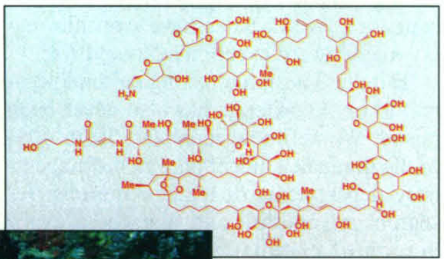
chemistry, and the study of basic chemical principles, have recently flourished. I would not trade my training in the competitive environment of total synthesis for any other. I



The structure of polytoxin (right), a compound from *Palythoa vestitis*, a soft coral (left)

owe my professional spirit and any future successes to this background.

Synthesis, with all of its facets, must persevere as a mainstay of the chemical frontier. Chemistry as a whole will always enjoy a steady advance sprinkled with dramatic breakthroughs. For decades, the steady advance has been fueled in good measure by the example and excitement of total synthesis. Dramatic breakthroughs in chemistry will often be made by those schooled in total synthesis. Total "synthetikers" enjoy the advantage of being able to make any molecules we want by simply "taking known reactions and putting them in a new order" (humor intended). We can think deeply about chemistry from broad experience, and so extend our imaginations and productivity to any chemical problem we choose. What other concern can claim this continuing impact?

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Facts about Artificial Intelligence

Ray Kurzweil (Letters, *Science*'s Compass, 16 July, p. 339) responds to my review (*Science*'s Compass, 30 Apr., p. 745) of his *The Age of Spiritual Machines* (Viking, New York, 1999) as follows.

1) My review "mires the reader in obscure and misleading factual objections." Kurzweil attempts a history of computing; in history, facts matter. He challenges only one of my historical objections, concerning the UNIVAC computer. His book, in an entry labeled "1950," says, "Eckert and Mauchley develop UNIVAC, the first commercially marketed computer. It is used to compile the results of the U.S. census" (p. 269). In fact UNIVAC was under more or less continuous development from 1947; it was not the first commercially marketed computer, nor was it operational until 1951.

2) I "drag out old anti–artificial-intelligence (AI) arguments." I do not. Rather, I hold that make-believe about basic conceptual issues, such as we find in Kurzweil's book, are hindering AI.

3) I complain "about anthropomorphizing, but there is no harm...." In AI, anthropomorphizing leads to an emphasis on human qualities that are irrelevant to, and a distraction from, the real aims of AI.

4) My review "ignores [the book's] salient arguments...." I do not detect any, only fantasy, Kurzweil's own "laws" of physics, unjustified assertions, and factual errors.

His letter is no different. For example, Kurzweil insists that Wittgenstein's *Tractatus* is about the brain, supporting this with a fallacious argument. In fact, the *Tractatus* is a technical work of symbolic and philosophical logic and abstract metaphysics and has nothing to say about the brain. Moreover, when Wittgenstein later did discuss the brain, he denied precisely Kurzweil's argument, that to talk about "thinking" or "knowing" is to talk about brain activity. Kurzweil also says that "there is nothing to prevent these efforts [modest connectionist experiments] from scaling up to the entire human brain." How could he, or anyone else, possibly know this, given the vast discrepancy in scale that is involved (there are perhaps as many as 10^{14} neurons in the human brain)?

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Chimp Cultural Diversity

The special News Focus of 25 June (p. 2070) by Gretchen Vogel highlights papers in *Nature* and the *Journal of Human Evolution* reporting that chimpanzees show regional learned behavioral differences (multiculturalism), but it does not mention that phylogeographic studies would lead us to expect such differences (*1*, *2*). What is often erroneously referred to as "the chimpanzee" comprises at least two well-differentiated allopatric populations that have diverged genetically for more than 1.5 million years. The same heterogeneity is now recognized in "the gorilla" and "the orangutan." There is several times more mitochondrial DNA variation in a single chimpanzee social group than in the entire human species (*2*) and more sequence variation at chimpanzee nuclear coding (MHC) and noncoding (HOXB6) regions than in humans (*3*). It is perhaps more surprising that there is any cultural variation in our own relatively homogeneous species than that there is any in our far more variable hominoid relatives. Although a few scholars still deny any role for genetics in the regulation of behaviors, and others posit the existence of nongenetic mental replicators (memes) to account for cultural transmission, we can no longer ignore the genetic diversity of the chimpanzees.

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Vogel quotes Carel van Schaik as speculating that tool-using in early hominids became more common as a result of higher "social tolerance." John Fleagle is quoted as agreeing with this speculation, noting that the reduction in canine tooth size seen in the early hominid fossil record was probably indicative of increased tolerance.

In 1993, we proposed a mechanism that would have led to increased social tolerance in basal hominids (*1*). The social change that led both to greater tolerance and to the origin of habitual bipedal posture evolved as an extension of the behavioral complex of bipedal threat displays and appeasement behaviors observed in great apes. These behaviors evolved in ape societies as means to mitigate aggression and avoid physically injurious confrontation. We speculated that these behaviors became more important in prehominid populations of the late Miocene in Africa, in part because of environmental changes. We also indicated that this behavioral change would have led to a reduction in canine size because conflict resolution would have increasingly relied on bluff and display rather than physical attacks involving biting. We have since demonstrated, using a demographic model (*2*), that a behavioral innovation leading to greater social tolerance that was effective at reducing morbidity and mortality in long-lived ape species would have been strongly favored by natural selection. This mechanism is best seen as an exaptation which, by promoting habitual bipedalism, made possible the anatomical and neurological changes associated with increased manual dexterity and tool use. One need search no farther than this to understand the origins of increased social tolerance in human ancestors.

CREDITS: (LEFT TO RIGHT) PHOTO: L.S. ROBERTS/VISUALS UNLIMITED/SOURCE: NICOLAOU *ET AL.*, *JOURNAL OF CHEMICAL EDUCATION*, *75*, NO. 10 (1998); BRUCE DAVIDSON/ANIMALS ANIMALS

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DNA Discovery

In a News section of the "Evolution" special issue (25 June, p. 2107), Virginia Morell writes, "he [Charles Darwin] wrote 100 years before DNA was discovered." She was in all likelihood referring to Watson and Crick's classic 1953 paper suggesting a structure for DNA, not its discovery. Any student of biology will be aware of the delightful irony that Mendel's seminal results were first reported in 1865, just 6 years after *On the Origin of Species* was published, although it was not until the modern synthesis some 70 years later that the two fields became integrated. What is not so well known is that Frederick Miescher first isolated DNA from pus-laden bandages in Tubingen Castle in Germany in 1869, although once again, the hereditary function of DNA was not conclusively demonstrated until the 1940s. We are now seeing a synthesis of evolutionary genetics and molecular biology, ultimately deriving from these three results, remarkably published within a decade of each other in the 19th century.

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Mitochondrial Recombination? (Continued)

In her article "Can mitochondrial clocks keep time?" (News of the Week, 5 Mar., p. 1435), Evelyn Strauss references E. Hagelberg *et al.* (*1*) as providing evidence for recombination in human mitochondrial DNA (mtDNA). Those authors suggest that a genetic mutation (at 16076 in HVS I) found in all three haplogroups among a study population of Nguna islanders is best explained "by paternal leakage of mtDNA and subsequent recombination" (*1*, p. 490). They also suggest that previously identified "hypervariable" mtDNA sites are actually ancient substitutions present in multiple haplogroups that result from recombination with paternal mtDNA.

We agree with Peter Arctander (Letters, 25 June, p. 2090) that these are improbable suggestions. Paternal mtDNA transmission in humans has not, to our knowledge, been confirmed. Paternal mtDNA in interspecific crosses of mice is apparently eliminated in early embryogenesis (*2*); "leakage [is] restricted to the first interspecific cross, and it did not spill over to subsequent backcrossing" (*3*, p. 885).

Recombination should disrupt the linkage between mutations within haplogroups. We estimated linkage disequilibrium (*4*) between all pairs of variable sites in HVS I for the 41 Nguna (*1*), 376 Native Americans, and 695 European individuals from a mtDNA database (*5*). Ninety-nine percent, 96%, and 93%, respectively, of all D^1 values indicated complete linkage (or nonlinkage) of variable sites. The incompletely linked sites were compared to sites previously identified as hypervariable (*6*). Within the region surveyed by Wakeley (*6*), four of six in the Nguna, five of six in the Amerind, and nine of 13 in the European samples were identified as hypervariable. Thus, most variable sites are completely linked or unlinked, and the great majority of the incompletely linked sites are "traditional" hypervariable sites.

There is little evidence for recombination outside of the D-loop (*7*) or between it and the coding regions (*8*). Because migration and recombination are presumably rare, the combination of these events is extremely unlikely. Alternative explanations for the 16076 polymorphism include that it is a hypervariable site specific to the Nguna or the result of systematic sequencing errors. Either way, better evidence would be required before recombination could be considered as a viable explanation for this polymorphism.

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Protein Crystallization at NASA: Well Grounded

The article "Negative review galls space crystallographers" by Jennifer Couzin (News of the Week, 24 July 1998, p. 497) summarized a previous report by the Amer-