 100 hypothermic bloodless perfusion experiments in one year on a budget approximately equivalent to the annual salary of one junior scientist.

Telling the World About It

All this should make apparent the value of the cryobiological research which has been conducted and continues to be conducted by scientists at BACS, Trans Time, the University of California at Berkeley, and BPRD. We have brought this research to the attention of the general public by the broadcast media — both television and radio — and by the print media. We have alerted the financial community. There is this modest little piece in the current issue of CRYONICS (not to mention previous editions of BAY AREA UPDATE in earlier editions of the Newsletter), and we have been noticed by other publications in the immortalist community.

Perhaps most importantly, we have been active in the world of scholarship, where we have begun to be listened to with increasing interest and respect.

The World of Scholarship

Previous editions of BAY AREA UPDATE have reported Northern California research activities in cryobiology which have been honored by the scholarly community. Two recent events are these:

1. "Reviving Hamsters After Hypothermic Asanguineous Perfusion," Harold D. Waitz, Hoyt Yee, Sandra Gann [sic], Paul E. Segall, Cryobiology, Vol. 1, p. 699, an abstract of an oral presentation by Paul Segall at the 21st annual meeting of the Society for Cryobiology, Aug. 21-24, 1984, University of California, San Diego, La Jolla, California. The abstract was based on the low-temperature hamster research of the cited authors.

2. "Ice-Cold Blood-Substituted Hamsters Revive," S. C. Gan, P. E. Segall, H. D. Waitz, H. Sternberg, accepted for oral presentation at the 69th Annual Meeting of the Federation of the American Societies for Experimental Biology, Apr. 21-26, 1985, Anaheim, California. A written abstract was published in the FASEB Proceedings which reported that the research it describes was supported by BACS and the Foundation for the Enhancement and Extension of Life (FEEL).

These two papers are important steps in sharing with the scientific community the details of the Model T research model discussed above.

Optimistic Outlook

Fellow cryonicists, immortalists, and life-extenders, I have a feeling in my still-to-be-frozen bones that we're going to make it! Researchers at BACS, Trans Time, BPRD, the University of California, Alcor, Cryovita, in South Florida, Michigan, Australia, France, and wherever people love life and abhor (not fear, but abhor) death, working cooperatively and imaginatively, and managing to cope ingeniously and resolutely with limited resources, buoyed by the support, understanding, and admiration of the rest of us as we rise above our petty differences, are going to persist in their battle against humankind's ancient enemies — aging and death — until these terrible, cosmic injustices and absurdities are eliminated.

Purple prose, maybe, but words to live and keep on living by.

Prospects and Applications for Genesis and Ultra Mass Production of Sub-Millimeter Machines, Devices, and Replicating Systems

(Part 1 of 3)

by Conrad Schneiker

INTRODUCTION

This paper examines the potential of some developing technologies for automated mass production of a wide range of miniature machinery and other microtechnology (MT) structures in very large quantities (10^6 to 10^{21}). These MT items may range in size from the just barely visible, submillimeter domain, down to the molecular, nanometer domain. The long-term prospects of molecular engineering and molecular automata are considered (Feynman, 1960: Drexler, 1981), as are much more near term, larger scale, intermediate MT products and some eclectic implementation schemes. The latter may permit the development of exponentially replicating computing machinery, energy generating devices, or life-saving medical instrumentation 5-15 years earlier than the former: in either case, the possibilities seem spectacular. A variety of potential applications are discussed, since they suggest and justify productive directions for MT R&D. **It is argued that the development of artificial replicating MT (ARMT) is possible in this century,** and further, that its development could open up so many new possibilities of such great value in science, engineering, medicine, and industry, that, logically it deserves at least the same level of support given Project Apollo, the Japanese 5th generation computer project, fusion energy research, or cancer research. ARMT has such broad practical implications, of such a radical character, that its development may amount to an industrial revolution.

Many ideas discussed below are not, individually, especially new or novel. However, they seem to have been rarely considered together or in this particular context. Hence, their combined potential has not been appreciated enough to generate development efforts comparable to the above-mentioned projects. Many others have made important contributions to the field of MT and ARMT engineering (often indirectly and unwittingly), but without the recognition their work deserves. To remedy this situation, and to encourage greatly increased levels of multi-disciplinary research and development along these lines, extensive references are provided. The current status of ARMT, especially considering Von Neumann (1966), Feynman (1960), and Moore (1956) is reminiscent of the development of the Eniac computer of the late 1940's: **"What puzzles me most is that there wasn't anything in the Eniac in the way of components that wasn't available 10, and possibly 15, years before.... The Eniac could have been invented 10 or 15 years earlier, and the real question is, why wasn't it done sooner?"** (J. Presper Eckert, Jr.).

The glossary of Carter (1982a) is recommended for readers unfamiliar with the technical terms used below in the rest of this paper.

HISTORY AND BACKGROUND

Ideas for MT systems come from many fields. These are a source of many good ideas, analogies, and examples for potential MT components and systems. This is especially true of biology, **where whether a proposed theoretical**

molecular mechanism in biology is or is not in fact used by nature, it still may be ultimately practical (perhaps with modification) for artificial MT machines. Similarly, some principles governing the formation, structure, and operation of biological molecular components also apply to artificial systems with larger size scales or different physical environments.

Molecular biology has revealed a fantastic and diverse array of molecular machinery. Examples include DNA information storage and state machines, mRNA message systems, tRNA parts delivery systems, peptide signalling systems, programmed ribosome protein constructors, membrane pumps, flagellar motors, enzyme clamps with cutting and joining functions, chlorophyll solar power converters, very sensitive protein light sensors, semiconducting proteins, protein actuators, etc. (Drexler, 1981; Hopfield, 1974; Robb & Barron, 1982; Stryer, 1981). Current work in biochemistry and biophysics is dramatically increasing our understanding of how such molecular structures work. Likewise, the search for the origins of life has stimulated considerations of much simpler molecular machinery involving small numbers of components for building primitive replicating chemical information storage systems (Baker & Allen, 1971; Eigen & Schuster, 1979, Eigen & Winkler-Ostwatitsch, 1981a, 1981b; Price, 1974; Root-Bernstein, 1982a, 1982b). Even more simple clay and crystal replicators have been suggested in Cairns-Smith (1971, 1981, 1982).

In the 1950's, the development of automata theory began as a distinct field (Von Neumann, 1951), and later included serious study of abstract self-replication, producing a replication model as proof of its feasibility (Von Neumann, 1966). This model was later refined by Codd (1968). Generalizations of such models and their relations to other scientific questions have been considered by Arbib (1967a, 1967b), Myhill (1964), and Smith (1976). More biophysical or implementation-oriented discussions of self-replicating machines are in Conrad (1982b), Jantsch (1980), Laing (1975, 1976), Martinez (1979), Penrose, (1959), Kemeny (1955), Miller (1978), and Taneja and Walsh (1981). Moore (1956) proposes manufacturing self-reproducing artificial plants to be harvested for their products. Long and Healy (1980) propose a replicating lunar industrial system. Applications of replicators to supply energy and to rapidly terraform planets are suggested in Dyson (1981). With the advent of genetic engineering, there has been a surge of interest in constructing computers from biological components (Angier, 1982; Bussert, 1982; McGill, 1982; Ostroff, 1983). A competing approach to molecular computing involves chemical synthesis of molecular electronic devices (Carter, 1982a, 1982b). The capabilities, structures, and functions of natural molecular computing and regulatory systems are discussed in Conrad (1972a, 1972b, 1973, 1974a, 1974b, 1976, 1982b), Conrad and Rosenthal (1981), Conrad and Liberman (1982), Conrad and Rossler (1982), and Liberman (1979a). A large number of molecular-scale, energy-related storage, transduction, gating, amplifying, and effector mechanisms are known, and may have potential applications to MT tools, robots, teleoperators, switching, and computing systems. These biological structures are discussed in Avery (1964), Avery and Pavildou (1974), Bard (1980), Chance (1979), Cope (1970, 1973a, 1973b, 1975, 1982), Davydov (1977, 1982), Fox (1982), Goldfein (1980), Gomer (1982), Hagen and Reid (1980), Hamerhoff and Watt (1981, 1982), Hartline (1979), Hopfield (1974), Koshland, Golbeter, and Stock (1982), Liberman (1979b), Lipinski (1982), McClaire (1971), McGiness, Corry, and Proctor (1974), Polonsky (1964), Popp (1979), Popp, Becker, Konig, and Peschka (1979), Savageau (1981), Savageau and Lapointe (1981), Stein (1982), Straub (1974), Szent-Gyorgyi (1968), and Thompson (1982a, 1982b). The symmetry principles governing the shape, structure, and evolution of biomolecules in Kilkson (1968, 1969, 1970, 1975)

might be extended and applied to prediction and design of larger or nonbiological artificial structures, in addition to suggesting a great variety of potentially useful molecular structures which natural selection necessarily failed to invent or otherwise bypassed. The ultimate miniaturization and performance limits for computing and other functions are considered in Bailey (1978), Freiser and Marcus (1969), Gilbert (1961), Keyes (1969, 1970, 1972, 1975), McClaire (1971), and Simon (1978). Von Neumann's attempts to understand how very complex systems with very large numbers of unreliable parts may function reliably may be found in Von Neumann (1951). Winograd and Cowan (1963) show how such systems may be realized.

ULTRA MASS PRODUCTION AND REPLICATING SYSTEMS

One reason for concentrating on miniature (submillimeter to submicron) robot and teleoperator construction systems rather than larger macro scale robots is **relative economy of resources and greatly reduced costs for large volume production of miniature robots and tools.** This is important if research in those domains of applied automata theory needing large numbers of similar or special purpose automata is to be both feasible and economical. Scaling down makes resources relatively more abundant and less expensive in the ratios of the corresponding volumes, expanding the limits of growth of robot populations by factors of millions or trillions, depending on size. Tiny gadgets built from tiny parts can take advantage of the inexpensive mass-produced products of biotechnology and photolithographic processes. For many products (including computers, communications equipment, and various types of biomedical instrumentation), there are positive gains in speed, ruggedness, power efficiency, and range of applications, due to decreased size.

Fully automated, MT production systems with relatively large and sufficiently cheap resource pools can expand their immediate or potential maximal production levels at rates equal to: (a) the time of their operation squared; (b) the time of their operation cubed; (c) the exponential of their time of operation; or even at (d) super-exponential functions of time. Rate (a) may be achieved by mass-producing MT factories, (b) may be achieved by mass-producing the factories of (a) above, (c) may be achieved through self-replication, and (d) may be achieved via cooperative replication. Linear speedup may be obtained simply by parallel operation of machines, where for instance, one teleoperator or robot controller might guide thousands or millions of identical machines through (effectively) identical operations. Very large linear speedup (or parallelism) occurs naturally in bulk chemical reactions, and most elegantly in the self-assembly of large biological macromolecules. Larger scale analogs of these processes may be worth developing using larger electric or magnetic field patterns in static or dynamic configurations.

The desire to realize the tremendous potential of exponential production via replicating systems has led to the examination of very large, 100-ton replicators (Long & Healy, 1980) and of very small, molecular scale replicators (Drexler, 1981). Although replicators of both scales will likely be developed and prove very valuable ultimately, intermediate scale replicators should be much easier to develop initially, and thus could be available substantially earlier. This is encouraging, since replicators of any scale should be quite valuable by virtue of exponential production. **Replicators in the 1 mm to 1 micron range may be the best range for initial development: they would be small enough to keep materials costs relatively low, they would be both large and**

small enough to most easily use parts grown by or derived from biological replicators (i.e., cells), they would be large enough to permit easy optical inspection, they would be large enough for current generation micromanipulators to operate on,they would be comparable in scale to the previous and current generations of Very Large Scale Integration (VLSI) technology which would be used to produce development tools, etc. This seems like the easiest level to create and debug artificial replicators, all things considered.

Replicators (as distinguished from self-replicators) need not be single, autonomous machines. A replicator may be a distributed system of specialized machines working together to replicate the entire system. A group of replicating machines may be synchronously operated in parallel by teleoperators under human control. These types of replicators may be much easier to develop than self-replicators and yet could still generate exponential production increases for a fixed labor input. As an example of these possible variants, our industrial economy may be conceived of as an evolving replicating system with a doubling time of about 30 years (Henson, 1983).

The initial generation of replicators need only simple capabilities (in addition to replication) in order to be very valuable. For instance, if each replicator can build a few thousand bits of computer memory or simple computer functional units and join them with similar components, very large numbers of very powerful computers with gigantic memory could be built for relatively low cost. This would permit the realization of a significant fraction of the economic and component count scaling benefits of molecular computing in advance of its development. This same principle applies to other technology that scales well as a function of large component counts. Such replicators could then be successively transformed into both larger and smaller replicators, and may also be combined in a symbiotic manner with biological cellular replicators. The stages of protein MMT development outlined by Drexler (1981) could be used by these larger replicators (and their products) well in advance of the time when their intended application for general purpose molecular assemblers and replicators would be possible, promoting more rapid development of these intermediate components by making them immediately useful.

Very large volume mass production can be accomplished without replication by using the multiple stage production (MSP) methods of (b), and especially (c) above. For many applications requiring only a few billion or quadrillion of a given product, these may frequently be better than replication for two reasons: (1) Exponential replication will eventually be limited to quadratic or cubic growth in 2- or 3-dimensional media with finite transport speeds, and so will limit the marginal value of replicators. (2) Designing replicators is, in general, a much more complicated task than designing MSP MT (MSPMT) systems, which would delay production of the desired end product for years or decades.

BOOTSTRAPPING TECHNIQUES

There are several ways that initial micro and molecular robot tools might be developed. These include: (1) using small precision machine tools to build still smaller tools of still greater precision, and so on, in a descending hierarchy until the desired size is reached; (2) using modified VLSI or nanolithography masking, etching, and deposition technology to make tiny parts out of a wide variety of materials; (3) genetic engineering techniques; (4) extraction and use of molecular structures from plants and animals. These are

discussed below. In practice, a number of combinations of these techniques may be used.

(1) Feynman (1960) proposed the development of a series of increasingly smaller teleoperated machine tools, each set of which would be used to build the next smaller set and so on down to the atomic level. At each level, much larger numbers of machines would be built and operated in parallel. Various operations to produce more precise flat surfaces and other structures would be needed at each level. Changes in machine design would be needed at each level to compensate for, and take advantage of, molecular forces and other effects encountered in the manufacture of each smaller generation of machinery.

(2) **Many intermediate levels of machinery in Feynman's program may be skipped by modifying existing photolithography processes developed for VLSI** circuit fabrication, or electron beam lithography (Isaacson & Muray, 1982). These micro fabrication methods give feature sizes in the 0.5 - 5 micron range and in the 2 - 4 nanometer range, respectively. **These would greatly simplify Feynman's proposal by starting out with a (physically) far smaller set of initial tools which would be nearly the same size as their anticipated products.** Actuators and force sensors might be manufactured from piezoceramic materials (Henry, 1969; Ruby, 1982; Von Randeraat & Setterington, 1974) or from silicon (Barth & Angell, 1981; Hu, 1981; Peterson, 1978). Additional information on microscience and microfabrication may be found in Krumhansl & Pao (1979), Wohltjen (1982), Wolf (1979), and Gilbert (1961).

(3) The construction of molecular computers from genetically engineered molecules was proposed by McAlear & Wehrung (1982) and Ulmer (1982). A much more ambitious set of capabilities is aimed for in the farsighted proposals of Drexler (1981, 1982b), where advanced protein design techniques would be used to produce a protein-based Molecular MT (MMT) for construction of a wide range of more general purpose molecular scale machinery, including protein machine tools robots, and computers. This technology base would then be used to bootstrap non-protein machinery with still greater capabilities and operable in a much wider range of temperatures, pressures, and chemical environments. This approach depends on great advances in computer prediction of protein conformation, although the task may be simplified somewhat by selecting amino acid sequences which make the task of prediction easier. Some progress is being made here in the design of enzymes (Breslow, 1982; Ulmer, 1983) and other organic structures (Wolken, 1980). A simplification of this approach starts with known conformations of prefolded polypeptide backbones and then picks amino acid combinations to stabilize them and provide desired reactive groups (Pabo, 1983).

These schemes may be improved in several ways. Lists of many examples of biomolecular analogs to macroscale technology, including beams, cables, actuators, motors, production lines, and numerical control systems are given in Drexler (1981). Rather than design new versions of these things from scratch, one could find and manipulate the DNA sequences which already code for similar functions. For instance, two common proteins, cytochrome oxidase and melanin, show semiconducting activity, and so might serve for molecular electronic parts (Cope, 1975; McGiness, Corry, & Proctor, 1974). Many biopolymers are also semiconductors (Simonescu, Dumitrescu, & Percec, 1978). There is increasing evidence that some biomolecules are dilute organic superconductors at physiological temperatures (Cope, 1982; Goldfein, 1980). Visual pigments may be a basis for molecular switches (Honig, 1982). Many other types of energy trans-

duction, switching, storage, recognition, and effector molecules have already been discovered in biological cells (Bard, 1980; Chance, 1980; Changeux, 1970; Cope, 1970, 1973a, 1973b, 1975, 1982; DeLuca & McElroy, 1981; Hopfield, 1974; Lipinski, 1982; Popp, 1979; Simonescu, Dumitrescu, & Percec, 1978; Stryer, 1981; Szent-Gyorgyi, 1968; Thompson, 1982a). This suggests an easier general approach which could, perhaps, be completed in one decade instead of two or more: since we already may have most of the needed protein tools, the main task (which is far simpler than ab initio design!) would involve suitable duplication and modification of these molecules and coupling them or directly connecting them via initial synthesis, genetic segment recombination, self-assembly, micro-teleoperators, micro-robots, or other mechanisms. (See the section on computer-aided heuristic design for suggested methods of doing this.) Since only a tiny fraction of all existing proteins and other naturally occurring molecules have been examined at present, our current knowledge base of protein molecular mechanisms could, if desired, be greatly extended by sequencing and characterizing the bulk of the more interesting human, plant, bacterial, and viral proteins. This task seems well suited for automated, brute force attack with present technology (Hunkapiller & Hood, 1983), and is an extension of a similar proposed project to map all the human proteins and DNA for medical applications (Wade, 1981).

Another possibility is to replace the redundant codon assignments in the genetic code, allowing for (say) twice as many amino acid types to be used. The new types of amino acids could contain new types of functional groups (organo-metallic structures, isotope labeled molecules, fluorescent molecules, etc.) or even be bound to preassembled protein (or other) modules. These could also be selected or designed on the basis of the ease with which their conformation might be predicted or controlled. Many distinct sets of codon and amino acid pairings may prove useful. They might be synthesized and bound to the appropriate tRNAs outside of cells before being assembled by ribosomes.

(4) The various molecular parts and products of phages, microbes, cells, plants, and animals provide a vast array of potential parts for MT structures. They have the advantage of being inexpensive, prefabricated, and standardized. The main problems with using them are those of identification, characterization, extraction, recombination, and implementation of useful components. These may be used as is, or may serve as molds, forms, templates, etc., for further processing. Thus some MT parts might be grown, say, in insects, or tissue cultures, or vats of cells. These parts may require some form of processing for preservation, and so on. Microsurgical and other micromanipulator technology (El-Badry, 1963; Johnstone, 1973), combined with teleoperators (Bejczy, 1980; Minsky, 1980) or robot controllers could be used for the separation and reassembly of biological parts, together with other artificial parts, into desired MT products. Very small parts consisting of large macromolecules, viral components, etc., might be fetched and oriented using specific antibody or other recognition molecules attached to ultra micromanipulators consisting of large conformation-changing proteins which in turn may be bound or mounted on still larger structures.

To be continued

BIBLIOGRAPHY OF PART 1

Angier, N. (1982), The Organic Computer, Discover, 76-79 (May, 1982).

Arbib, M.A. (1967a), Automata Theory and Development: Part I, J. Theor. Biol., 14(2), 131-156 (1967).

Arbib, M.A. (1967b), Some Comments on Self-Reproducing Automata, in Systems and Computer Science, J.F. Hart and Satoru Tasasu, eds., University of Toronto Press, 1967, pp 42-59.

Avery J. (1964), Excitation Migration and Biological Systems, in Electronic Aspects of Biochemistry, B. Pullman, ed., Academic Press, New York, 1964, pp 29-41.

Avery, J. and C.M.E. Pavlidou (1974), A General Perspective of the Quantum Mechanical Foundations of Energy Transduction, Ann. New York Acad. Sci., 227, 651-668 (1974).

Bailey, F.R. (1978), Computational Limits on Scientific Applications, IEEE CH, 1328 301-303 (April, 1978).

Baker, J.W. and G.E. Allen (1971), Matter, Energy, and Life, Addison-Wesley, Reading, MA, 1981.

Bard A.J. (1980), Photoelectrochemistry, Science, 207, 139-144 (1980).

Barth, P.W., and J.B. Angell (1981), Miniature Silicon Sensors: Present Status and Future Prospects, Proc. of the 1st Sensor Symposium, Tsukuba City, Japan, 1981, pp 1-8.

Bejczy, A.K. (1980), Sensors, Controls, and Man-Machine Interfaces for Advanced Teleoperation, Science, 208, 1327-1335 (1980).

Breslow, R. (1982), Artificial Enzymes, Science, 218, 532-537 (1982).

Bussert, J. (1982), Are Biochips the New Wave?, Military Electronics/Countermeasures, 27-30 (June, 1982).

Cairns-Smith, A.G. (1971), The Life Puzzle, Univ. of Toronto Press, Toronto, 1971.

Cairns-Smith, A.G. (1981), Beginnings of Organic Evolution, in The Study of Time IV, J.T. Fraser, N. Lawrence, and D. Park, eds., Springer-Verlag, New York, 1981, pp 15-33.

Cairns-Smith, A.G. (1982), Genetic Takeover, Cambridge University Press, Cambridge, 1982.

Carter, F.L. (1982a), ed., Molecular Electronic Devices, Marcel Dekker, New York, 1982.

Carter, F.L. (1982b), Conformational Switching at the Molecular Level, in Molecular Electronic Devices, F.L. Carter, ed., Marcel Dekker, New York, 1982, pp 51-71.

Chance, B. (1979), Tunneling in Biological Systems, Academic Press, New York, 1979.

Chance, B. (1980), Biological Membranes, Physics Today, 33(10), 32-38 (1980).

Chang, T.M.S. (1972), Artificial Cells, Thomas Books, Springfield, IL, 1972.

Changeux, J.P. (1970), Allosteric Interactions in Regulatory Proteins and Excitable Membranes, in Physical Problems in Biological Systems, C. DeWitt and J. Matricon, eds., Gordon and Breach, New York, 1970, pp 81-121.

Codd, E.F. (1968), Cellular Automata, Academic Press, New York, 1968.

Conrad, M. (1972a), Information Processing in Molecular Systems, Currents in Modern Biology, 5, 1-14 (1972).

Conrad, M. (1972b), Statistical and Hierarchial Aspects of Biological Organization, in Towards a Theoretical Biology, III, C.H. Waddington, ed., Aldine, Chicago, 1972, pp 189-221.

Conrad, M. (1973), Is the Brain an Effective Computer?, Intern. J. Neuroscience, 5, 167-170 (1973).

Conrad, M. (1974a), The Limits of Biological Simulation, J. Theor. Biol., 45, 585-590 (1974).

Conrad, M. (1974b), Evolutionary Learning Circuits, J. Theor. Biol., 46, 167-188 (1974).

Conrad, M. (1976), Molecular Information Structures in the Brain, J. Neuroscience Research, 2, 233-254 (1976).

Conrad, M. (1982b), Bootstrapping Model of the Origin of Life, BioSystems, 15(3), 209-219 (1982).

Conrad, M., and E.A. Liberman (1982), Molecular Computing as a Link Between Biological and Physical Theory, J. Theor. Biol., 98, 239-252 (1982).

Conrad, M., and A. Rosenthal (1981), Limits on the Computing Power of Biological Systems, Bull. Math. Biol., 43, 59-67 (1981).

Conrad, M., and O. Rossler (1982), Example of a System Which is Computation-Universal but not Effectively Programmable, Bull Math. Biol., 44(3), 443-447 (1982)

Cope, F.W. (1970), The Solid-State Physics of Electron and Ion Transport in Biology, Adv. Biol. Med. Phys., 13, 1-42 (1970).

Cope, F.W. (1973a), Piezoelectricity and Pyroelectricity as a Basis for Force and Temperature Detection by Nerve Receptors, Bull. Math. Biol., 35, 31-41 (1973).

Cope, F.W. (1973b), Electron-Phonon (Trapped-Photon) Coupling and Infrared Coaxial Transmission Line Theory of Energy Transport in Mitochondria and Nerves, Bull. Math. Biol., 35, 627-644 (1973).

Cope, F.W. (1975), A Review of the Applications of Solid State Physics Concepts to Biological Systems, J. Biol. Phys., 3, 1-41 (1975).

Cope, F.W. (1982), Electronic Conduction and Mechanoelectrical Transduction in Biological Materials, B. Lipinski, ed., Marcel Dekker, New York, 1982, pp 99-124.

Davydov, A.S. (1977), Solitons and Energy Transfer Along Protein Molecules, J. Theor. Biol., 66, 379-387 (1977).

Davydov, A.S. (1982), Biology and Quantum Mechanics, Pergamon, Oxford, 1982.

DeLuca, M.A., and W.D. McElroy (1981), eds., Bioluminescence and Chemiluminescence, Academic Press, New York, 1981.

Drexler, K.E. (1981), Molecular Engineering: An Approach to the Development of General Capabilities for Molecular Manipulation, Proc. Natl. Acad. Sci. USA (Chem), 78(9), 5275-5278 (1981).

Drexler, K.E. (1982a), Personal Communication, 1982.

Drexler, K.E. (1982b), When Atoms Will Do The Work, Smithsonian, 13(8), 145-154 (Nov, 1982).

Dyson, F. (1981), Disturbing the Universe, Harper Colophon, New York, 1981.

Eigen, M., and P. Schuster (1979), The Hypercycle, A Principle of Natural Self-Organization, Springer-Verlag, New York, 1979.

Eigen, M., and R. Winkler-Oswatitsch (1981a), Transfer-RNA: The Earlier Adaptor, Naturwissenschaften, 68, 217-228 (1981).

Eigen, M., and R. Winkler-Oswatitsch (1981b), Transfer-RNA, An Early Gene?, Naturwissenschaften, 68, 282-292 (1981).

El-Badry, H.M. (1963), Micromanipulators and Micromanipulation, Academic Press, New York, 1963.

Feynman, R.P. (1960), There's Plenty of Room at the Bottom, Engrg. & Sci. (Cal. Tech.), 22-36 (Feb, 1960), and in Miniaturization, H.D. Gilbert, ed., Reinhold, New York, 1961, pp 282-296.

Fox, R.F. (1982), Biological Energy Transduction: The Uroboros, John Wiley & Sons, New York, 1982.

Freiser, M.J., and P.M. Marcus (1969), A Survey of Some Physical Limitations on Computer Elements, IEEE Trans. Magnetics, 5(2), 82-90 (1969).

Gilbert, H.D. (1961), ed., Miniaturization, Reinhold, New York, 1961.

Goldfein, S. (1980), Some Speculations on Biological Superconductors, Nerve Electrical Conduction, and Retrieval and Storage of Information, Speculations in Science and Technology, 3(2), 127-136 (1980).

Gomer, D. (1982), Surface Diffusion, Scientific American, 247(2), 98-109 (1982).
Hagan, B.E., and B.L. Reid (1980), The Mathematical Translation of Growth and Form - I: Transferring the Wave-Particle Duality from Physics to Biology and Proposing Wave Interaction as a Key Determinant of Biological Structure, Medical Hypotheses, 6, 559-609 (1980).
Hamerhoff, S.R., and R.C. Watt (1982a), Microtubules: Biological Microprocessors?, in Molecular Electronic Devices, F.L. Carter, ed., Marcel Dekker, New York, 1982, pp 341-356.
Hamerhoff, S.R., and R.C. Watt (1982b), Information Processing in Microtubules, J. Theor. Biol., 98, 549-561 (1982).
Hartline, F.F. (1979), Biological Applications for Voltage Sensitive Dyes, Science, 203, 992-994 (1979).
Henry, E.C. (1969), Electronic Ceramics, Doubleday & Co., Garden City, NY, 1969.
Henson, H.K. (1983), Personal Communication.
Honig, B. (1982), Visual Pigments: A New Type of Molecular Switching Device, in Molecular Electronic Devices, F.L. Carter, ed., Marcel Dekker, New York, 1982, pp 137-139.
Hopfield, J.J. (1974), Kinetic Proofreading: A New Mechanism for Reducing Errors in Biosynthetic Processes Requiring High Specificity, Proc. Nat. Acad. Sci. USA, 71(10), 4135-4139 (1974).
Hu, E.L. (1981), New Approaches to the Fabrication of Submicron Switches, American Scientist, 69, 517-521 (Sept/Oct, 1981).
Hunkapiller, M.W., and L.E. Hood (1983), Protein Sequence Analysis: Automated Microsequencing, Science, 219, 650-659 (1983).
Isaacson, M., and A. Muray (1982), Nanolithography Using In Situ Electron Beam Vaporization of Very Low Molecular Weight Resists, in Molecular Electronic Devices, F.L. Carter, ed., Marcel Dekker, New York, 1982, pp 165-174.
Jantsch, E. (1980), The Self-Organizing Universe, Pergamon Press, New York, 1980.
Johnstone, K.I. (1973), Micromanipulation of Bacteria, Churchill-Livingstone, London, 1973.
Kemeny, J.G. (1955), Man Viewed as a Machine, Scientific American, 192(4), 58-67 (1955).
Keyes, R.W. (1969), Physical Problems and Limits in Computer Logic, IEEE Spectrum, 6(5), 36-45 (May, 1969).
Keyes, R.W. (1970), Power Dissipation in Information Processing, Science, 168, 796-801 (1970).
Keyes, R.W. (1972), Physical Limitations of Small Structures in Electronics, Proc. IEEE, 60(9), 1055-1062 (1972).
Keyes, R.W. (1975), Physical Limits in Digital Electronics, Proc. IEEE, 63(5), 740-767 (1975).
Kilkson, R. (1968), Evolution of Chromosomes and Viruses, Derivation Of Structure, Quarterly Reviews of Biophysics I, 3, 265-308 (1968).
Kilkson, R. (1969), Membrane Structure and Transitions, A Molecular Basis of Regulation, in Nobel Symposium 11, A. Engstrom and B. Strandberg, eds., Almquist and Wiksell, Stockholm, 1969, pp 257-266.
Kilkson, R. (1970), Biomolecular Structure and Specialization, Limits and Pathways of Evolution, FEBS Symposium, 21, 255-266 (1970).
Kilkson, R. (1975), Intrinsic Asymmetry of Oligomer Transitions and Biomolecular Evolution, J. Mol. Evol., 5, 125-130 (1975).
Koshland, D.E., Jr., A. Goldbeter, and J.B. Stock (1982), Amplification and Adaption in Regulatory and Sensory Systems, Science, 217, 220-225 (1982).
Krumhansl, J.A., and Y. Pao (1979), Microscience: An Overview, Physics Today, 25-32 (Nov, 1979).

Laing, R. (1975), Some Alternative Reproductive Strategies in Artificial Molecular Machines, J. Theor. Biol., 54, 63-84 (1975).

Laing, R. (1976), Automation Inspection, J. Comp. Sys. Sciences, 13, 172-183 (1976).

Liberman, E.A. (1979a), Analog-Digital Molecular Cell Computer, BioSystems, 11(2-3, 111-124 (1979).

Liberman, E.A. (1979b), Biological Physics and the Physics of the Real World, BioSystems, 11, 323-327 (1979).

Lipinski, B. (1982), ed., Electronic Conduction and Mechanoelectrical Transduction in Biological Materials, Marcel Dekker, New York, 1982.

Long, J.E., and T.J. Healy (1980), Advanced Automation for Space Missions--Technical Summary: A Report of the 1980 NASA/American Society for Engineering Education Summer Study on the Feasibility of Using Machine Intelligence in Space Applications, (Sept, 1980).

Martinez, H.M. (1979), An Automation Analogue of Unicellularity, BioSystems, 11, 133-162 (1979).

McAlear, J.H., and J.M. Wehrung (1982), Biotechnical Electron Devices, in Molecular Electronic Devices, F.L. Carter, ed., Marcel Dekker, New York, 1982, pp 175-179.

McClaire, W.F. (1971), Chemical Machines, Maxwell's Demon, and Living Organisms, J. Theor. Biol., 30, 1-34 (1971).

McGill, P. (1982), Japan on the Road to a Biological Computer, New Scientist, 11, 358 (Nov, 1982).

McGiness, J., P. Corry, and P. Proctor (1974), Amorphous Semiconductor Switching in Melanins, Science, 183, 853-855 (1974).

Miller, J.E. (1978), A Proposal for the Genetic Manipulation of Plant Metabolism, J. Theor. Biol., 74, 153-154 (1978).

Minsky, M. (1980), Telepresence, Omni, 2, 45-52 (June, 1980).

Moore, E.F. (1956), Artificial Living Plants, Scientific American, 195(4), 118-126 (1956).

Myhill, J. (1964), The Abstract Theory of Self-Reproduction, in Views on General Systems Theory, M.D. Mesarovic, ed., John Wiley & Sons, New York, pp 106-118.

Ostroff, J. (1983), Biochips, Venture, 65-68 (Feb, 1983).

Pabo, C. (1983), Designing Proteins and Peptides, Nature, 301, 200 (1983).

Penrose, L.S. (1959), Self-Reproducing Machines, Scientific American, 200(6), 105-114 (June, 1959).

Peterson, K.E. (1978), Dynamic Micromechanics on Silicon: Techniques and Devices, IEEE Trans. Electron Devices, 25, 1241-1250 (1978).

Polonsky, F.R. (1964), Biochemical Macromolecules Considered as Specific Information Generators at Very Low Temperatures, in Electronic Aspects of Biochemistry, B. Pullman, ed., Academic Press, New York, 1964, pp 481-502.

Popp, F.A. (1979), Photon Storage in Biological Systems, in Electromagnetic Bio-Information Proceedings, F.A. Popp, G. Becker, H.L. Konig, and W. Peschka, eds., Urban & Schwarzenberg, Baltimore, 1979, pp 123-149.

Popp, F.A., G. Becker, H.L. Konig, and W. Peschka (1979), eds., Electromagnetic Bio-Information Proceedings, Urban & Schwarzenberg, Baltimore, 1979.

Price, C.C. (1974), ed., Synthesis of Life, Dowden, Hutchinson, & Ross, Stroudsburg, PA, 1974.

Robb, E.J., and G.L. Barron (1982), Nature's Ballistic Missile, Science, 218, 1221-1222 (1982).

Root-Bernstein, R.S. (1982a), Amino Acid Pairing, J. Theor. Biol., 94, 885-894 (1982).

Root-Bernstein, R.S. (1982b), On the Origin of the Genetic Code, J. Theor. Biol., 94, 895-904 (1982).

Ruby, D. (1982), Piezoceramic Devices, Popular Science, 69-71 (July, 1982).

Savageau, M.A. (1981), Accuracy of Proofreading with Zero Energy Cost, J. Theor. Biol., 93, 179-195 (1981).

Savageau, M.A., and D.S. Lapointe (1981), Optimization of Kinetic Proofreading: A General Method for Derivation of the Constraint Relations and an Exploration of a Specific Case, J. Theor. Biol., 93, 157-177 (1981).

Simon, J. (1978), The Limit of Computing Speed, Comm. ACM, 21(10) 876-877 (1978).

Simonescu, C.R., S.V. Dumitrescu, and V. Percec (1978), Semiconducting Biopolymers and Their Part in Biochemical Phenomena, in Topics in Bioelectrochemistry and Bioenergetics, Vol. 2, G. Milazzo, ed., John Wiley & Sons, New York, 1978, pp 151-204.

Smith III, A.R. (1976), Introduction to and Survey of Polyautomata Theory, in Automata, Languages, Development, A. Lindenmayer and G. Rozenberg, eds., North-Holland, New York, 1976, pp 405-422.

Stein, W.D. (1982), Replicating RNA Duplexes and the Epigenetic Address, J. Theor. Biol., 94, 869-883 (1982).

Straub, K.D. (1974), A Solid-State Theory of Oxidative Phosphorylation, J. Theor. Biol., 44, 191-206 (1974).

Stryer, L. (1981), Biochemistry (2nd Ed.), W.H. Freeman, San Francisco, 1981.

Szent-Gyorgyi, A. (1968), Bioelectronics, Academic Press, New York, 1968.

Taneja, V., and P.J. Walsh (1981), Growth Consideration of a Self-Replicating Field Dependent on External Factors, IEEE Tran. on Systems, Man, and Cybernetics, SMC-11, 8, 558-563 (1981).

Thompson, D.E. (1982a), Nerve Electricity Studied In Vitro, Science News, 121(12), 196 (1982).

Thompson, D.E. (1982b), Self-Assembly: Biology—Physics, Science News, 121(20), 334 (1982).

Ulmer, K.M. (1982), Biological Assembly of Molecular Ultracircuits, in Molecular Electronic Devices, F.L. Carter, ed., Marcel Dekker, New York, 1982, pp 213-222.

Ulmer, K.M. (1983), Protein Engineering, Science, 219, 666-671 (1983).

Von Neumann, J. (1951), The General and Logical Theory of Automata, in Cerebral Mechanisms in Behavior: The Hixon Symposium, L.A. Jeffress, ed., John Wiley & Sons, New York, 1951, pp 1-2, 15-31.

Von Neumann, J. (1966), Theory of Self-Reproducing Automata, (Completed and edited by A.W. Burks), Univ. Illinois Press, Urbana, IL, 1966.

Von Randeraat, J., and R.E. Setterington (1974), Piezoelectric Ceramics, Mullard, London, U.K., 1974.

Wade, N. (1981), The Complete Index to Man, Science, 211, 33-35 (1981).

Winograd, S., and J.D. Cowan (1963), Reliable Computation in the Presence of Noise, MIT Press, Cambridge, MA, 1963.

Wohltjen, H. (1982), Microfabrication Techniques: Current and Future, in Molecular Electronic Devices, F.L. Carter, ed., Marcel Dekker, New York, 1982, pp 231-243.

Wolf, E.D. (1979), The National Submicron Facility, Physics Today, 32(11), 34-36 (Nov, 1979).

Wolken, G., Jr. (1980), Computer Design of Organic Structures for Desired Properties, Industrial Research & Development, 22(10), 157-160 (Oct, 1980).

SCIENCE UPDATES

by Thomas Donaldson

MORE ON CAUSES OF DAMAGE IN BRAIN ISCHEMIA

Besides dynorphin and verapamil, yet another scientist has come up with yet another drug which may greatly help recovery from stroke and other kinds of brain ischemia. Moreover, this drug may tell us something quite significant about the mechanism of injury in brain ischemia.

B.S. Meldrum, R.P. Simon, J.H. Swan, and T. Griffiths, at the Department of Neurology, Institute of Psychiatry, in London reported recently in SCIENCE that 2-amino-7-phosphonoheptanoic acid (which these scientists thoughtfully renamed APH), given to rats before injury, would protect their brains from the usual degeneration which happens after ischemia.

The drug APH acts by preventing one particular neurotransmitter (methyl aspartate, baptized MNDA), from acting on the neurons. APH is a very strong anticonvulsant; what may happen to neurons when they are injured by ischemia is that they start firing convulsively as soon as blood flow reestablishes itself. This convulsive firing can injure the brain cells; in fact, severe artificial convulsions can cause brain damage resembling that of ischemia, a fact which deserves to rank as an interesting clue. R.P. Simon et al, by their recent experiment, have basically shown very strong evidence that convulsive firing of the neurons underlies a large part of the injury due to ischemia.

Their experiment was quite simple. They administered APH by direct injection into one side of the brain before injury to their test rats. They then injured both sides of the brains of their rats by blocking off blood flow through their carotid arteries for 30 minutes. Blood flow was cut down even more by inducing low blood pressure. After two hours of recovery, they killed their test animals and examined the state of their brains.

As it turned out, the APH, given before brain injury, protected brain cells very well against ischemic damage. Often the protected side of their animal's brains looked normal; the APH protected all cell types in a sphere one to two millimeters in diameter surrounding the location of injection of APH into the brains.

The interest in this drug lies not in its value as a practical treatment for brain ischemia, but for what the experiment shows about the nature of injury. Blaine White, in Detroit, has already tried verapamil as a treatment for prolonged absence of blood flow to the brain in cases of accidental death, with some startling success. Verapamil is a calcium blocker, which is to say that it prevents the entry of calcium into the neurons, among other cells. It's a very interesting fact, therefore, that convulsive firing of the neurons injures them precisely because it produces a massive accumulation of calcium in the neurons. This experiment of Meldrum et al gives us a very clear idea of just how ischemia damages neurons.

CIRCADIAN RHYTHMS AND AGING

For quite some time, I have felt that exploring the connection between circadian rhythms and aging might give us very important clues as to the mechanism of aging itself. The reason why this might be so is that one or several of our ordinary body clocks might also be measuring time for the sake of aging itself; if we found some way to reset the clock, then we would have a way to prevent or delay aging.

Some scientists, motivated by this hypothesis, have done experiments on insects. In 1978, U. von Saint Paul and J. Aschoff (J COMP PHYS, D127, 191 (1978)) tried exposing the blowfly to continuous light as one means of testing a possible effect of disrupted circadian rhythms on lifespan. Their experiment SHORTENED the lifespan of the blowflies. Several other scientists have also done experiments of this kind. In 1972, C.S. Pittendrigh and D.H. Minis (PROC NAT ACAD SCI USA, 69, 1537 (1972)) found that exposure to continuous light would shorten the lifespan of fruit flies. N.G. Hairston (PROC NAT ACAD SCI USA, 73, 971 (1976)) found that continuous light would shorten the lifespan of a copepod (a very small marine crustacean) unless high levels of pigment protected it.

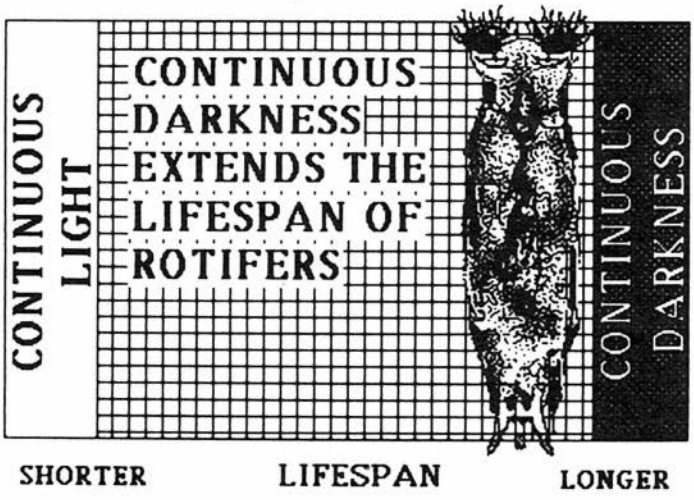
Interfering with the circadian cycle is difficult. For instance, if we use drugs, we don't know that the drug might have a toxic effect which negates any (theoretical) effect upon lifespan. Putting insects into a regimen of continuous light might cause toxic effects too.

The interesting thing is that continuous DARKNESS seems to work much better than continuous light in prolonging lifespan. An early experiment, by R. Allemand et al (EXPERIMENTAL GERONTOLOGY, 8, 279 (1973)) demonstrated that continuous darkness prolonged lifespan in fruit flies. A recent interesting paper by M. Sawada and H.E. Enesco (EXPERIMENTAL GERONTOLOGY, 19, 335-343 (1984)) has also approached the study of aging and circadian rhythms in lower animals by studying the effect of continuous darkness on ROTIFERS.

They exposed the rotifers (a microscopic aquatic animal) to continuous darkness for 20 generations. They also exposed a second group of rotifers to continuous light, and an third group (the controls) to a normal 12/12 light/dark cycle. All three groups were bred equally well. However, those rotifers on a schedule of continuous darkness lived 22% longer than those on either of the other two cycles.

This is intriguing. Could it be that DARKNESS rather than the PERIOD OF THE CYCLE caused the increase in lifespan? They tried another set of experiments, exposing rotifers to 18 hours of darkness and 6 hours of light. these rotifers lived about 18% longer than controls.

The authors of this study feel that that continuous darkness caused a change in the circadian



rhythms of their rotifers. This change increased their lifespan. I personally believe that the experiment was a worthy attempt to work out relationships between circadian rhythms and lifespan.

However, I cannot agree with their conclusion. The main difficulty is that most animals will establish their own periodic cycling in the absence of all outside clues. Once they have a periodic cycling, then their lifespan would depend on THAT cycle. Cues from outside aren't necessary. If there are no outside cues (for instance, if the animals live in continuous darkness), then we wouldn't expect any effect on lifespan. I believe that their experiment really shows that DARKNESS has some unknown effect increasing lifespan in rotifers.

The sort of experiment they need to do is one in which they expose their animals to a cycle of, say, 15 hours of light and 15 hours of darkness. That is, a cycle LONGER than the normal 24-hour cycle.

On the plus side, their paper is one of very few which attempt to piece out an effect of rhythmic cycling on lifespan. I feel that it deserves attention for this reason.

MAY-JUNE 1985 MEETING CALENDAR

ALCOR meetings are usually held on the first Sunday of the month. Guests are welcome. Unless otherwise noted, meetings start at 1:ØØ PM. For meeting directions, or if you get lost, call ALCOR at (714) 738-5569.

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The MAY meeting will be at the home of:

(SUN, 5 MAY 1985) Paul Genteman
535 S. Alexandria, #325
Los Angeles, CA

DIRECTIONS: From the Santa Monica Freeway (Interstate 1Ø), exit at Vermont Avenue , and go north to 6th St.
From the Hollywood Freeway (US 1Ø1), exit at Vermont Avenue, and go south to 6th St.
Go west on 6th 4 blocks to Alexandria, and turn right. 535 is the first apartment building on the west side of the street. Ring #325 and someone will come down to let you in.

The JUNE meeting will be at the home of:

(SUN, 2 JUN 1985) Hugh Hixon
289 Cerritos Avenue
Long Beach, CA

DIRECTIONS: Take the Long Beach Freeway (State 7) to Long Beach, and get off downtown at the Broadway exit (goes east). Continue on Broadway to Alamitos, where Broadway turns into a 2-way street. Bearing to the right, continue two blocks on Broadway to Cerritos and turn north (left). 289 is in the old apartments on the SE corner of 3rd and Cerritos.

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