Evolution's Greatest Mistakes

As miraculous as living things might seem at first glance, a closer look reveals that evolution's blind blunderings often fall well short of perfection. Claire Ainsworth and Michael Le Page peek under the hood of life to assess the parts and processes where things seem to have gone spectacularly wrong.

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Bad ventilation

THE ascent of Mount Everest's 8848 metres without bottled oxygen in 1978 suggests that human lungs are pretty impressive organs. But that achievement pales in comparison with the feat of the griffon vulture that set the record for the highest recorded bird flight in 1975 when it was sucked into the engine of a plane flying at 11,264 metres.

Birds can fly so high partly because of the way their lungs work. Air flows through bird lungs in one direction only, pumped through by interlinked air sacs on either side. This gives them numerous advantages over lungs like our own. In mammals' two-way lungs, not as much fresh air reaches the deepest parts of the lungs, and incoming air is diluted by the oxygen-poor air that remains after we breathe out. Our air passages end in air sacs, or alveoli, which unlike the tubes of bird lungs have to be relatively large to ensure adequate air flow. This means less surface area for gas exchange. Large alveoli also need thick walls for support, but these reduce gas exchange. As a result, humans have delicate alveolar walls that are prone to become damaged, leading to a condition called emphysema.

Verdict: Bird lungs are far superior to ours and, the more they are studied, the longer the list of their advantages becomes. We mammals might have been even more successful had we inherited or evolved similar lungs.

Mutant maker

Our DNA is our most precious possession. So you would expect the polymerase enzymes that copy it when cells divide to be painstakingly accurate. Some are, but surprisingly, most are not.

Of our 14 known DNA polymerases, just four are highly accurate, making about one error for every million bases of DNA. The rest are sloppier, with some erring as often as 1 base per 100 copied. The typos in this paragraph show just what this could do to our genome.

So why do we have them? Accurate polymerases fit the DNA bases they are copying very precisely. But when bases become damaged they change shape, and if the damage isn't repaired before DNA is copied, the polymerase can no longer recognise them. This halts replication, and risks cell death. "It's a pretty dire situation if you can't get past damage in any way," says Alan Lehmann of the Centre for Genome Damage and Stability at the University of Sussex in the UK.

Sloppy polymerases save the day by being able to read through damaged bases, but they make lots of mistakes even where DNA is undamaged. So a higher mutation rate is thus the price we pay for avoiding a high rate of cell death during division. It can sometimes be a benefit: it's partly

how the immune system generates novel antibodies, while certain bacteria switch to using error-prone polymerases in times of stress, perhaps to encourage mutations that might help a few members of a population to survive. The vast majority of mutations, however, either have no effect or are harmful. With this in mind, there are efforts under way to see if it is possible to deactivate the error-prone polymerases in our cells to help prevent cancer (Cancer Letters, vol 241, p 13).

Verdict: A blunder from an individual point of view, increasing the risk of cancer and of our children having genetic diseases. A triumph if you don't care if many offspring have harmful mutations so long as a few emerge slightly fitter.

All mixed up

Imagine that you are creating the blueprint for humans. Would you design it in a way that means big chunks are prone to being lost, duplicated or ending up back-to-front? This is exactly what happens to our genome as it is passed down the generations, causing genetic disorders or making us more susceptible to one disease or another. On the face of it, this seems like a pretty serious flaw.

One of the main ways in which these mix-ups occur is when things go wrong with a process called recombination. During the production of eggs and sperm, pairs of chromosomes line up and swap matching sections. This helps to eliminate harmful mutations because it leaves some offspring with fewer of them, while others--destined for evolutionary oblivion--end up with more. The trouble is, all the duplicated and repetitive sequences in our DNA can cause chromosomes to line up wrongly, resulting in one getting an extra chunk of DNA and the other losing that chunk. This can lead to all sorts of problems, such as leaving us with too few or too many copies of some genes.

However, the consequences are not always bad. Extra copies of genes can provide the raw material for evolution. While one copy holds the fort and performs its normal functions, the extra copy is free to mutate and take on new functions. Primates have an unusually large number of duplications compared with other mammals -with humans and chimpanzees having the most--and many of these duplicated genes appear to have evolved rapidly (Nature Reviews Genetics, vol 7, p 552).

Verdict: If you want to guarantee that children are always as genetically healthy as their parents, duplications are a huge mistake. As a means of generating the diversity on which evolution depends, however, it is brilliant.

Burning blueprint

Inside every one of our cells are dozens of little sacs called mitochondria, in which sugars are "burned" to produce the energy that powers the cells. The process also produces highly damaging molecules called free radicals, so the interior of a mitochondrion is hardly the safest place for vital DNA--and yet it is home to the genes for 13 crucial mitochondrial proteins.

It's a crazy design: like keeping the repair manual for a steam engine by the furnace, where it inevitably becomes charred and unreadable. The slow loss of function as mutations accumulate in mitochondrial DNA may be the main cause of ageing and, some believe, of many age-related diseases, from diabetes to Alzheimer's.

The DNA is there because of our evolutionary history. Mitochondria are the remnants of a once independent bacterium that formed a symbiotic alliance with our cells around 2 billion years ago. Over time, many of the bacterium's original genes have been lost or jumped to the cell nucleus, but human mitochondria still retain 13 genes.

Anti-ageing research is already exploring ways of moving the remaining genes to the safety of the

nucleus. It will not be easy. The 13 genes cannot simply be moved to the nuclear genome, because then the 13 proteins will be made outside the mitochondria where they are needed. A solution might be to get the mRNA recipes for proteins delivered to the mitochondria, so the genes reside in the nucleus but the proteins are still made inside the mitochondria.

Verdict: If you wanted to build humans to last, mitochondria are the last place you'd put DNA.

Ineffective enzyme

It's the planet's most plentiful protein because it is so useless at what it does.

Nearly all life on Earth depends upon the enzyme called RuBisCo. It turns carbon dioxide from the air into the chains of carbon that are the building blocks of all life. But as well as being one of the world's most sluggish enzymes, it is apparently too stupid to tell the difference between carbon dioxide and oxygen. If this isn't one of evolution's greatest mistakes, then what is?

RuBisCo "fixes" C[O.sub.2] by attaching it to a sugar called ribulose bisphosphate. But it is easily confused, and sometimes picks up an oxygen molecule and attaches that instead, causing a series of reactions that result in the loss of both carbon and energy. Worse still, RuBisCo enzymes catalyse the reaction of only about three molecules per second. Other common enzymes catalyse tens of thousands.

These shortcomings make photosynthesis far less efficient than it might be, though some plants have come up with ways to reduce the chances of RuBisCo adding oxygen. These tricks have evolved independently on many different occasions.

RuBisCo's failings have been attributed to the fact that when it evolved, levels of oxygen were far lower than they are now, so mistaking oxygen for C[O.sub.2] would have mattered far less. Research published last year, however, suggests that far from being a dunce, RuBisCo has a streak of genius. [O.sub.2] and C[O.sub.2] have some similar physical features that make it hard for any enzyme to discriminate between them. RuBisCo maximises the chance that a C[O.sub.2] molecule rather than a molecule of the much more abundant oxygen reacts with the substrate, by grabbing the biphosphate molecule and twisting it (Proceedings of the National Academy of Sciences, vol 103, p 7246). The trade-off is that this twisting makes it hard for RuBisCo to release the end product-hence its slowness. "Arguably, RuBisCo is not inefficient, it's as good as it could get," says Howard Griffiths, a plant scientist at the University of Cambridge.

Verdict: The tricks plants have evolved to try to compensate for RuBisCo's inefficiency show what a limiting factor it is, but it remains to be seen whether the protein itself can be improved. Lots of genetic engineers are trying, though.

Not made to last

How often have you heard people complain that the gadgets and appliances we buy aren't designed to last very long? Well neither, it seems, are we. From our twenties onwards, our bodies start declining. But why?

The discovery in recent decades of a cellular signalling system that controls the rate of ageing in worms and possibly other animals seemed to support a long-abandoned idea: ageing evolved to get rid of Old animals to make room for the next generation. Most biologists, however, see ageing merely as an unfortunate side effect of how natural selection works.

It is clear that there will be less selection for genes that benefit creatures late in life, because not many individuals survive for that long. What's more, genes that have detrimental effects in old age can still be favoured if they have a beneficial effect in youth. The result is that organisms have

evolved to spend more energy on growth and reproduction than on repairing the damage that underlies ageing. It's equivalent to the idea that while manufacturers do not necessarily build-in obsolescence, they don't waste money building products to last ether.

It is now thought the signalling system merely controls the trade-off between repair and reproduction: mutant worms that live longer produce fewer offspring. This trade-off, however, results in very different lifespans in different species. Animals like mice, which run a high risk of being killed by predators, reproduce as quickly as possible, age fast and die young. Other animals, including many reptiles and fish, age extremely slowly. Some produce ever more offspring as they get older, while their mortality rate actually drops--a phenomenon called negative senescence.

In fact, ageing seems to be particularly intense in mammals. Some speculate that this is because during the reign of dinosaurs, the breed-fast, die-young strategy of early mammals led to the loss of some of the abilities that help stave off decline. For instance we cannot regrow teeth indefinitely, like most reptiles, or regenerate damaged hair cells in the ear, as birds can.

During recent human evolution, by contrast, there may have been strong selection for longer lifespans. The "grandmother hypothesis" proposes that individuals with long-lived grandparents to support them and pass down knowledge have more children who survive (New Scientist, 10 July 2004, p 14).

Verdict: Ageing may not have evolved to kill off old animals, but nor can it really be seen as a mistake from an evolutionary standpoint. This is no comfort when you have to look in the mirror each morning, of course.

Blind spot

Critics of Darwin like to ask how something so complex and as apparently perfect as the eye could possibly have evolved gradually, and the man himself devoted several pages of later editions of On the Origin of Species to refuting their arguments. Perhaps he need not have worried. Eyes are complex, but their structure reveals the unplanned nature of evolution.

The most famous flaw is found in vertebrate eyes. Their light-sensing structure, the retina, is wired up back-to-front, with the light-sensitive cells behind the nerves and blood vessels that support it. Not only does light have to pass through this layer first, obscuring the image, but the nerves and blood vessels have to dive through the retina, creating a blind spot in each eye.

In cephalopods, such as squid and octopuses, the eyes are built the "right" way around, so why not in vertebrates too? The answer is that when eyes first evolved in the ancestors of modern vertebrates, the retina arose from an in folding of the developing brain, and the cells that could form light receptors happened to end up on the inside of this fold. "Once you have done something like this it's very hard to change," says Michael Land, a specialist in eye physiology at the University of Sussex, UK.

As always, evolution has made the best of a bad job. Vertebrates have a number of adaptations to compensate for the ancestral blunder. One is the fovea in primates, a patch of retina where the nerves and blood vessels are swept aside and which is jam-packed with light receptors. This has to be kept small to ensure it gets enough oxygen, giving us fuzzy peripheral vision but sharp central vision. "The cephalopod eye is not as good as ours," says Land. But again, birds have outdone us, eliminating most blood vessels from the retina thanks to a structure called the pecten. This means the animal with the sharpest eyesight of all is the hawk.

Verdict: Back-to-front retinas are a mistake whichever way you look at them.

The list goes on ...

THE FEMALE PELVIS Human adaptation to walking upright has made giving birth more dangerous for women than for any other primate

LINEAR CHROMOSOMES The ends of linear chromosomes erode as cells divide, something that cannot happen with circular chromosomes

EXTERNAL TESTICLES In harm's way VAGINA AND URETHRA NEAR ANUS Leaves women prone to genital and urinary infections

WISDOM TEETH Many of us have jaws that are too small for these third molars

MUTANT GLO GENE Like most primates, humans cannot make vitamin C, rendering us vulnerable to scurvy unless we get plenty in our diet

THE APPENDIX No known function but if it gets infected it can kill you

WINDPIPE NEXT TO THE GULLET Means choking is not uncommon

ULNAR NERVE Runs behind the elbow, where it is unprotected (think funny bone), instead of in front of it

VULNERABLE BRAIN CELLS A few minutes of oxygen deprivation causes permanent brain damage in humans, yet an epaulette shark can survive for over an hour without oxygen

PARASITIC DNA Our genome is littered with "jumping genes" that can cause genetic diseases

ODONTOID PROCESS This extension of the last neck vertebra can easily fracture and damage the brainstem

FEET After coming down from the trees, we ended up walking on the "wrists" of our lower limbs, leading to all sorts of structural weaknesses

THE Y CHROMOSOME It is gathering mutations because it can't swap DNA with the X chromosome

VULNERABLE HEARTS A little heart damage triggers a disastrous cascade of events that causes further damage

HAIRY BOTTOMS Who needs them?