leaving dental features to support its identification as a whale. In this context, note that several early whales from the Eocene of Pakistan, *Gandakasia* and *Ichthylestes*, known only from teeth, were originally described as mesonychids (*11*). Rather than use Prothero's definition of a whale, Thewissen *et al.* use other characters to establish *Ambulocetus* as a whale, including an inflated ectotympanic that is poorly attached to the skull and bears a sigmoid process, reduced zygomatic arch, long narrow muzzle, broad supraorbital process, and teeth that resemble other archeocetes. Before these purported whale characters can be used in a phylogenetic definition of whales, however, the possibility that some of them may have a broader distribution (for example, in mesonychids) needs to be examined.

While the study of Thewissen *et al.* provides new information at the base of whale evolution, recent molecular data have challenged traditional views of later whale evolution. According to Milinkovitch *et al.* (*12*), data from mitochondrial DNA suggest that odontocete whales might not be a monophyletic group; that is, they do not comprise a lineage that includes the common ancestor and all of its descendants. A closer relationship is suggested between the sperm whales and the baleen whales than between the sperm whales and other alleged odontocetes. These molecular results have intriguing evolutionary implications (*13*). Either baleen whales secondarily lost the ability to navigate using echolocation or, alternatively, echolocation in whales may have evolved twice, once within the sperm whale + baleen whale clade and once within other odontocetes. The molecular view of odontocetes as a nonmonophyletic group is not supported by morphologic evidence, although few studies have addressed the problem using comprehensive data sets (including both fossil and recent taxa) and rigorous phylogenetic methods (*14, 15*).

Molecular as well as morphologic studies compel us to reexamine whale phylogeny. Although its relationship to other whales is uncertain, *Ambulocetus natans* is a whale, using a definition based on ancestry. This discovery is significant in providing a more complete picture of morphologic diversity at the base of whale evolution, particularly in documenting the locomotory transition in whales from land to the sea. More importantly, perhaps, it directs us to what is most needed now, an expanded study of the phylogenetic relationships of all whales and their close relatives, including extinct as well as recent taxa.

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What Are We? Where Did We Come From? Where Are We Going?

Luke O'Neill, Michael Murphy, Richard B. Gallagher

If an angel appeared before you and granted the answer to one question, what would that question be? If your burning desire is to know whether there is intelligent life elsewhere in the universe, you are in good company. A group of eminent physicists, chemists, and biologists agree that this is *the* "angel question." It remains, for the time being, unanswerable, but questions almost as fanciful—what are we, where did we come from, and where are we going—are at least beginning to be tackled in a meaningful scientific way. These were the themes that dominated a recent meeting in Dublin (*1*), held to commemorate the series of lectures given in Trinity College 50 years ago by Erwin Schrödinger.

Those original Schrödinger lectures, entitled "What Is Life?", electrified public audiences in Dublin half a century ago and, when published by Cambridge University Press in 1944, had a major influence on the development of molecular biology. In them, Schrödinger put forward two propositions. First, "order from order": Inspired by studies of Delbrück on the rate of mutation in fruit flies exposed to x-rays, he discussed the physical nature of the gene and the mechanism of heredity. His suggestion of it being an aperiodic crystal was a remarkably prophetic description of the structure of DNA. Second, "order from disorder": an outline of how living organisms maintain order while being displaced from equilibrium, a feat made possible by the metabolism of food or, as Schrödinger termed it, negative entropy. Speakers at the 50th anniversary meeting were invited to speculate on the future of biology in the spirit of Schrödinger's original lectures.

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What Are We?

Genetically, that is, in terms of information content, humans are 99 percent identical to chimpanzees. Indeed, argues Jared Diamond, a visitor from outer space would classify humans as a third species of chimpanzee, not with the separate classification that we award ourselves. How, then, did we become so successful? What sets us apart from other species? Diamond, professor of biology at the University of California, Los Angeles, proposed that it is human inventiveness, a talent developed as a consequence of the acquisition of language. The first signs of inventiveness appeared around 50,000 years ago, judging from the evidence of elaborate tools, art, and burial of the dead. It is possible that changes in the voice box facilitating efficient transmission of information allowed this development of inventiveness. It was pointed out by Stephen Jay Gould (Harvard University) that early language would have had a selective value that could have been co-opted by early man in acquiring inventiveness, so language and inventiveness probably co-evolved. John Maynard Smith (University

of Sussex) agreed that it is the ability to use grammar, the awareness of the importance of word order, that sets humans apart from other animals. He illustrated the complex genetic basis of language by citing an inherited genetic defect in which affected family members are unable to follow certain basic rules of grammar, but can learn them on a case-by-case basis.

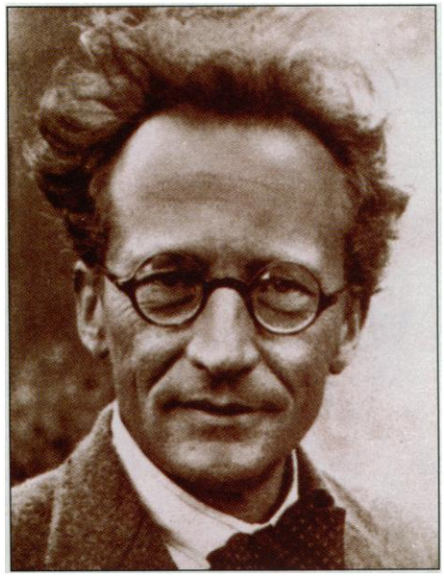
For Schrödinger, the world was a construct of our sensations, perceptions, and memories. This construct is slowly being resolved, with some recent advances in the study of perception. Nobel laureate Gerald Edelman (Scripps Research Institute, La Jolla), who acknowledged the influence of Schrödinger's theories on his early career, outlined his approach. He explained that the hard-wired model of the brain as machine is inadequate because it does not take into account the accrual of numerous small factors that act in parallel and that make brain function context-dependent. In its stead he proposed a somatic selection model: Random circuits are developed during embryogenesis, and these differentiate and adapt as a result of experience. Furthermore, reimprinting or "mapping of maps" adds to the plasticity and complexity. These concepts are being mimicked by increasingly sophisticated perception machines. One of the latest, Darwin III, can discriminate between light at the center of its field of vision and light and stimulation at the periphery. Through the strengthening and selection of particular circuits as a result of the experience acquired, the automaton can track signals from lit objects. This ability to select groups of "synapses" makes Darwin III closer to the human brain than any other computer-based simulation so far attempted. Edelman felt, however, that attempts to make a perception machine that is actually conscious, using a Turing machine-based computer, is bound to fail owing to the dynamic and selective processes at work in the human brain.

Moving to the still more mysterious subject of consciousness, Roger Penrose, professor of mathematics at the University of Oxford, argued convincingly that consciousness will not be understood on a computational basis. He proposed that it will require a fuller understanding of quantum mechanics, specifically the application of micro quantum mechanics to macro events.

Where Did We Come From?

RNA almost certainly came before both DNA and proteins: RNA contains replicable information and can have enzymatic coenzyme activity. In fact, the concept of an early "RNA world" is now widely accepted. But how did RNA evolve in the first place? And how did the RNA world evolve into the nucleic acid–protein world?

In response to the first of these questions, Leslie Orgel (Salk Institute, San Diego) took up the theme of "order from order," exploring the self-replication of copolymers made up of, but more reactive than, the constituent monomers. In the



Erwin Schrödinger.

test tube, simple copolymers comprising poly-C and poly-G nucleotides spontaneously replicate. However, these are but "periodic crystals"; more complex, RNA-like molecules (aperiodic crystals) have not been shown to be capable of self-replication. This prompted speculation on the involvement of a cofactor (or cofactors), for example amino acids, which are thought to have been present in the pre-RNA world. The story was taken up by Nobelist Christian de Duve (International Institute of Cellular and Molecular Pathology, Brussels) who made the point that the emergence of RNA depended on robust chemical reactions—it is wrong to imagine that some fantastic single accidental event supported the development of the RNA world. The emerging RNA world contained information, catalytic activity, and replication machinery (ribozymes and cofactors). Ribozyme utilization of amino acids may eventually have led to the appearance of enzymes. It is generally accepted that this process took a very long time—perhaps hundreds of millions of years—but de Duve suggested that, on the contrary, for such a complex chemical process to succeed it must have been relatively fast in order to avoid decay and loss of information.

There still remain the questions of translation and the origin of the genetic code. John Maynard-Smith offered one scenario for the emergence of these features: the use of amino acids and cofactors by ribozymes. Due to their relative size and structure, the most likely interaction was between a single amino acid and three nucleotides (hence the triplet code). As the number of amino acids used as cofactors increased, each with its own nucleic acid triplet, so the possibility of two, three, and four amino acids being brought together arose. Some of these emerging peptides would be functional, and the nucleic acid sequence would have a selective advantage. Maynard-Smith felt that this illustrated a point that must not be overlooked in the study of evolution, namely, that adaptation of function may obscure the origin of structure: A case in point is the feather, evolved for flight from the original purpose of maintaining warmth.

A stark alternative to the ideas of gradually increasing complexity of protometabolism came from Stuart Kaufmann, professor of biology at the University of Pennsylvania. In considering an enormous set of random chemical reactions, such as may have occurred on the planet in the immediate pre-biotic era, Kaufmann provided some astonishing statistical analyses. These suggested that closed networks of chemical reactions, in which each product catalyzed a different component of the network, may have arisen spontaneously. As an analogy he described a floor on which pegs have been scattered: The pegs are gradually tied together, one to another, by pieces of string. Suddenly, at some critical phase of the process, most of the pegs are connected to form a net. Life may have its origins in a similar phase change, in which a network of interdependently replicating molecules arose from a set of independent chemical reactions. This may explain why even the simplest of life forms comprise an extraordinarily complex series of reactions.

Where Are We Going?

This was a question dealt with on several levels. Where is biological research going? What is the future of the planet? And what are the possible evolutionary developments of the species?

Despite the enormous changes that we have wreaked on our environment, major evolutionary changes in humans will not occur. Stephen Jay Gould dismissed the idea that the species is "going somewhere" under natural selection and described how most successful species are stable through their geological lifetimes. Furthermore, given the relative pace of cultural change and lack of isolation of human populations, there is little propensity for speciation. This is not to say that underlying natural selection is not occurring on numerous fronts—of course it is. It is most readily studied in genetic resistance and susceptibility to infectious disease, vividly demonstrated by

the relative resistance of a small fraction of the population to acquired immunodeficiency syndrome (AIDS), in itself a massive experiment on human natural selection.

Several speakers speculated on the developments that the study of life might witness in the next 50 years: cures for still-intractable infectious diseases, a deeper understanding of the origins of life, a reasonable insight into how the brain works, and the emergence of a blueprint for the development of organisms are all on the agenda. All agreed that an increasing proportion of biologists' time will be spent on experiments *in silico*, that is, by computer modeling. The discussions on the fate of the species, and indeed of the planet, were rather more pessimistic. Manfred Eigen, Nobel laureate and director of the Max Planck Institute in Göttingen, wove together the future of biology and the future of the planet. Of the many serious problems confronting humans, the most urgent is that of population growth. According to Eigen, to feed the world's population in 50 years' time will require all our ingenuity, including the use of nuclear power and genetic engineering to increase crop yields. He urged scientists to become involved in the great debates on these subjects that currently grip society, and he emphasized that time is of the essence: We do not have much time left to prove that we are not the products of a lethal mutation.

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1. The meeting "What Is Life?" was held in Dublin, Ireland, on 20 to 22 September 1993.

Surprising Signals in Plant Cells

Alan M. Jones

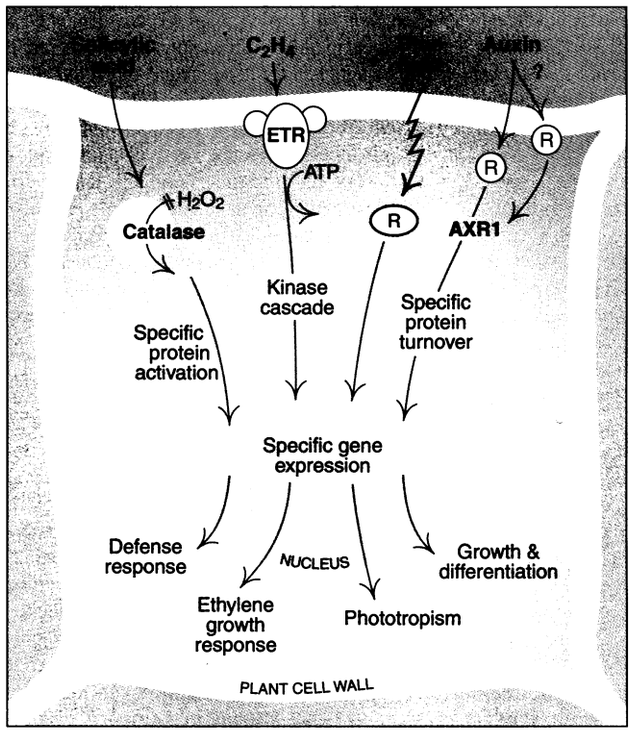
Plants, like animals, must respond to environmental cues. In the past few months, some surprising specifics of how plants perceive and transduce these signals have come to light. Working independently, four research groups have found new signal perception mechanisms in plants not described before for any eukaryotic cell: We now know something about how plants sense blue light and the plant hormones salicylic acid, ethylene, and the class of growth-promoting hormones designated as auxins, of which indole-3-acetic acid is the representative member.

Salicylic Acid

In *Science*, Chen and co-workers of the Klessig group (*1*) reported the identity of a receptor for salicylic acid, the endogenous signal required for the systemic acquired resistance (SAR) response of plants. SAR is part of a defense response that is induced locally by pathogen or pest attack but that spreads systemically to protect the entire plant. Salicylic acid likely mediates this response: Application of salicylic acid or certain analogs such as aspirin (acetylsalicylic acid) induces the rapid expression of the pathogenesis-related genes, which serve as molecular markers for the SAR response (*2*). Moreover, the timing is right. Salicylic acid increases throughout the plant after only one part of the plant is attacked by a pathogen, and this increase occurs before the expression of the pathogen-related genes (*3*).

Chen and co-workers found that the cellular binding protein for salicylic acid shares high sequence identity with some members of the catalase family of enzymes (*1*). Catalases reduce and effectively inactivate hydrogen peroxides, one type of reactive oxygen species (ROS) in eukaryotic cells. Could this member of the catalase family be the salicylic acid receptor that mediates the SAR response? Several pieces of evidence suggest that it is. The binding of salicylic acid to catalase is regulatory and inhibits its enzymatic activity, at least in vitro. The resulting increase in ROS could possibly activate specific transcription factors, as active oxygen species do in animal cells (*4*). Chen and co-workers therefore tested whether pathogen-related gene expression is increased by the addition of compounds that increase the amounts of ROS in the cell. Their results suggest that ROS can induce pathogen-related gene expression. Other data also point to the induction of SAR by salicylic acid as being mediated through catalase: The binding affinity of salicylic acid and its analogs to catalase parallels the inhibitory action of these compounds on hydrogen peroxide reduction and, of critical importance, parallels their ability to induce SAR. This observation links the action of catalase to SAR, thereby diminishing the trivial possibility that salicylic acid and its analogs are nonspecifically binding to catalase (for example, by the ability of salicylic acid to chelate the iron cofactor of catalase).

That ROS may transduce the signal that mediates the response to pathogen attack fits with the observation that extracellular ROS elicit local defense mechanisms. Triggers of SAR such as fungal cell wall glycans and glutathione cause local oxidative crosslinking of cell wall proteins well in advance of the effect on gene transcription (*5*). This is the first action of the plant in response to a pathogen attack—erection of a local barricade by stiffening of the cell wall through intermolecular crosslinks. Thereafter, the plant systemically induces defense- and wound-related genes that provide further resistance. Both actions are mediated by ROS. These ROS, although certainly toxic at high concentrations, now must be considered true secondary messengers when present at lower concentrations. We may even eventually find that ROS are important messengers for growth and development as well.



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Surprising signals. The recently discovered mechanisms by which plants sense their environments.

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