



Why sex  
is worth  
losing your  
head for

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For nearly a century sex has been biology's biggest mystery, says **Nick Lane**. Now it's becoming clear not only why it evolved, but when



**S**EX is the ultimate absurdity. Forget the hormonal rushes, the sweat and contorted posturing. Forget about the heartache, the flowers, the bad poems and the costly divorce, just think about the biology. It's nuts. Cloning makes far more sense.

A clone, after all, just quietly gets on with copying itself. And since every clone can produce more clones, cloning produces far more offspring. There is no need for males – a waste of space, as hard-line feminists and evolutionists agree.

What's more, each clone has a combination of genes that has already been found fit for purpose. Sex, by contrast, randomly mixes genes into new and untested amalgams. And the horrors of sex don't end there. There is the problem of finding a mate, and fighting off rivals. Not to mention the risk of picking up horrible diseases like AIDS and all sorts of selfish replicators that exploit sex to spread themselves through the genome.

All this made sex the “queen of evolutionary problems” in the 20th century, taxing some of the finest minds in biology. The issue isn't just explaining why almost all plants and animals engage in sex. It is also explaining why the life forms that ruled the planet for billions of years and remain by far the most abundant – the bacteria – manage fine without it.

That suggests that the ubiquity of sex among complex organisms has something to do with their ancient evolutionary history, not just the recent more past. Could there be some deep connection between the evolution of sex and the evolution of complex cells more than a billion years ago?

As you were probably taught at school, the seemingly obvious answer to the question, why bother with sex, is that sex generates variation, the raw material for natural selection. As environments change, sexual species can therefore evolve and adapt faster.

In reality, though, most individuals live in an environment very similar to that of preceding generations. And if some start reproducing by cloning, the clones – being equally well adapted to the environment – should rapidly drive the sexuals to extinction by dint of producing far more offspring competing for the same resources.

Sure, sex should be an advantage in the long term, over thousands and millions of years, but evolution doesn't work like that. It doesn't plan ahead. And the environment rarely changes enough in the short term, over years and decades, to favour sex.

Not so fast, argued the great evolutionary biologist Bill Hamilton. The environment that really matters is on the inside, he said. Parasites lynch us from within, and evolve so quickly that clones can't cope.

## Cloning beats sex

By throwing up new mixtures of genes each generation, sex enables at least a few individuals to escape the parasitic lynch mob. This is known as the Red Queen hypothesis because, like Alice, we have to run fast just to keep up with the ever-changing throng.

Problem solved? Unfortunately, no. From the mid-1990s onwards, it became clear that even parasites can't explain the prevalence of sex. Parasites give sex a decisive advantage only when parasite transmission is very high and their effects are dire.

Models developed by population geneticist Sally Otto of the University of British Columbia, Vancouver, Canada, suggest that under most circumstances a diverse population of clones (which accumulate differences over time as a result of mutations) outperforms sexuals. Most population geneticists agree. Parasites account for some sex over the time, but not for the ubiquity of sex in complex organisms.

Then there are the bacteria: if sex is such a big thing, then why don't they bother with it? Yes, bacteria do swap some bits of DNA, but “bacterial sex” doesn't begin to compare with the no-holds-barred approach of complex cells, the eukaryotes.

To understand why eukaryotes resorted to full-on sex, it would help to know when it happened. There are plenty of eukaryotes that multiply by cloning rather than sex, but almost all turned celibate only very recently.

There was thought to be one exception, however, in the form of *Giardia*, a single-celled parasite with a nasty effect on people. *Giardia* is very distantly related to animals and fungi, and some think it resembles the very first eukaryotes. Having never been caught in flagrante, it was taken to be asexual: a living fossil from the time before sex.

In the past years, this idea has been overturned. There is now unequivocal evidence of sexual recombination in *Giardia* – which suggests sex got off to a very early

Male praying mantises sometimes pay the ultimate price for sex

start. “Sex most definitely evolved in the last common ancestor of eukaryotes,” says phylogeneticist Joel Dacks at the University of Alberta in Edmonton, Canada. “That much one can say with extreme confidence.”

There’s no shortage of clever ideas about what came between bacteria and full-blown eukaryotic sex. But sex would not have evolved unless each intermediate step offered an advantage. And if each step is an advantage, then why don’t we see any bacteria indulging? They just don’t look interested.

“All these theories of sex seem to be missing something,” says biochemist Bill Martin at the University of Düsseldorf, Germany. And he thinks he knows what it is: mitochondria, one of the defining characteristics of eukaryotes.

Mitochondria are the power-houses of eukaryotic cells, generating almost all energy we use. A few eukaryotes, though, like *Giardia*, appeared to have none and this was long taken to be another primitive trait.

But a few years ago, *Giardia* turned out to have mitochondria after all. The same story has been repeated for a host of primitive eukaryotes once believed to be mitochondria-free, all of which in fact have structures derived from mitochondria, or at least a few genes that betray mitochondrial ancestry.

Last year the final bastion fell. An obscure single-celled flagellate with a  like a character from an *Asterix* book  *astix* – also turned out to have mitochondrial genes. As phylogeneticist Andrew Roger at Dalhousie University in Halifax, Canada, puts it: “We can now say definitively that all known living eukaryotic lineages descend from a common ancestor that  mitochondria.”

So the last  mon ancestor of all eukaryotes had both sex and mitochondria. We also know that the acquisition of mitochondria had profound effects on the host genome. “The ancestors of the mitochondria were once free-living bacteria,” Martin says. “When they got inside cells, if any died they would have bombarded the host cell chromosome with bacterial DNA.”

Back then, the mitochondria didn’t have stunted genomes as they do today, but normal bacterial chromosomes with several thousand genes. Martin has shown that, of the



It’s absurd: male barnacles have to go to great lengths to have sex, flatworms engage in “penis fencing” and blue sea slugs risk having their penises eaten

eukaryotic genes whose ancestry can be traced, 75 per cent or more came from bacteria rather than the host cell.

This bombardment has dwindled to a trickle today, but occasionally still makes itself felt by disrupting genes in the nucleus, causing genetic diseases. In the human lineage in just the past 50 million years or so, there have been hundreds of separate, independent transfers of mitochondrial genes to the nucleus.

### Parasitic genes

What’s more, in the early days of the eukaryotic cell, the mitochondria didn’t bombard their host with genes alone. Eukaryotes are odd in that their genes are in pieces, rather than continuous. A typical gene has a mixture of coding regions, which stipulate the sequence of proteins, and non-coding regions known as introns. Today, introns are commonly found in the same places in the same genes, even in eukaryotes as distantly related as algae and humans.

In other words, a good many introns, too, must have been present in the last common ancestor of all living eukaryotes. Introns retain

certain similarities with each other but also, intriguingly, with a type of parasitic jumping gene. Strikingly, as geneticist Steve Zimmerly at the University of Calgary in Alberta, Canada, and others have shown, these jumping genes are found in the bacterial ancestors of mitochondria, as well as in other bacteria.

So introns probably came from bacteria via the mitochondria. Even doubters give credence to the idea. Dacks, for example, hedges his bets. “I am not entirely convinced that introns necessarily came from mitochondria  even that bacteria pass around their genes  today, although they certainly could have.”

What if they did? The jumping introns would have proliferated for a while, wreaking havoc, but ultimately decaying into the inert, fixed introns we see today, as they accumulated mutations. “It looks as if there was a turbulent phase of genome evolution in the wake of mitochondrial origin,” says Martin. “Introns invaded the host cell chromosomes and ran amok. They spread into hundreds, perhaps thousands, of positions that have been conserved to the present.”

Much of this picture has been obscured by

“Is there some deep connection between the evolution of sex and the evolution of complex cells a billion or so years ago”

the swirling controversies that surround the origin of the eukaryotic cell. No topic is more bitterly contested among biologists – except sex, of course. Nonetheless, a coherent picture is slowly emerging of the early eukaryotic cell. It had mitochondria. It had sex. And it suffered an extraordinary bombardment of DNA from its troublesome guests. And that makes a lot of sense in the light of new work on why we all have sex anyway.

As the Red Queen fell out of favour, researchers began to cast around for other possibilities. Unexpectedly, the most promising lead came from dusty old models of population genetics, raised from their deathly hallows in undergraduate textbooks.

The old models fell from fashion because they never seemed to show any advantage to sex when compared with cloning, but that was not the only way in which they failed to match the real world. For reasons of mathematical purity, they all assumed an infinite population size. In an infinite population, anything that can happen will happen. But real-life populations are never infinite, and even vast populations are divided into partially isolated groups.

When Otto teamed up with Nick Barton, now at the Institute of Science and Technology in Klosterneuberg, Austria, and considered finite populations, they found, as you would expect, that there are some circumstances when sex helps individuals.

Imagine a new mutation arising in a gene. In clones, the genes are effectively tied together like beads on a string. There is no reshuffling as there is during sexual reproduction. This means the fate of each gene in clonal species depends on the entire ensemble – the whole

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genome – rather than on the merits of individual genes as in sexuals. Most mutations that occur are detrimental, but not so bad that they sink an otherwise good genome there and then. However, they gradually sap genetic vigour, imperceptibly undermining fitness.

When set against this second-rate background, beneficial mutations can wreak havoc. One of two things can happen. Either the spread of the mutation is retarded by the second-rate company it keeps, or it isn't. In the first case, strong positive selection for the gene is dissipated by weak selection against hundreds of others. Such “selective interference” means that most beneficial mutations are simply lost again.

But if the new mutation does spread throughout a population, the scenario is even worse. Because the gene can't be isolated from any others, it can only spread at the expense of all other genomes in the population. If 500 variants exist in a population, 499 of them will disappear. So selective interference can portend a disastrous loss of genetic diversity. Much the same thing has happened to the notoriously degenerate male Y chromosome, now a stump of its former self.

Otto and Barton modelled the impact of a gene that promotes sex in individuals that can have it both ways, reproducing either clonally or sexually. They found that the sex gene

frequently spreads through the population, turning more and more individuals to sex.

“Sex improves the efficiency of selection, allowing good genes to recombine away from the junk residing in their genetic backgrounds,” says Otto. “As the good genes spread, they then carry along the sex genes, beating out the genes for cloning, and often overcoming the costs of sex.”

Exactly how often these circumstances apply is uncertain. “It's still not clear that selective interference gives a strong enough individual advantage to maintain high rates of sex and recombination,” says Barton. “There needs to be a lot of selection, which is plausible but not definitely established as yet.”

One possibility that certainly ropes in lots of selection is the battle against parasites, so selective interference embraces the Red Queen hypothesis rather pleasingly. Even more pleasing is its relevance to early eukaryotic cells. According to Otto, sex is most advantageous when there's a lot of variation in a population, when mutation rates are high and selection pressures are great.

That combination is a killer for clones. They are particularly vulnerable to high mutation rates which undermine genetic vigour. Heavy selection puts a premium on the genes that work, and means beneficial mutations are more likely to be selected at the expense of diversity. And diverse populations have the most to lose whenever there's a selective sweep for a particular gene in this way.

The first eukaryotic cells faced all three problems in spades. As a result of the early gene bombardment from mitochondria, the mutation rate surely shot through the roof. Selection pressures must have been heavy, too, with parasitic introns proliferating throughout the genome. And with such rapid genome evolution, the population could be nothing but diverse.

Sex was the only answer. Total sex. Recombination of genes across all chromosomes. The big question now is not so much why sex evolved – but how? ■



A beautiful couple but highly vulnerable while mating

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