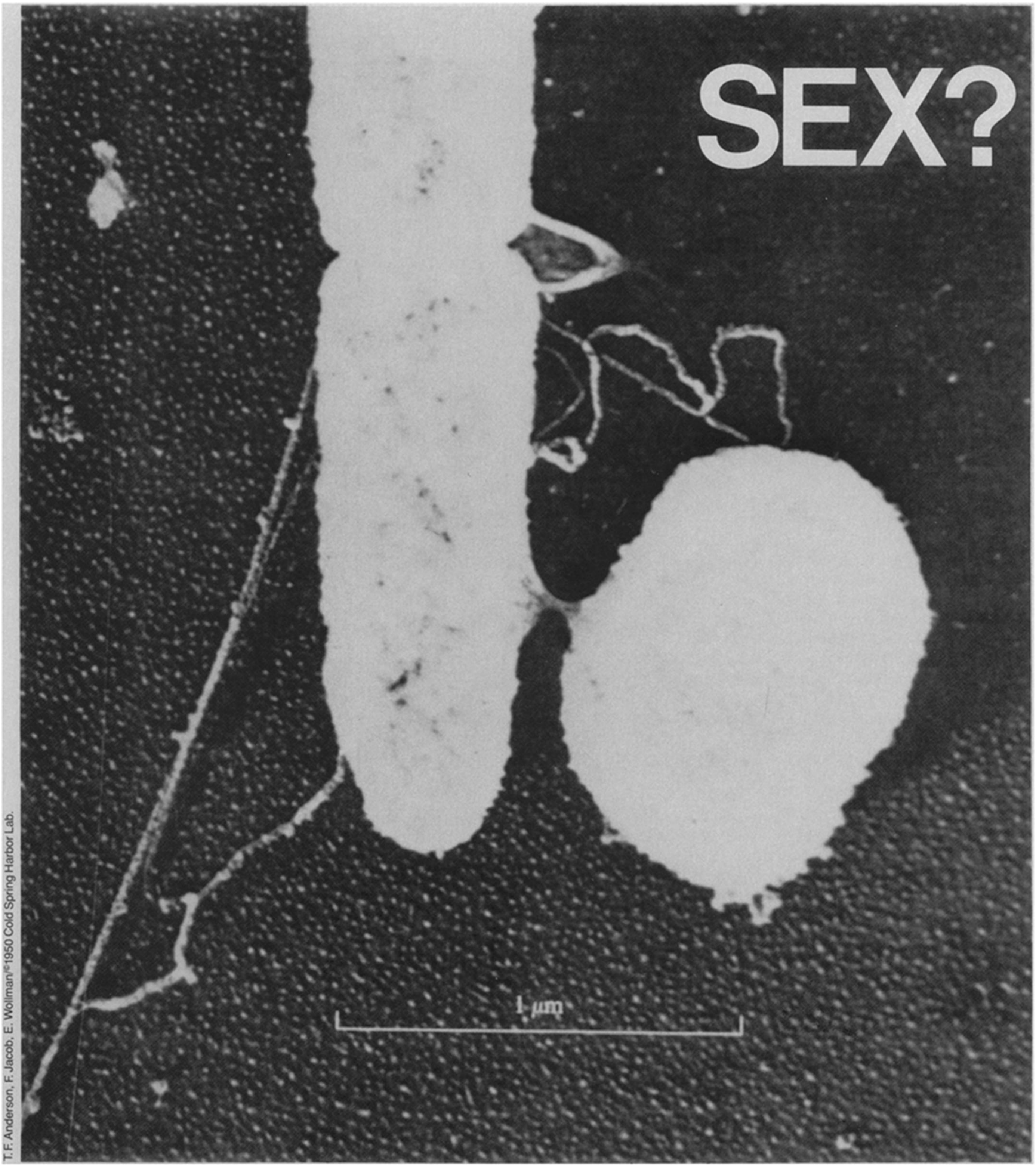
WHY IS



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By GARDINER MORSE

A huge amount is known about how sex is done. Library stacks and magazine stands overflow with those observations. But there's a larger question that's gotten far less attention: *Why* is sex? "We do not even in the least know the final cause of sexuality," wrote Charles Darwin in 1862. "The whole subject is as yet hidden in darkness." He might have been writing today.

"Sex is the queen of problems in evolutionary biology," wrote Graham Bell, an evolutionary biologist at McGill University in Montreal, in 1982. Why such a thing exists at all, he says, is "the largest and least ignorable and most obdurate" of life's fundamental questions. Bell was one of over a hundred scientists from around the United States, Canada and Europe who gathered recently to explore this question during a four-day symposium held at the Marine Biological Laboratory in Woods Hole, Mass. The symposium, entitled "The Origin and Evolution of Sex," is thought to be the first of its kind, says the meeting's principal organizer, Harlyn O. Halvorson of Brandeis University in Waltham, Mass.

While "sex" means different things to different people, a definition emerged that seemed satisfactory to the scientists attending the symposium. Sex, most agreed, is "the process whereby a cell containing a new combination of genes is produced from two genetically different parent cells."

Biologists trying to discover how sex first arose have some daunting problems: As Bell puts it in his book *The Masterpiece of Nature*, "sex does not fossilize well." We may never learn how it first happened. Complicating the question is disagreement among biologists about whether the origin of sex in prokaryotes — cells without nuclei, such as bacteria — is at all connected with the origin of sex in eukaryotes — higher organisms, such as fungi and human beings, whose cells have nuclei and other internal membranes. Sex in these two groups of creatures seems so dissimilar that some biologists wonder if the eukaryotes didn't "reinvent the wheel" (in Halvorson's words) rather than simply elaborate on the prokaryote system.

It's also unclear why sex has survived in higher organisms. The familiar high school biology text explanation that sex brings about genetic variations that fuel the process of evolution isn't satisfying to some scientists. Norton Zinder, a molecular geneticist at Rockefeller University in New York, explains the problem this way: "How could an organism that only passed half of its genes to its offspring [through sexual reproduction] ever have competed with [an asexual] progenitor that passed all of them? It seems unlikely that the offspring produced sexually were 'fitter' than their asexually produced relatives." That question is so disturbing to biologist George C. Williams that he wrote his book *Sex and Evolution* "from a conviction that the prevalence of sexual reproduction in higher plants and animals is inconsistent with current evolutionary theory."

One idea those attending the sex symposium seemed to agree on is that no one knows why sex persists. Nonetheless, Zinder and others made a stab at explaining why it exists in the first place by summarizing some theories about how it got off the ground several billion years ago in the ancestors of modern bacteria.

To think about sex in ancient microbes, it's useful first to look at how modern ones do it. Bacterial sex isn't trivial; it's evolved into a fine-tuned system for exchanging genetic information in ways that make microbes among earth's most adaptable creatures. Resistance to certain antibiotics is one advantage sex — gene exchange — can confer on bacteria. Detoxification of heavy metals and the ability to make bacteriocidal chemicals are others.

When two bacteria conjugate (mate), their membranes fuse at some point to form a channel between them. The male bacterium (called "male" because it is the gene donor) can donate small, autonomously replicating circles of DNA called plasmids, which can carry genes for useful traits such as those just mentioned. Plasmids can also pick up genes from the larger, circular chromosome in the cell they inhabit and carry them into other bacteria during sex. Some plasmids can mobilize one strand of the double-stranded bacterial chromosome to transfer from one bacterium to another. Once inside the recipient bacterium, these transferred genes sometimes insert into the recipient bacterium's chromosome by a process called recombination. Recombination results in a chromosome with a novel collection of genes and requires a bevy of enzymes to orchestrate the breaking, insertion and ligation (gluing) of DNA strands.

Viruses also figure into the bacterial sex scene. Viral DNA in an infected cell can pick up genes from the host's chromosome. Later, when the virus leaves this host and infects another bacterium, the passenger genes go with it, a process called transduction. Bacterial genes carried into the new host by the virus may then recombine with the host's chromosome, resulting in a new gene combination. Some scientists say transduction is sex.

How could these elaborate systems have gotten off the ground? Zinder, who co-discovered transduction by viruses in 1951, offered some speculations (both his own and others') at the sex symposium about the chance migrations of DNA that might have set the process of sex in motion. Sex may have resulted, he says, from the evolution of "molecular parasites" that, in developing systems to assure their own survival, became useful to their hosts and established themselves as mediators in bacterial sex. Adds Edward Adelberg of Yale University in New Haven, Conn., "sexuality first [may have] begun in bacteria... as an accidental outcome of the selection for the spread of plasmids and viruses."

The idea is this: The earliest bacteria, living perhaps 3.5 billion years ago, had replicating chromosomes, but there weren't plasmids or viruses, and there wasn't sex. As happens today, dead bacteria liberated fragments of DNA that were taken up by living ones (a process called transformation). Some of those chromosome fragments, Zinder says, must have contained the chromosome's "origin of replication," the short stretch of DNA that instructs DNA-copying enzymes where to begin. If such a fragment left a dead bacterium and entered a live one, enzymes in the live bacterium might copy it just as they copy the intact chromosome. These fragments, "free, autonomous little replicating entities," as Adelberg describes them, would be copied and passed down through the generations.

"But this idea was picked on," says Zinder, "because... when it starts, it's not of advantage." Why would these little entities, these molecular parasites, be maintained if they accomplished nothing for their host? Two strategies may explain how they exploited their toehold even without host complicity. Those parasites that could capture proteins from the host might have been able to escape intact through the host's membrane and enter other cells. "A plasmid which can be replicated and transfer a copy of itself to another cell is at a great advantage over a plasmid that cannot do that — it will spread like an epidemic through the host population," says Adelberg. Thus while the plasmid did nothing for its host, it did develop mechanisms to guarantee its own survival at the host's expense. The earliest viruses may have been such independent, protein-coated DNAs.

The plasmid's second exploitative strategy was probably to evolve genes encoding proteins that permit conjugation, Zinder suggests, such as those for the male's sex pilus, an appendage that seems to connect mating bacteria and may act as a tube through which DNA can pass. Conjugation would be of obvious use to the plasmid, but like the early virus device, wouldn't seem to help the host at all. (Interestingly, most genes involved in conjugation occur on plasmids, and not on the chromosomes of modern bacteria.)

Left: When bacteria conjugate (mate), a bridge called the sex pilus forms and their membranes fuse, making a channel through which DNA can pass. Here, two Escherichia coli *mate.*

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The key to the plasmids' success may have been that they developed ways to give their hosts an advantage over uninfected cells—such as acquiring antibiotic resistance genes that could protect their hosts.

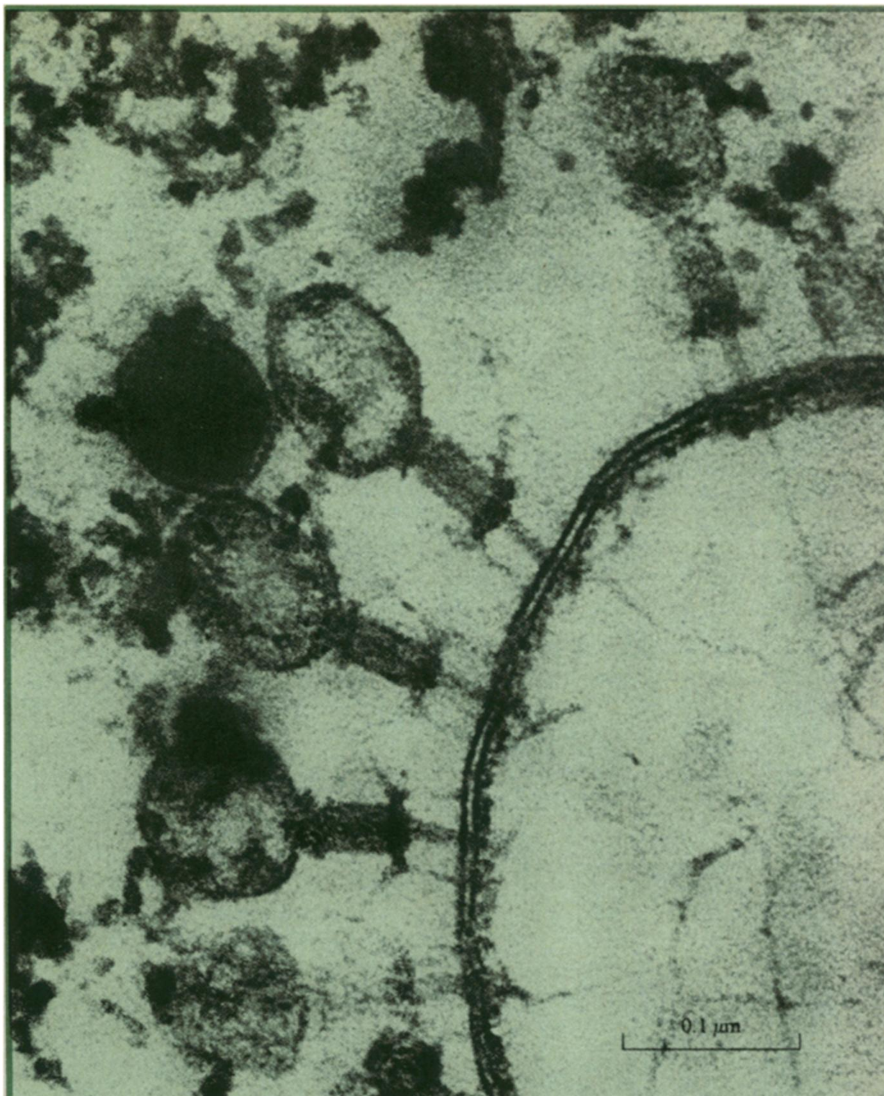
The evolutionary step that completes the transition from parasitism to sex is the debut of recombination — the exchange of fragments between DNAs. "I represent a very classical genetic point of view," Zinder says, "that sex arose and has a selective advantage in populations ... because it will allow evolution to proceed faster by the ability to shuffle genes," which yields new variations. Recombination in bacteria should do just that — bring about new combinations of genes by inserting genes from one bacterium into the chromosome of another.

The elaborate enzymatic machinery needed for recombination, some scientists believe, was in place long before bacterial sex existed. Those enzymes probably first evolved to carry out DNA repair, a function essential to organisms whose DNA must have been constantly damaged by ambient radiation present then and miscopied by primitive and faulty DNA replication mechanisms. "The enzymes which make cuts and break and rejoin [DNA] as a repair process could have led quite naturally to that being exploited for gene exchange — bacterial sexuality," Adelberg says.

How does all this bear on the problem of sex in higher organisms? Unfortunately, if there is a link between prokaryotic and eukaryotic sex, it's missing. "We have no knowledge of intermediates between these two groups," Adelberg observes. "There's no fossil evidence, nothing living today that's an intermediate," he says.

The key difference between prokaryotic and eukaryotic sex is that eukaryotes prepare special cells (such as sperm or eggs) or cell nuclei, with half the normal chromosome number. These combine during sex, and initially are made by a process called meiosis. Sex between eukaryotes brings meiotic cells or nuclei together to form a new cell or nucleus with a complete chromosome complement resulting from the combination of donor genes. Prokaryotes have nothing like meiosis.

Bell finds the notion that prokaryote sexuality gradually evolved into eukaryote sexuality "improbable." The hunt for a creature with a sexual system midway between the prokaryote and eukaryote versions may fail because, he says, "if I'm right, there won't be an intermediate process." Zinder, on the other hand, notes that if we "consider sex in bacteria to be a consequence of the ability of DNA to be replicated and recombined," then "it is possible the sex in higher forms is no more than an elaboration of such mechanisms which formed their adaptive value only after existing."



T4 viruses appear to be inserting DNA into E. coli *bacterium. Viruses carrying bacterial genes can transfer them from one bacterium to another in this way.*

L.D. Simon, T.F. Anderson/VIROLOGY 32, 279, ©1967 Academic Press, Inc.

If there was an intermediate form of sex eons ago, but no fossil evidence remains, how can biologists even approach the problem? It may be that clues—if there are any — are hidden in the DNA of modern organisms, a number of scientists suggest. The only "watertight" way to show that there is or isn't a link between prokaryote and eukaryote sex, Bell believes, "is through the sort of serendipitous observations of the sort Peter Bruns is making." Bruns, of Cornell University in Ithaca, N.Y., has recently discovered that fruit flies, yeast and the protozoan *Tetrahymena thermophila* all share part of a gene that's associated with meiosis, one step of the *Tetrahymena* sexual process (SN: 8/11/8, p. 89). This finding implies an evolutionary link between that step in these three eukaryotic organisms. Bruns *didn't* find evidence of this "meiosis-associated" gene in the prokaryote *Bacillus subtilis*. If all or part of this gene *had* turned up in the bacterium, it would have implied an evolutionary connection between prokaryotic and eukaryotic sex.

This type of experiment, where DNA sequences linked with eukaryotic sex are searched for in prokaryotes, is a "conceivable approach" for probing the evolutionary relationship between these vastly different groups of organisms, Halvorson says.

Whether this link is shown either to exist or not, the basic question — *why* is sex — will still need to be answered. But speculation about how sex first came about, and what it accomplishes for the organisms that do it, should offer insights into why these systems for recombining genes exist. As if in response to Williams' worry that sex doesn't jibe with evolutionary theory, Zinder remarked at one point, "no one would go to all the trouble to elaborate such highly sophisticated mechanisms [for gene exchange] just to have the fun of banging two bacteria together. It's got to be fundamentally important at the genetic level—or God's playing a trick on us." □

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