

Table 1. Phenotypes of knockout mice, deficient in NOS (modified from ref. 10)

NOS subtype	Phenotype
nNOS or type 1	Pyloric stenosis; resistant to vascular stroke; inappropriate and excessive sexual and aggressive behaviour; normal hippocampal long-term potentiation (LTP) and cerebellar long-term depression
iNOS or type 2	More susceptible to <i>Listeria</i> and <i>Leishmania</i> infection and lymphoma cell proliferation; resistant to endotoxin, hypotension and corraegenan inflammation
eNOS or type 3	Deficient acetylcholine vasodilation; elevated mean blood pressure; L-N ^G -nitroarginine-induced hypotension

rings in response to acetylcholine and were unaffected by treatment with NOS inhibitor, L-N^G-nitroarginine (L-NAA). These observations substantiated the role of eNOS earlier envisaged in vasodilation. The mean blood pressure in eNOS⁻ mice was 35% higher than in control animals, confirming the role of endothelial NO in maintaining normal blood pressure, through its vasodilating function. The surprising result, however was that L-N^G-nitroarginine (NOS inhibitor), which raises blood pressure in wild-type mice, dramatically lowers blood pressure in eNOS⁻ mice, suggesting that there is a form of NOS other than eNOS, which contributes to increase in blood pressure, so that its activity is inhibited by NOS inhibitor, thus lowering the blood pressure. This other form of NOS may be nNOS in the adventitial neurons in blood vessels, and/or nNOS in skeletal muscles. NO

may also lead to contraction of skeletal muscles resulting in increase in blood pressure.

Note added in proof: In August/September, 1998, two reports^{11,12} appeared, where the role of NO in inducing defence response against pathogens in two plant species (tobacco and soybean) was demonstrated. In tobacco, induction of NOS was observed in resistant, but not in the susceptible plants¹¹. Similarly, in cultured soybean cells, both the activity of NOS and release of NO were observed in response to either a bacterial pathogen or molecules that elicit defence responses. Therefore, it is obvious that plants also produce NO in resistant genotypes using an enzymatic machinery similar to that found in animal cells. It is believed that NO collaborates with reactive oxygen intermediates (ROIs) to trigger transcriptional activation of

plant defence genes and the hypersensitive response¹³.

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COMMENTARY

Life beyond earth*

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Is there life beyond Earth? This question has occupied the minds of thinkers of all times and although the chances of

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finding life elsewhere are high, there has been no evidence so far that life exists outside the Earth. True, almost all of the planets and satellites of our solar system have been explored with high resolution cameras and specially designed instruments, samples of Moon have been analysed in the laboratories all over the world, experiments have

been carried out on Martian soil and cometary matter over the past few decades and we have surveyed the space around other stars in our galaxy with powerful antennas, yet not a trace of life elsewhere has been found. With further space missions planned in the near future and efforts for search of extra-terrestrial intelligence gathering

momentum, the coming century may provide us some clues to this problem.

The question of life beyond Earth is intimately related to the origin of life itself. Is there an origin of life? There are two lines of thinking about the way life first emerged. If life arose from abiotic processes, then it must exist everywhere, wherever chemical and biological evolution can lead to conditions that are suitable. Origin of life should, therefore, be an inevitable consequence of laws of physics as inherent in the Schrödinger's equation. With about 200 billion stars in our galaxy, and over 100 billion galaxies in the universe, we must have a large number of hospitable planets on which life could exist, as can be predicted by probability considerations given by the Drake equation. In our galaxy alone, the number of life-worthy planets may range between one and a million. The only limiting factor would be the small fraction of planets on which life can originate since origin of life is the most improbable event. Communication with such civilizations would be further restricted by the fraction of them which are technologically advanced enough to communicate and the length of time such advanced civilizations can survive extinction against natural or self-made catastrophes. Since we know that extinction is the ultimate fate of all forms of life, the last two factors may be very small. On the basis of the experience of just one example, namely ours, it is unlikely that a technological civilization can last much longer than a few thousand years. This is a very short period, making it improbable for us to receive a signal from another civilization. However, if we do not search, we may never find out and that is a strong enough reason to make an all out effort to look for our companions beyond the Earth.

As on Earth, it is reasonable to assume that life elsewhere must also be carbon and water based, although other possibilities like silicon-based structures have been discussed. If life exists anywhere else, it is unlikely to have shapes and forms similar to ours. So if we wish to look for life, we ought to define what exactly is meant by life. In brief, life must satisfy the conditions of reproduction and metabolic activity and be capable of change through these processes.

On the other hand, all experiments done hitherto on the Earth show that life can only arise from life. Chemists have been able to make complex organic molecules such as proteins, amino acids, DNA, RNA and other complex building blocks of life in the laboratory but no one has been able to synthesize a cell or put together simple structures such as mitochondria or chloroplasts from its constituents. Abiotic synthesis of a cell may, therefore, be the key to the origin of life. Whether life exists elsewhere or not would be determined by the probability of the formation of the first cell from the end products of chemical evolution, which clearly must have occurred in many parts of the universe.

Several lessons learnt from terrestrial life are useful for the present discussion. First of all we know from fossils found in deep sea sediment cores that, over the aeons, life has evolved from simple to complex forms. Fossil records on the Earth show that life started at about 3.5 billion years ago or even a few hundred million years earlier and the complexity has grown exponentially with time. Secondly, life occurs wherever conditions are favourable for its sustenance. Life has been found in diverse environments like Antarctica and in hydrothermal vents at the bottom of the oceans, where photosynthesis is not possible, due to lack of sunlight. Here, other alternative pathways such as fixation of sulphide have been adopted by nature for providing necessary energy for supporting life. If growth can be sustained, the number of species grows exponentially. Thus starting with a single bacteria, a colony as big as the whole earth can grow in a period as short as a week. We may therefore infer that, wherever life is found, it will be found in abundance.

Meteorites have provided crucial information about prebiotic chemistry. The carbonaceous meteorite which fell at Murchison, Australia in 1969 has provided valuable clues about abiotic synthesis. This meteorite formed very early, at the beginning of the formation of the solar system and contains besides carbon and hydrated minerals, several amino acids. Many of these occur in racemic proportion and the nitrogen isotopic ratios provide definite evidence that they are not terrestrial contaminants acquired after the fall of the meteorite. Urey-Miller synthesis of formation of

complex organic molecules in reducing environment containing CO_2 , CH_4 , H_2O , etc. have shown that it is easy to form these building blocks of life by abiotic processes. However, initiation of biotic processes, if at all it can occur from abiotic processes, is expected to take a long time. We know that the Earth formed early, within 50 or 60 million years of formation of the solar system (4.6 billion years ago) by collisional accretion of planetesimals. In the beginning, the Earth must have been extremely hot because of the terminal collision of a large planetesimal which is believed to have also resulted in the formation of the Moon. By about 4.2 billion years ago there is evidence from sedimentary deposits that the Earth's crust had cooled enough to have liquid water but by this time the second major episode of bombardment of the Earth by large planetesimals started and continued till about 3.8 b.y. ago. This Late Heavy Bombardment was quite cataclysmic, certainly not conducive to formation or preservation of life. But we already have fossil evidence of the first cells occurring on the Earth at this time or shortly thereafter. Thus, there was hardly any time available for transition from abiotic to biotic processes which is supposed to take a long time.

In this context the hypothesis of Panspermia advanced by Helmholtz, Arrhenius and recently favoured by Hoyle and Wickramasinghe is noteworthy. If life seeds are present everywhere in the universe, then life must occur wherever the conditions are conducive, within our planetary system and outside. If we survey various bodies of the solar system we find that Moon, Mars, Europa, Ganymede, Titan and comets in Kuiper belt or Oort's cloud have frozen water on or below their surface. Although the Moon was long believed not to have water and organic matter, the recent exciting findings of frozen water (probably brought in by comets over the ages) in its polar craters by the Prospector Mission of NASA have increased the probability of presence of some organic molecules as well.

Surface features and drainage channels seen on Mars indicate that liquid water once flowed there in the form of mighty rivers, very early in its history, although today it is in frozen form. There has been ample volcanic activity

on Mars in the past which could have provided favourable environment and source of heat for existence of life on Mars. Recent finding of minute carbonate globules in a meteorite which originated from Mars and fell at Allan Hills in Antarctica (ALHA 84001) about 13,000 years ago have rekindled the hopes of life occurring on Mars. Although there is some doubt whether the PAH (polycyclic aromatic hydrocarbons) and carbonate globules found in ALHA 84001 are biotic or chemical in origin, the findings have created renewed interest in the search for life on Mars. The Viking missions to Mars in 1976-77 did not provide any evidence of presence of bacterial activity there which were taken to indicate absence of living forms but further exploration and analysis of Martian soil is necessary to substantiate this conclusion.

Environment on Europa and Ganymede is not so conducive to sustain life albeit the presence of sub-surface ice which might, at times, get converted into liquid form, but the Kuiper belt comets (beyond the orbit of Neptune) show a slight reddening, not expected from inorganic molecules. Comets are known to contain complex organic molecules such as alcohols and formaldehyde, and a suggestion made by Wickramasinghe that this reddening is due to some organic or bacterial pigments, has created some interest in the possibility of comets harbouring life. Titan, the large satellite of Saturn, presently has an atmosphere (N_2 , CH_4 , H_2O) similar to what Earth had in the early days of its formation, except that the temperature there is very low. One has to wait for a space mission planned in the coming decade to see if complex organic molecules or primitive life indeed occurs there or not. In short, although there have been no traces of life elsewhere in our solar system, even in the most primitive form, and the Earth remains unique, possibilities do exist and the next few decades should be able to provide more definitive evidence.

Planets and protoplanetary discs have recently been found outside our solar system and as of now, at least twelve such star-planetary systems have been identified. Since their existence is inferred from the slight yanking of the star's orbit (sub milliarc seconds/year), only large planets having size compa-

rable to or bigger than Jupiter have so far been found. Some of them may even be brown dwarfs. Many of them are not only much bigger than the Earth, but also have a short period and are located too close to the central star to have the right temperatures for supporting life. The optimum location from the central star is where water can occur in liquid form. Still, it is possible that some may have the right conditions to support life. Bernard's star, for example, about 6 light years away from us has a planet orbiting around it. The British Interplanetary Society has carried out a feasibility study under Project Daedalus for a mission to Bernard's star using nuclear propulsion. The star, 51 Pegasus, has a planet which is about half the size of Jupiter but with an orbit even closer than that of Mercury around the Sun. 16 Cygni and 47 U Majoris have larger planets (1.6 to 2.4 times the mass of Jupiter) but their orbits are relatively farther (equivalent to the orbit of Mars around the Sun) and may be more favourable for supporting life. Some planet-like bodies have also been found to occur around pulsars (PSR 1257 + 12). In spite of the dissimilarity of their masses and orbits, compared to the Earth in the solar system, the existence of planetary objects around many stars has provided new thrust to search for life outside our solar system. In the next decade a Terrestrial Planetary Explorer, with two 6 m telescopes in interferometric configuration and improved photometric techniques, may look for Earth-like planets around many stars and may even be able to collect information about planetary geology, atmospheric constituents, etc.

It may be equally fruitful for starting a search for extraterrestrial intelligence (SETI) through radio communication. Starting with Project Ozma in 1960, more than 80 searches have been carried out over the past four decades using the existing radiotelescopes in various countries. The 21 cm line of neutral hydrogen, which is the most abundant element in the Universe is perhaps uniquely suited for radio communication as was suggested by Cocconi and Morrison in 1959. Although no signals have been detected so far, the searches continue with increasing efforts and sensitivity. Since direct communication through interstellar probes with intelli-

gent life far away would take an unrealistically long time, one has to resort to search for a radiosignal which may have been beamed towards us by such civilizations (eaves-dropping). The sensitivity of most searches made so far has ranged between 10^{-22} and 10^{-24} W/m^2 . Recently a more sensitive search has been carried out by the SETI Institute under Project Phoenix in the frequency range of 1.2 to 3 GHz using a spectrometer having 28 million channels achieving a resolution of 1 Hz. About 200 solar type stars have been surveyed in the southern sky by the Phoenix team with a sensitivity of about 3×10^{-25} W/m^2 using 64 m diameter parabolic dish antenna at Parkes, Australia. Over the next two years, the SETI Institute plans to observe another 800 stars in the declination range of about 0° to 40°N using the Arecibo Telescopes with a sensitivity of 5×10^{-27} W/m^2 . Several other SETI projects with comparable or better sensitivity are being carried out in Argentina, Australia, Italy, France and USA. Most searches have used a narrow band spectrometer with a band width of less than one Hz to minimize the detection levels. An upper limit of detection limit 5×10^{-27} implies that no transmitters with power exceeding about 10 MW connected to a 64 meter dish and radiating at about 21 cm wavelength were beamed towards the Earth from a distance of about 1000 light years, during the small period of time (minutes) during which the searches were made. Transmitting power limits would be lower for nearby locations according to the inverse square law. Searches are also being carried out for pulsed signals at optical wavelengths.

The Giant Meterwave Radio Telescope (GMRT) recently set up near Pune can provide a powerful means to carry out this search for ETI signals. The GMRT consists of 30 fully steerable antennas of 45 m diameter and can look at 90% of the entire sky. It is the world's largest radiotelescope operating in the frequency range of 38 to 1430 MHz. Although designed for radioastronomy, it is an excellent facility to search for ETI. For this purpose, it is desirable to build a 128×10^6 channel spectrometer with a resolution of 0.5 Hz. An additional advantage is that radio noise is low in India.

This is obviously one effort which can be made in India with some advantage. There are other experiments which can be taken up in India. Realizing that one meteorite, Murchison, has transformed our concepts and provided a firm evidence of abiotic synthesis of complex molecules in the outer space, search and analysis of fresh meteorite falls may be an easy and effective way to pursue this problem. So far satellites have not been used to photograph

meteor trails and such a programme can be taken up here using Indian satellites. Since about 10–20 meteorites fall on the Earth every year, there is a good chance of quick recovery of a meteorite in India provided its trail is determined photographically. It can be expected that some of them may turn out to be unique and may shed further light on problems related to the origin of life in our solar system.

In spite of the absence of any evidence so far for existence of life beyond

Earth, the subject remains extremely fascinating. It is hoped that with improved technology, the coming century may provide an answer to the question whether we are alone in the universe or if there are some companions out there waiting for us to communicate.

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OPINION

New trends and fashions in science and apathy of funding authorities towards areas in classical science

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The role of fashion in science has been dealt with in some detail by Erwin Chargaff in his essay 'Triviality in Science: a brief meditation on fashions'. Later in his autobiographical book *Heracleian Fire*² Erwin Chargaff says 'The onset of molecular biology was accompanied by an orgy of model-building, much of it of a transparent stupidity. The journals were full of models no sooner published than discarded. Even then I counselled moderation, thus contributing to my reputation as a "controversial figure".' Another author Stephen Jay Gould³ speaks of modern trends in science in his 1991 Science Book Prize winning work *Wonderful Life* where he points out, 'The sciences of historical complexity have been demoted in status and generally occupy a position of low esteem among professionals... These distinctions have entered our language and our metaphors the "hard" versus the "soft" sciences the "rigorously experimental" versus the "merely descriptive". Several years ago Harvard University, in an uncharacteristic act of educational innovation broke conceptual ground by organizing the sciences according to procedural style rather than conventional discipline within the core curriculum. We did not make the usual two-fold division into physical versus biological but recog-

nized the two styles just discussed, the experimental-predictive and the historical. We designated each category by a letter rather than a name. Guess which division became Science A and Science B? My course in the history of earth and life is called Science B-16.' In one of my earlier articles I too have dealt with this subject⁴.

In my present article on this topic, I wish to deal with the new trends in science, particularly in Indian science with special reference to life sciences. In doing so, I must first outline the process of scientific investigation which is the study of nature and natural phenomena by observation through our sensory organs. In the modern age, we supplement our senses by different gadgets which augment our observations. However, our observations are only the beginning of science, these are followed by a process in the mind which classifies and reasons out our observations, draws conclusions and makes generalizations. The fall of an apple and Newton's law of gravitation is a familiar example. These generalizations then have to be tested by experiments wherever possible, by artificially creating the conditions and these generalizations are now called laws or theories. The phenomena and laws thus discovered are next utilized to perform difficult jobs or

activities. Up to the discovery of the phenomena and making generalizations about them, the process is science but thereafter the skill in performing jobs with that scientific knowledge is technology, although it may be difficult at times to say where science ends and where technology begins. Citing examples from the field of biology, the persons who domesticated wheat or rice plants by creating conditions for their culture under cultivation were doing science but those who repeated the cultivation for ages by improving conditions of cultivation were doing technology but here again those who discovered better breeds in nature or bred new varieties by crossing or by other genetic processes were scientists. Taking another example from the field of medical science, when Ronald Ross found that bites of *Anopheles* mosquito were responsible for injecting malarial parasite in the blood stream in humans and these thereafter multiplied in the body and caused malarial fever in man, he was doing science, but the doctor who prescribes quinine or other drugs to cure malaria is only a technician, but once again a doctor who discovers a new drug or new treatment for malaria is a scientist.

And I must also mention here cases like those of James Lovelock, the author