Going by the book

A group of Chinese scientists has discovered the main biochemical pathways in drug addiction—and without having to do a single experiment

MODERN biology has a lot of “omes”. The genome—all the genes that go to make up an organism—is a familiar idea. The proteome—all the different proteins—is becoming so. But there are also the transcriptome (RNA), the glycome (sugars), the lipidome (fats) and the metabolome (all the miscellaneous odds and ends not covered by the others). And then there is the bibliome—all the mentions in research papers of known biomolecules. There are now so many of these papers, and the databases linking them are so good, that it is possible to use scientific methods to investigate the bibliome in its own right, just as any of the other, wetter “omes” may be investigated. Which is exactly what a group of researchers from Peking University, led by Wei Liping, have done to get at the biochemical heart of drug addiction.

Dr Wei and her colleagues wanted to answer three questions. First, what are the genes and biochemical pathways in addiction? Second, does addiction to different substances involve the same core biochemical mechanisms? Third, does anything in those mechanisms explain why addiction is so hard to shake off?

Many people, of course, have asked these questions before, and partial answers have emerged. What Dr Wei hoped to do was to take these fragmentary answers and patch them together to make something approaching the whole truth. And, in a paper just published in the Public Library of Science, she seems to have managed just that.

It looks good on paper

Dr Wei's group looked at more than 1,000 studies of the biochemistry and genetics of drug addiction. They were interested in the four sorts of drug reckoned most addictive: alcohol, cocaine, nicotine and opiates (heroin, methadone and so on). About 1,500 genes were implicated by one or more of the studies, but in only 396 cases was that implication backed by at least two independent lines of evidence. It was on these confirmed cases that Dr Wei concentrated her fire.

Biochemistry is about pathways and networks of pathways. A pathway is a series of enzymes (each of which is encoded in a gene) that perform a task in sequence, like workers on an assembly line. Dr Wei therefore ran her 396 genes through a database of all known pathways to see which involved several enzymes encoded by those genes.

She found 18 that were involved in addiction to at least one type of drug. Five, however, were common to all four types, and these five pathways therefore look as though they are at the core of the process of addiction. Three of the five were already under suspicion. Dr Wei's result provided strong statistical evidence to back up what had just been hunches. Two other pathways, however, had not previously been considered as being involved in addiction.

The existence of these five central pathways helps explain a lot about addiction. First, it gives weight to the belief that some people are more susceptible to all sorts of addiction than others are. That contrasts with the thought that addictions are substance-by-substance phenomena, though the two ideas are not mutually exclusive since changes in the 13 substance-specific pathways clearly also result in addiction.

Second, the particular pathways involved help to explain why addiction is so hard to reverse. Several of them take part in strengthening the connections between nerve cells, which is the underlying basis of learning. Unlearning something by breaking these connections is hard.

Third, Dr Wei was able to link the five central pathways together into a network, and show that this network has four positive-feedback loops in it. Work on other species in other contexts suggests that the mixture of loops she found was one that often results in rapid and irreversible biological processes—which is exactly what is seen in addiction.

None of this, of course, directly helps the addict, though it reinforces the message that it is better not to start taking these drugs in the first place. But working out how the addiction machine operates may point those looking for therapies in the right direction. And this study also shows that the old cry “more research is necessary” is not always true. Sometimes all you need to do is look at what you already have in a different way.

Astronomy

Where the shadows lie

A rare double ring illuminates the dark matter of the early universe

EINSTEIN himself reckoned that, although they must exist, they would be impossible to spot. Yet the great man was mistaken. Astronomers have seen “Einstein rings”, formed when light from a distant galaxy is bent by the presence of a nearer massive object, usually another galaxy, that lies directly in its path to Earth. Now they have discovered something even rarer: a double Einstein ring formed by two such intervening objects. The resulting image casts light, as it were, on the question of how “dark matter” was distributed in the early universe. The exact nature of this type of matter is unknown, but it seems to make up a quarter of the contents of the universe. The latest result suggests it is more widely spread than the visible matter that is clumped together to form galaxies, with implications for how those galaxies formed.

In his general theory of relativity, Einstein proposed that space and time are distorted by the presence of massive objects. Light, which normally and famously travels in straight lines, thus appears to follow a curved path when it passes near a heavy thing such as a galaxy. This effect is known as gravitational lensing, and the heavy object that causes it as a gravitational lens. If source, lens and observer are exactly aligned, the result is a luminous ring that appears to surround the lens.

Einstein despaired of ever finding a source and a lens precisely aligned with an observer on Earth and thought that, even if they did exist, telescopes would never be powerful enough to see the resulting ring. Nevertheless, the first such ring was observed in 1987. Now, a group of astronomers led by Tommaso Treu of the University of California, Santa Barbara, have seen two concentric rings.

Dr Treu and his colleagues first identified the most promising places to look for Einstein rings—parts of the sky where two or more clusters of galaxies can be seen one behind the other. They then searched these areas for galaxies that appeared to have two different spectrums, suggesting that what looked like a single object actually had another one sitting behind it. Having found a promising one in the constellation Leo, they turned the Hubble space telescope on it.

As they hoped, the image of the first galaxy, which lies about 2 billion light years away, was surrounded by a ring of light from the second one, which lies 6 billion light years away. To their surprise, however, they spotted a second ring, formed by light from a third galaxy 11 billion light years away.

This discovery, which Dr Treu presented to a meeting of the American Astronomical Society held in Austin, Texas, on January 10th, represents more than an unusual and pretty stamp for the astronomers' collection. The diameter of the rings depends not only on the distance to the galaxies that caused them but also on the masses of those galaxies. The more massive they are, the more the light is bent.

Dr Treu and his colleagues compared the mass the rings suggested was present with what they could actually see. They were thus able to study the distribution of dark matter. Earlier work had suggested that dark matter seeded the early universe, acting as nuclei around which visible matter clumped into galaxies. But Dr Treu found that the dark matter extended further than the visible matter, forming a halo around it. If that turns out to be true elsewhere, it makes galaxy formation harder to explain.

Having a double ring could also help explain dark energy, a mysterious force that is thought to pervade the universe, causing its expansion to accelerate. The outer ring is created by a galaxy that is some 5 billion years older than the inner one. If further double rings are discovered, and Dr Treu is optimistic that they will be, it should be possible to tell whether the amount of dark energy around has remained constant, or has changed over the course of time.

Einstein proposed the existence of something he called the cosmological constant, to fulfil the role now assigned to dark energy. As its name suggests, it was not expected to vary as the universe aged. But if it did, it would not be the first time that Einstein erred.

Co-operative breeding

The perils of togetherness

Family support is rare. That might be because its spreads diseases

ANYONE with children knows the benefits of sympathetic grandparents, aunts and cousins. From babysitting to emotional support when the kids set fire to the carpet, having family around is invaluable. Such co-operative breeding is common in birds as well as humans. It usually involves young adults delaying their own reproduction for a year or two to help their parents raise the helpers' younger siblings. In some species, grandparents also assist their offspring when their own breeding time is over. The nest is thus better defended, more food is gathered and the nestlings are better educated in the ways and wiles of their species. In fact, the benefits of co-operative breeding are so great that many researchers wonder why it is not more common.

A study just published in Behavioral Ecology and Sociobiology, by Claire Spottiswoode of Cambridge University, suggests the reason is that other organisms also benefit. Pathogens and parasites are able to take advantage of avian co-operation, imposing a price that is not always worth paying.

Dr Spottiswoode spent three years capturing and testing wild birds of many different species in South Africa and Malawi. She injected them with phytohaemagglutinin (PHA), a substance that induces an immune reaction. In particular, when PHA is inserted beneath the thin skin of a bird's wing, it causes a swelling a bit like a mosquito bite.

Dr Spottiswoode reasoned that the amount of swelling from a dose of PHA should reveal the activity of a bird's immune system. Individuals from species at risk of disease will respond swiftly and strongly. That response, however, comes at a price. The larger the swelling, the greater the immune stress on the bird and the more energy its immune system is consuming to fight off the effects of pathogens.

Measuring the swelling with pressure-sensitive callipers allowed Dr Spottiswoode to determine the strength of each bird's immune system. She found, as she had hypothesised, that co-operatively breeding birds routinely have stronger immune responses to PHA than closely related species that do not breed co-operatively. This suggests there is something about co-operative breeding that forces the immune system to work harder than it otherwise would. She argues that this something is the increased transmission of pathogens within family groups. Not only do co-operative breeders interact closely with many more individuals than non-co-operative birds, but these individuals are also usually close relatives. That means they share a genetic susceptibility to the same strains of disease.

Though Dr Spottiswoode's research focused on birds, the principle is likely to apply to other social species, people included. Indeed, the evidence is that many human infections — malaria, measles and influenza, for example — stem from the crowded living that came about when people settled down to farm. Moreover, studies of modern human evolution suggest that several recent genetic changes are responses to such diseases.

People and birds are similar in many ways. A lot of bird species form more-or-less exclusive, more-or-less long-term pair bonds in which both parents raise the offspring. That is a pattern rarely found in mammals. Co-operative breeding in both groups is, in some ways, an extension of this pattern. The benefits are the same. So are the costs that have to be overcome.

How to find a mate

The scent of a woman (and a man)

A new kind of dating agency relies on matching people by their body odour

ONE of life's little mysteries is why particular people fancy each other—or, rather, why they do not when on paper they ought to. One answer is that human consciousness, and thus human thought, is dominated by vision. Beauty is said to be in the eye of the beholder, regardless of the other senses. However, as the multi-billion-dollar perfume industry attests, beauty is in the nose of the beholder, too.

ScientificMatch.com, a Boston-based internet-dating site launched in December, was created to turn this insight into money. Its founder, an engineer (and self-confessed serial dater) called Eric Holzle is drawing on an observation made over a decade ago by Claus Wedekind, a researcher at the University of Bern, in Switzerland.

In his original study Dr Wedekind recruited female volunteers to sniff men's three-day-old T-shirts and rate them for attractiveness. He then analysed the men's and women's DNA, looking in particular at the genes that build a part of the immune system known as the major histocompatability complex (MHC). Dr Wedekind knew, from studies on mice, that besides fending off infection, the MHC has a role in sexual attractiveness. It changes odours in ways the mice can detect (with mice, the odours are in the urine), and that detection is translated into preferences for particular mates. What is true for mice is often true for men, so he had a punt on the idea that the MHC might affect the smell of human sweat, as well.

It did. Women preferred T-shirts from men whose MHC was most different from their own. What was more, women with similar MHCs favoured the use of similar commercial perfumes. This suggests that the role of such perfumes may be to flag up the underlying body scent rather than mask it, as a more traditional view of the aesthetics of body odour might suggest.

That makes evolutionary sense. The children of couples with a wide range of MHC genes, and thus of immune responses, will be better protected from disease. As the previous article suggests, that could be particularly important in a collaborative, group-living species such as humanity. Moreover, comparing MHCs could be a proxy for comparing kinship, and thus help to prevent inbreeding.

The promise of an MHC-based match is not only that your partner's old laundry will smell better but all sorts of other benefits too. The biological compatibility created by complementary immune systems apparently promises better orgasms, a lower likelihood of cuckoldry, more happiness and so on. Nor are heterosexuals the only ones who can benefit. Gay men and women respond as strongly to MHC-derived smells as straight people do—though, as might be expected, their response is to the smell of people of the same sex, rather than the opposite one.

Indeed, the only people for whom MHC matching might not be expected to work are women on the Pill. Chemical contraception, which mimics pregnancy, messes up the system because of an intriguing twist. When women are pregnant, they prefer the smell of MHCs that are similar to their own. This means they are happier in the company of their relatives, which may, as the previous article also suggests, bring evolutionary benefits of its own.

ScientificMatch.com does not rely entirely on the MHC. Besides sending off a swab taken from the inside of their cheek and a cheque for $1,995, hopeful singles have to answer the usual questionnaire about income, background and details such as whether they would prefer a skiing holiday to one spent sketching. They are not, however, asked whether they wear their T-shirts for three days on the trot.