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11 pp → 70 minutes.

Terry Lectures, Yale University

Thurs - Fri :

April 6, 7 and April 13, 14 1989

I feel deeply moved and honored to have been invited to return to Yale to give the Terry Lectures. As you know, I came to Yale in 1946 to work with Professor Ed Tatum on a one semester's leave from Columbia Medical School. I marvel that the Jane Coffin Childs Fund was willing to make such a gamble! The research I did that summer, discovering genetic recombination in bacteria, disrupted my life plans, and led to my completing a Ph. D. at Yale; and I am glad to express my appreciation once again for that launching of the career I actually followed. I am not going to bore you with any further reminiscence -- that is more appropriate for the published book that is the promised fruit of the lectureship. That work will afford an opportunity to deal in appropriate detail and context with the matters I will merely sketch out in my verbal presentation. It will also include a further account of my own history, as the secular scientist son of an orthodox rabbi, which may give some further justification for my qualifications to speak on an endowment that refers to religion. My concordat with my father was an acknowledgment that there are many paths to the truth, that the most important manifestation of the religious impulse is that there be a quest, for self-understanding as well as for the comprehension of the external universe.

The self-conscious awareness of history is certainly unique to the human species. Each of us looks back to a cultural tradition that has molded our personality, our language, his capacity to cope with the external world. We look ahead to a posterity and around ourselves to a community of other people on whom our own lives inevitably impinge.

Religion is then also this consciousness of the species, the insight that man in complete isolation is nothing, that our life can have a meaning only in communication across time and space with our past and future traditions and with our fellows.

My approach to science, as a matter of philosophical principle, is that of unmitigated mechanistic reductionism - the only path I know that encourages bold experimentation. The hardest question for me as a scientist to answer is "why bother to do it." I have to look to extra-scientific values to respond to that. #P189-199. SAM 52

My four lectures will carry us far afield, but all will relate in some fashion to the

religious impulse, so construed.

1. The origin and extension of life. -- a cosmological perspective
2. The human organism -- what biological science can tell us about human nature, and how this impinges on our adaptation to a man-made environment, its consequences for our own health and mortality.
3. Science and Policy By which I mean the social and ethical role of the scientist. I could have said Science and History.
4. Science as a vocation -- the motivations and vicissitudes of the scientific career, and how this is shaped by changing institutions.

These are vast subjects, beyond my capability to address in rounded depth within the compass of the lectures. I will try to give some general background, and then proceed somewhat epigrammatically to stress where my own thought may deviate from the common wisdom, if only because the latter is hard to find. Inevitably, I will be sacrificing coherence to avoid redundancy. Perhaps I have also chosen unwisely in the progression of topics, my first two will assume more familiarity with biological theory; and I hope that does not deter some of you from trying again next week.

proceed to .1

(P/272.1)

Introduction See P/272.0 75 lines

P/272.1 Origin and extent of Life.

In this first lecture I will begin with a cosmological perspective.

a) Universal order: applicability of laws of physics over 35 orders of magnitude -- application of studies on nuclear structure to the origin of the universe.

b) Human quest for insight on ultimate questions of his origin and being, quite apart from the merely utilitarian: an awesome physics, and a creature born of that milieu capable of awe.

c) How humble we must feel when we contemplate our rather limited, or rather mediocre place in the physical universe.

I hope you are all familiar with the Morrisons' "Powers of Ten". It reminds us that human scale is roughly half way, 10 powers of 10, between the atom and the solar system:

SLIDE

Powers of 10.

-10 to the atom

+11 to the solar system

+16 nearest stars

+20 galaxy

+26 visible universe

Scaled 10^{10} above the atom, the human organism is of a complexity to challenge every power of intelligence; the same complexity gives us the apparatus to raise the question.

Most of you are familiar with the standard cosmological model. I will briefly recapitulate what is commonly accepted today, passing quickly over what I must borrow

from others:

Ultimate origins remain a great mystery; in greatly simplified shorthand:

~ 10-15E: universe. Big Bang. Expanding gas. condensation into nuclear particles, protons, neutrons, electrons. Aggregation to galaxies, stars. Burning H -> He -> C, N, O, -> elements up to Fe. Collapsing stars reemit all these into the interstellar medium.

Local process:

Earth, solar system ~4.5E

Cosmic abundance: per table. -- TABLE ...

Cosmic Abundance

Earth very strongly fractionated; some argument whether any or what trace of the lighter elements are primitive to the earth, or may be later accretions. Most of the HCNO of earth has been distilled away under radiation pressure during aggregation and evaporation from the atmosphere subsequently, escaping earth's limited gravitational pull, especially for H.

In surprisingly short time Primitive life ~ 3E. That is, for most of its history, our own planet has been shaped by the activity of living organisms. Most obviously, we are in gross chemical disequilibrium -- one does not have to subscribe to Gaian religion to be impressed that we have an atmosphere containing 20% oxygen entirely the product of plant photosynthesis.

0.6 - ~ 1 E differentiation of cells more readily recognizable as fossils. We can be fairly sure that DNA as a common element of heredity goes back a billion years. Compare that to ~5MM for humanoid, ~1MM "human", 50K for recognizable culture, 10K for the neolithic, 5K for "history". It is banal to remark on the acceleration of technology and of human expansion: who would dare to guess the planetary condition 100 years hence, keeping in mind not only the technological explosion, what can be foreseen with computers, space travel, biotechnology but the political problematics of the species.

Return to what I call "eobiology", the dawn of life. This remains the sorest point of biological theory.

How do we model the creation of structures as complex as the cell from the chemistry of a primitive planetary atmosphere? As we learned of the role of DNA, we could be more

concrete about the requisites of a self-reproducing system; and they redoubled the problem:

DNA -> RNA -> protein enzymes

TABLE

DNA →

We found ourselves in the ultimate chicken-egg dilemma: How make the egg (the protein) without a pre-existent chicken (DNA) whose replication depends on the egg! Until recently only DNA was attributed with properties of replication of information content, this through template-directed-assembly. That is an existing polymer chain was the framework on which a new copy was assembled, unit by unit being taken from the milieu in proper order. Very recently, we have been enlightened by the discovery of ribozymes, Cech, Altman and others: RNA itself is capable of folding into special convoluted shapes that give it catalytic enzyme-like activity. In a milieu of concentrated RNA precursors (ribose, phosphates, purine and pyrimidine bases) an RNA molecule might be able to replicate itself and start an evolutionary pathway -- eventually discovering and collaborating with DNA and protein products. The proteins would assist the task of metabolism, of shaping the milieu to offer the best nourishment for RNA to proliferate.

There has been a substantial tradition of work on one element of this problem -- sources for the smaller organic molecules of which these polymers are comprised. Darwin, in 1871, had already speculated:

TABLE ...

Slide - Darwin

February 1, 1871

My dear Hooker:

-- It is often said that all the conditions for the first production of a living organism are now present, which could ever have been present. But if (and oh! what a big if!) we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, &c., present, that a protein compound was chemically formed ready to undergo still more complex changes, at the present day such matter would be instantly devoured or absorbed, which would not have been the case before living creatures were formed. --

Despite his having offered critical scientific evidence against spontaneous generation, Pasteur, in 1883, was willing to invoke electromagnetism and polarized light as a way to achieve the asymmetric synthesis that he pointed to as a hallmark of life.

Darwin's important insight is that the scarcity of precursor organics in our atmosphere and oceans is at least partly attributable to the action of voracious organisms. Hence, inorganic processes at an earlier stage might have provided a much richer environment for spontaneous generation than anything we see today. In 1945, Norman Horowitz added the further theoretical insight of the backward evolution of biosynthetic processes: as a given nutrient became depleted, there would be strong selective impetus for its production from existing materials as feedstocks. In this way, complex pathways could be evolved stepwise, back from the end products -- relieving the need to evoke intelligent foresight in the design from CO₂ to DNA.

Darwin's speculation was elaborated in a more modern framework in 1924 by Oparin, and by Haldane soon after, and given some experimental substantiation by Urey & Miller (1953) that amino acids and a host of other building blocks (sugars, purines and pyrimidines) could be generated by the irradiation of gas mixtures simulating the atmosphere of primitive earth: H₂O, CH₄, NH₃, CO₂ are all that are needed. Such radiations produce active reagents like C₂H₂, HCN and CH₂O -- and one can readily go from there to the synthesis in some concentration of virtually any organic molecule. These findings have dispelled any mystique about the source of "organic" molecules, a

mechanistic revelation that we should credit to Wohler in 1828 when he synthesized urea (an "organic" substance) from NH_4CNO , ammonium cyanate, an "inorganic salt".

There remains a yawning gap between the "thin soup", Haldane's metaphor for Darwin's little warm pond, and the self-replicating informational polymer, RNA being today's main champion.

Lacking a clearcut experimental paradigm, very few biologists are actively engaged in further study, notable exceptions being Leslie Orgel's examination of the simplest RNA-like segments capable of showing self-catalyzed assembly.

Some, like Francis Crick, find the gap so daunting that they invoke panspermia, that seeds of life have drifted to earth from other sources, perhaps that these are merely the garbage discarded from the extraterrestrials' space ships. That displaces the question of origin to other times and places, perhaps even to other universes -- having the advantage of terminating a line of experimental enquiry that some may feel to be an utter waste, and certainly removing all constraints of time and chemical parameters. We have no way to dismiss such conjectures; and there have been many serious proposals of migration of particles from one planet to another after cataclysms like cometary impacts.

I will, however, set this group of theories aside in order to make another point about the intersection of cosmology and molecular biology.

RNA seems entirely plausible as an intermediate in the evolution of the gene. It could only function in a milieu that was already quite rich in its specific precursors: the sugar, the bases and phosphate. Also, there dare not be an overabundance of other reactive species; and I would worry about the assembly and replication of an RNA in a medium dominated by more primary and active reagents like CH_2O . The relative scarcity of P relative to C, N in the cosmic abundance (and earth's surface) is also worrisome. Even with specific enzymes, we need to limit the variety of precursors we put in the reaction mix. How much more troublesome these would be before the evolution of that high specificity. Perhaps some day there will be demonstrated a chromatographic fraction of the RNA precursors on clay columns that will account for the segregation needed to make such a system work: that is at least an experimental challenge.

Meanwhile my own thoughts have leaned a) to still more primitive potential polymer

systems, and b) to richer "habitats" for their production and variety.

For b), I have particularly in mind that astronomers have long neglected what is plain from the cosmic abundance of the elements: the molecular chemistry of the entire universe, not just of an earth's atmosphere, must be dominated by organic chemistry -- a subject not usually in their curriculum. Molecules have, of course, a limited role in astronomical description: the principal observable is the radiation from galaxies and stars, reflecting temperatures inconsistent with molecular states of matter. A substantial part of the cosmic mass is, however, represented by interstellar "dust" or "smoke or frost", micron-scale particles that can hardly be other than aggregates of the simple ices, hydrides (OH₂, NH₃, and CH₄) and other molecular species. Larger organic molecules may well play a critical role in the nucleation of the dispersed cosmic gas to form such grains, the first step in the condensation of matter to form the stars and galaxies.

Comets are likely to be the closest accessible analogues of these grains, together with the major planets like Jupiter which are massive enough, and cool enough, to have retained most of their primitive composition. We now have observational evidence, from microwave spectroscopy for the interstellar medium, and direct mass spectrometry for Halley's comet of the great abundance of many organic molecules in space.

TABLE incl. Halley

Halley paper
Halley chem.
Mols. in space

This matter is coupled to earth by continued meteoritic infall, even to the present time. This must have been far more prevalent 3 billion years ago; and some have argued that most of the earth's water (and therefore of other hydrogenaceous matter) came from those sources. The cometary impacts that are invoked as sources of faunal cataclysms, of evolutionary wipeouts, some say every 28 million years, are of a kind with some of the sources of chemical precursors of life. Besides obscuration, these recent inputs may also have been pre-industrial chemical pollution of the atmosphere.

We have little detailed knowledge of cometary chemical synthesis, though many of its products are familiar structures. It is a low temperature regime, hence not in liquid aqueous phase, though water is abundant as ice. But we should explore those processes as a major input to the chemical origins of life. It is a very long gamble, but we may find a channeling of synthetic processes in that regime that will give us obvious clues to more plausible starting points for eobiology.

My further remarks on a):

"What some primitive polymers might have been?" are still more speculative, if that is possible! My tactic is to attend to ABUNDANT molecular species, and gamble that some of them may offer some special chemical properties pertinent to template directed assembly. That is the inverse of starting from RNA, and gambling on a way to make it. All of these exercises would be wasted effort if they do not suggest some concrete avenues of experimentation.

A couple of hints:

1. Graphite, "spherical graphite" - fullerene. Extended sheets of aromatic rings form in huge abundance in carbonaceous smoke. These will certainly incorporate odd N- O- and H- atoms in their structure: that is precisely what activated charcoal is; with occasional Fe atoms, catalytic activity is well known.

"Assembly" of these grains occurs either at very high temperatures in fires and exptl. laboratory; or in dilute gas phase in space. No good ideas on self-replication; not clear how to study it. A/C insolubility may be of limited relevance to replication in aqueous systems; since Warburg's oxidase models we have to respect the catalytic capabilities of this material. Immense quantities can't be ignored as part of the environment. Huge amount of "smoke" in space consistent with these kinds of structures. 2200 Å absorption feature. (Kroto- Sussex; Smalley-Curl+ - Houston).

TABLE fullerene and graphite

Fullerene

At this point, mention our surprising ignorance of what happens to charcoal in the earth's natural environment. Depending on its temperature history, charcoal is micro-crystalline -graphitic, with many imperfections; but of course highly insoluble. About 20 years ago (1966) Elie Shneour, working in my lab at Stanford looked for microbiological degradation of C-14 labelled charcoal in soil samples, with no conclusive finding. He used soils near old fire sites that should have enriched for charcoal utilization over many years. What then is the natural sink for charcoal in the natural C cycle. To my knowledge, no other work on this subject; yet we do not observe huge accumulations in most soils. Speculate: a) anaerobic processes -- we did not investigate (trapped CO₂ in base); b) simply too slow to be picked up with our methods; c) even a slow spontaneous oxidation; d) possible role of fungi, protozoa, invertebrates, that may not have been

incorporated in our samples. Wide open for reexamination. As a better defined chemical entity, fullerene may be an attractive option -- either to find it in abundance in soils, or to find out how it is metabolized.

2. A second avenue of (re)investigation is the exploration of the smaller reactive molecules like CO, CH₂O, C₂H₂, HCN, HCNO and the hydrides. These are readily available from either atmospheric or primitive pre-planetary sources. Most of the laboratory product is a tar, hard to analyze except for prejudged targets. And of course one manipulates the laboratory parameters to optimize those expectations.

There has been little systematic exploration of potentially paired structures that can be basis of template- directed assembly. One starts with hypotheses; and I am not the most skilled in the structural theory needed to criticize them. It is hard to mobilize those who are in such a disreputable venture.

In fact, there are a limited range of structures, starting from elementary addends that preserve approximate equimolarity of C N and O (to match the abundance ratios, keeping in mind that the overabundance of H will sequester much of the O as H₂O.)

I observe that

SLIDE

HEAD shows

feedstocks like:

H₂ H₂O NH₃ CO₂ CH₄ CO demonstrably ->

HCN HCOOH CH₂O HCNO --> HCO-NH₂ H₂N-COOH H₂N-CO-NH₂

and can hypothetically give rise to chains like:

-(NH-CH₂)- polymethylamine;

and more interestingly:

polycarbamate; urea-formaldehyde; polyglycine

-(NH-CO-NH-CO)- -(NH-CO-NH-CH₂)- -(CO-CH₂-NH)-

-(CO-NH-CO-NH)- -(CO-NH-CH₂-NH)- -(NH-CH₂-CO)-

and I just put those forward for your attention as primitive backbones. They can potentially pair as hydrogen-bonded aggregates; polyglycine also permits of a hydrophobic interaction. Formaldehyde, forming Schiff bases with imido groups, would be sufficient to add side chains allowing configurational and informational complexity, eventually catalytic specificity. Mixed backbones, i.e., with choices among these and similar units, might also offer some avenue for directed replication by selecting monomer units for assembly. The primitive system does not have to be perfect: mutation rates of 40% per generation would still preserve the original structures, and give abundant latitude for experimentation. (We have to marvel that mutation rates have been evolved to be so low in contemporary organisms, now that the mechanisms work with some efficiency.) Initially, selection would drive the composition of polymers to those most successful at retaining their informational identity in the complex milieu, at extracting their monomeric inputs; eventually to those with some catalytic advantage.

I am not asking anyone to believe that these are the eomolecules! I do suggest that research on the properties of simple polymers could give us fresh insight on the strategy of construction. I have not done even the elementary model building that would be needed to make the best choices among these primitive polymeric structures.

EXO

Planetary exploration as an experimental approach.

I hope you will permit me an anecdote on how I came to this subject:

When Sputnik was launched on October 4, 1957, I was in Melbourne, Australia, a Fulbright scholar from the University of Wisconsin, visiting MacFarlane Burnet's laboratory. Of course, as many of you will remember, the event prompted intense excitement about its scientific- technological as well as military-political implications.

A month later, November 6, 1957, I arrived in Calcutta to visit J.B.S. Haldane. Haldane was notorious as a committed communist, who then broke with the party over the Lysenkoist suppression of genetics. In India, he regarded himself as a "refugee from the US occupation of Britain". That day was the occasion of a lunar eclipse, with

religious processions in the crowded streets.

The eclipse was the main topic of conversation at dinner: Haldane remarked that this was the 40th anniversary of the "October" revolution: it might be a second coup, after Sputnik, were the Russians to plant a red star on the moon during the eclipse! We calculated that a thermonuclear demonstration, accenting the military prowess signified by Sputnik, might indeed be visible from earth. It was depressing to me that we had even to contemplate the possibility. Our political views diverged sharply, but we shared the lament that this magnificent scientific opportunity, the beginning of human exploration of space, would likely be marred by the geopolitical competition, that it would be used for propaganda demonstration rather than scientific inquiry. Furthermore, we might have to take measures to protect the moon and other planets from inadvertent radioactive or biological contamination arising as byproducts of the circus.

Since childhood, I had been intrigued by the scientific debate over the possibilities of extra-terrestrial life. As a thirteen-year old I had listened with amusement to Orson Welles' notorious radio broadcast modelled on H. G. Wells' novel, "War of the Worlds". I had thought that the subsequent news reports of public panic were part of the Halloween spoof itself! Twenty years later, my main professional work, on the genetics of microbes, inevitably focussed my interest in the ultimate origins of life. The possibility of its divergent evolution elsewhere than on our own planet was self-evidently one of the most important challenges to biological science. The tools to meet them were finally in our grasp.

Promptly after returning to Madison I steeped myself more deeply in the general physical and astronomical background of space inquiry, and of rocketry and space travel. I also addressed the policy issues of putting more science into the new agency, NASA, and was gratified at the active support given this by the National Academy of Sciences. Shortly after I moved to Stanford in February 1959, I had working with me, on a panel to study the problems of planetary quarantine, and biological scientific opportunities in space travel, such wonderful people as Melvin Calvin, Norman Horowitz, Dan Mazia, Matt Meselson, Aaron Novick, Roger Stanier, Gunther Stent, Harold Urey, C. B. van Niel and Harold Weaver. One of my more important discoveries was Carl Sagan, then completing his graduate work at the University of Chicago. A cognate group met on the East Coast with Salvador Luria, Paul Doty, Tom Gold, Keffer Hartline, Martin Kamen, Cy Levinthal, Stanley Miller, F. O. Schmitt, and Wolf Vishniac. (Wolf we lament as a casualty-in-action: he died in 1973 of an accident in

Antarctica whilst conducting microbiological field surveys related to our collective experiments.)

My first preoccupations had been about planetary conservation, to protect the opportunity for investigating their virgin surfaces until the technical possibility emerged. The U.S. frantic efforts to emulate Sputnik in orbital flight succeeded only on January 31, 1958; and it seemed premature to many to be contemplating lunar, much less planetary, landings. This was precisely my concern: that early approaches to the moon or planets would be crude crash landings most likely to result in contamination, e.g. from radio-isotope electric generators.

~~In my meetings with various NASA representatives and at JPL, Al Hibbs and others put it to me that I should be undertaking a constructive as well as critical role: why didn't I take a positive part in the development of biological instrumentation for space exploration? Accordingly we established an instrumentation research laboratory at Stanford and began our experimental program in "Cytochemical Studies of Planetary Microorganisms". That was an arch title: the only planetary organisms we had were terrestrial ones. But we pondered the methodology by which life might be most efficiently sensed by instruments on a lander on Mars. My implicit assumption was an automated unmanned mission. The question is not really whether human intelligence should play a part in space exploration, but whether it is more effective in ground control stations or in the spacecraft -- where the human presence imposes enormous logistic costs, and the imperative of return flight. The controversy continues to the present day.~~

At around this time, I coined the term "exobiology", a smaller mouthful than "the scientific study of extraterrestrial life". Exobiology has been panned as one of the few scientific disciplines that may have an empty set as its experimental objects. Regardless, what we have called biology until now should be limned "esobiology", which can be backformed into "earth's own biology". It may be unique in the solar system, perhaps even the cosmos -- howbeit, it is still parochial.

Planetary travel was a reality far sooner than any of my scientific colleagues would have allowed. By 1976, not one but two Viking landers were thriving on the Mars surface, but they were returning pictures and chemical analytic data of a bleak surface, rather discouraging (no trace of organic carbon according to the mass spectrometer) for any prospect of life.

Today, the most that one can say about a Martian exobiota is that a number of

habitats on the planet, particularly at high latitudes, remain to be explored. Permafrosts probably do retain some moisture, and internal heat and chemical seepage arguably could support living organisms at some depth underground -- not unlike the thermal vents on the floor of earth's oceans. Many large scale topographic features seem to signify ancient (if now desiccated) oceans and rivers, and these may bear fossils of a more hospitable epoch in Mars' history.

In my view, there is a race between the showmanship of a manned expedition to Mars, and further automated exploration, particularly with a roving vehicle to sample more of the surface. There is not necessarily a great hurry to do either; but I fear that what Haldane and I worried about in November 1957 has come to pass in the fundamental orientation of how we explore space. Meanwhile, some of the military programs, namely reconnaissance from orbit have given enormous advantage to sustaining world peace through the verification of strategic arms control agreements; and satellite communications have truly unified a world economic culture.

Signs of Life.

In our contemplation of candidate experiments for exobiology, we gave great thought to the most reliable signatures of life, those least dependent on familiar terrestrial models. With Pasteur, we agreed that optical activity was a necessary concomitant: there is a general argument. Three dimensional configurations cannot be defined without specifying left- or right-handedness of the parts. Once asymmetric catalytic systems are established, they are bound to discriminate between optical isomers. The spontaneous condensation of formaldehyde gives equal parts of D- and L-glucose. The latter is almost unknown in living organisms.

On the other hand, it is difficult to point to fundamental processes that would have predetermined for earth which isomer should predominate: I suspect that is one of many mutational accidents in the history of the planet. By the same token, either isomer (if the molecule is found at all) is equally likely to characterize another planet.

More generally, we concluded that almost any out-of-equilibrium singularity would be a clue. A Martian who could simultaneously detect oxygen and traces of methane in our atmosphere would almost certainly attribute that conjunction to life. The hypothesis is the residual when no inorganic process can be invoked. Likewise, optical fibers (or iron

rails) stretching for kilometers; or bottles of tritium would be be certain telltales of "intelligence" -- though the latter drives one to seek subcategories. Our final experimental recommendations for Viking 1975 focussed on chemical analysis of the soil with mass spectrometry: that gave an unequivocal negative for organic matter, and overrode marginal findings from other instruments. In retrospect, one of our main regrets was having left off a simple measurement of electrical conductivity: salts in the soil would have been revealing about fossil oceans. But we did not know about the "river beds" when we launched.

ETI

With the prospect of any form of life elsewhere in the solar system so dim, we have all abandoned the expectation of extant intelligent evolution so close by. Our remaining recourse is to seek meaningful signals with our radiotelescopes. I hope the enigmatic collapse of the receiver at Green Bank, W Va. is not to be taken as such!

There is no persuasive argument for or against the likelihood of success of such searches; and it would certainly be an exciting day were we to receive a signal. Nevertheless, I have been until recently reluctant to spend much money on such programs. My argument had to do with the pace of our expanding technology to make such measurements. I felt it was worth waiting a decade to get a tenfold or more enhancement of capability per unit cost. A couple of decades have now gone by, and broader enthusiasm having been discouraged by unabashedly negative findings, I feel that it may now be timely: for a few million dollars today we can conduct signal analysis that would have been measured in billions then, owing to the enormous advances in digital computers. A few people are making a low key effort; they deserve our encouragement. We will soon have been able to survey the nearest hundred or thousand stars for signals specifically beamed at earth. By then, they may have intercepted what we emit in our broadcasts -- perhaps that is what deters them from any effort on their part.

It is not too soon to ponder what we might expect to hear, would wish to send. The Dutch logician Freudenthal has done some provocative work on the construction of a universal logical language, having posed the question: how do you communicate with a "creature" with whom you share nothing but limited signals and a common physical environment? He begins with mathematical universals, like the number series. Such work will also have important ramifications in machine intelligence -- the computer

being another kind of alien.

It is a disturbing question (since I can give no credit to UFO's): why haven't we heard already? If another few hundred years of technological advancement can be extrapolated from the last century, it is hard not to imagine an easy ability to communicate over interstellar distances, at least a few tens or hundreds of light years. A century or two is a minor fluctuation: a substantial proportion of "civilizations" should be a million years more advanced than ours, in the context of a billion years of cellular evolution. Is the evolution of life so rare? of intelligence so problematical? Or is an expansive, technological society doomed to self-destruct?