

# A miner's canary for modern civilization?

*When the buzz dies down it's time to worry ...*

More than 70 percent of the bees that used to pollinate crops along the east coast of the United States have disappeared since late last year, while the west coast has lost up to 60 percent of its bees. And the news from Europe is no better. About 30 percent of Europe's 13.6 million hives died last year, with losses that reached 80 percent in south-west Germany and 50 percent in Slovenia. Severe losses have also been reported from Canada, Britain, France, and Italy.

According to Gilles Ratia, president of Apimondia, the international beekeeping body: "With this level of mortality, European beekeepers can only survive another 8 to 10 years." It would seem that the sperm courier for almost 80% of commercial crop species, the European honeybee, is in a decline that promises to be terminal, perhaps within a decade or two. Meanwhile, the bee crisis appears to be spreading into Asia with reports of unspecified losses in India and China.

Mystery surrounds this wholesale disappearance of bees. Blame has been laid on pesticides, herbicides, parasites and industrial pollutants; on intensive monocultural farming, on genetically modified crops and even on radiation interference by mobile phones. However, scientists have found evidence of almost all known bee viruses in the few bees that have been left in the affected hives. Some had five or six infections at the same time and were infested with fungi—a sure sign, according to some experts, that the insects' immune system had been compromised to the point of collapse.

Curiously, the one country with no sign of this alarming phenomenon—commonly known as Colony Collapse Disorder (CCD)—is Australia. Australia has herbicides, pesticides, bee parasites, industrial pollutants and mobile phones a-plenty. And it also has the distinction of being almost entirely free of genetically modified crops. Currently however, there is no direct evidence that the artificially modified DNA of GM plants has had any detectable impact on bee genes, and so coincidence is the only linking factor between CCD and GM crops.

Despite their chain-like molecular structure and apparent fragility, genes are very durable. In fact, certain genes are known to have out-lived the rise and fall of mountains and the drift of continents from pole to pole. And yet species occasionally alter their structure and behaviour within relatively short periods of time, with no discernible change to their genetic code. This enigma has now been resolved by the discovery that all DNA is subject to an overriding molecular code which often alters in response to changes in the environment (see DNA diagram, p.4). Unfortunately, the existence of this external, or epi-genetic code is not yet widely accepted and there are even biologists who are unfamiliar with this explosive new field of genetic research.

The epigenetic code consists of a pattern of external hydrocarbon switches, or methyl groups, that are attached at various points to the side rails of DNA and determine whether or not particular genes or groups of genes are available for transcription. Only during the past decade or so it has been realised that the appropriate attachment of these carbon tags, known as methyl groups, is crucial to the proper functioning of all DNA. The methylation pattern even helps to determine gender by orchestrating sexual form and function in all sexually-reproducing species.

The particular pattern of methylation that an individual organism inherits from one or other of its parents is known as imprinting. Sexual imprinting was first noted in 1910 in certain types of ornamental corn. Its kernels are dark purple if a 'Red' gene is inherited from the egg (female), but they are blotchy lavender if the same gene is transmitted via sperm. Today we know that in corn pollen, which contains the plant's sperm cells, the Red gene is methylated. During kernel development the methyl tags are successively removed, thereby permitting full genetic expression to gradually appear as it matures. It is now known for example, that a number of genetic ailments in humans are due to faulty methylation, and dysfunctions such as Fragile X Syndrome are caused by flaws in the methylation pattern that have been passed on from one of the parents.

The methylation of a genome determines the pattern of folding that allows the chromatin strands of DNA to be squeezed into the nuclei of plant and animal cells. If all of the DNA present in each of our cells was stretched out in a line, it would be almost 3 meters (10 feet) long, so DNA must be tightly folded and compressed to fit inside the cell nucleus. Exactly how this is done plays a crucial role in determining which genes can be read and expressed as protein. In general, genes in tightly compressed DNA are poorly expressed,

while genes in more loosely packed DNA are more available to the machinery involved in transcribing the gene into messenger RNA, and ultimately into protein.

Appropriate DNA methylation is therefore essential for the normal development and functioning of all organisms and mice that have been genetically engineered so that they can't make the enzymes that attach methyl tags to DNA invariably die before birth. Of critical importance, however, is the fact that the methylation pattern is also vulnerable to interference by environmental factors during the life of the individual plant or animal. So it seems that the French biologist Jean Baptiste de Lamarck was right after all: the environment does indeed interact with plants and animals in heritable fashion—although not in the simplistic way that Lamarck proposed.

In the words of Professor Ryszard Maleszka, Senior fellow at the ANU School of Biological Sciences, "Genes and environments cannot be separated. For billions of years these two entities co-evolved to generate living forms. Any disturbance in an organism's environment must be sensed by its genome," he said, "and epigenetic mechanisms are responsible for maintaining the proper responses."

Maleszka maintains that this ancient feedback mechanism comes into clearest focus in the rigidly structured society of the European honeybee. In an article published last year Dr Maleszka described the research undertaken by he and his team into the making of a honey-bee queen. The queen and her army of female workers have identical genes, and yet the queen is a giant egg factory and the workers are small and sterile. The sole determining factor seems to be the exclusive diet of Royal Jelly that is fed to prospective queens when they are in larval form.

"Royal jelly is a thick, creamy, and highly concentrated source of proteins, essential amino acids, unusual fats, vitamins and other nutrients, and is produced by the head-glands of young worker-bees. A huge amount of royal jelly, in which a preselected queen larva virtually swims, sets her on her journey to become a very lucky creature. ... Her lifespan will be at least 20 times longer than that of a regular worker bee. ... In return for all these privileges and rewards she will lay up to 2000 eggs per day, equal to almost three times her bodyweight, for the next 2–3 years. ... The queen larva has exactly the same genetic composition as a regular worker larva, but these two virtually different organisms follow two very different developmental paths." (Maleszka, *Nature Neuroscience* vol.7 p.847, 2004)

The recent mapping of the honey-bee genome has meanwhile shown that the genes involved in the production of royal jelly are bacterial in origin and exist in only a few insects. They are known as the 'Yellow genes' and they represent an ancient bacterial invasion that became seamlessly incorporated into bee genomes during the past 100 million years of productive partnership. These genes not only help to feed the species, but by producing royal jelly, they also help to determine the complex social structure within the hive. And all this hinges on the pollen from which royal jelly is made.

Pollen grains are armoured sperm capsules that have been specifically crafted by natural selection to launch a plant's genetic material into the future. Whenever a cargo of plant sperm is hijacked by bees and injected into the hive's food reservoir it is essential that the genes in the plant sperm are fully compatible with Yellow genes and that they and their by-products do not dislodge any of the minute methyl tags that switch bee genes on or off.

When humans artificially embed alien bacterial genes in a plant's genome however, such old genetic partnerships are inevitably put at risk, and it is now known that bacterial genes can transfer between unrelated strains of bacteria just as easily as they can between bacteria of the same species.

In the case of Bt cotton, Bt corn and Bt canola the Bt refers to the fact that the plant genomes contain genes from *Bacillus thuringiensis*, a soil-dwelling bacterium related to anthrax. These genetically modified crop species produce leaf material that is toxic to the leaf-eating larvae of certain insects, especially, butterflies.

Alien bacterial genes such as this thereby have the potential to play Russian Roulette with the age-old epigenetic relationships between plant DNA and bee DNA, and especially between their relatively stable patterns of methylation. Dr Maleszka warns that any interaction between those alien genes and the Yellow genes that produce royal jelly in the head-glands of worker bees is entirely beyond our ability to predict, detect, or assess. And just as unfathomable is the ability of Bt genes to interfere with bee methylation.

Recent research has shown that DNA's epigenetic tags are remarkably vulnerable to interference by both internal and external factors. Geneticists at McGill University in Montreal have shown, for example, that inadequate grooming adds methyl groups to a particular gene in the DNA of baby rats, thereby altering their

behaviour as adults. In subsequent research they found that the injection of a common food supplement, L-methionine, also adds methyl groups to that same gene, generating very similar behaviour.<sup>1</sup>

This new research not only highlights the vulnerability of methylation to outside interference it spotlights the crucial question that faces us with GM crops: if a common amino acid and food supplement can alter the methylation pattern of rat DNA, then genetically modified pollen might well alter the methylation pattern and gene expression of bees when GM pollen is fed to their larvae.

Indeed, a 1990 study found that very high concentrations of *Bacillus thuringiensis* (var. *tenerionis*) "reduced longevity of honeybee adults."<sup>2</sup> This variety of Bt is widely used against insect pests such as the Colorado potato beetle, and although the reduced life-span in bees was not attributed to methylation interference at the time, our new knowledge of epigenetics makes this conclusion very hard to avoid.

The standard argument in favour of GM crops is that they will increase yields and thereby feed more people—and make large-scale monoculture more profitable, just as the Green Revolution did.

But such possibilities pale to insignificance when matched against the risks and stakes that are involved. Whether GM crops might increase harvest yields and thereby avert the growing threat of mass starvation among the world's poor is of minor importance when matched against the vastly greater threat that our species faces with the accelerating loss of the European honeybee. When the bee no longer pollinates our food crops starvation and social chaos will sweep civilization from the more habitable regions of the planet.

So ultimately, this is not an argument that GM crops have already interfered with bee genes or bee methylation. But it is indeed an argument that the potential for catastrophic interference clearly exists. Given the hair-trigger nature of the epigenetic code and the methylation process, and given the size of the stakes in this game of genetic Russian Roulette, the Precautionary Principle should therefore apply.

Sadly, the disappearance of bees is not the only current threat to agriculture and human survival. Consider some of the others: global warming and the accelerating release of methane from abyssal hydrates and Siberian marshlands, declining harvests due to deteriorating climate, rampant soil erosion, declining soil fertility and shrinking water supplies. Similarly, the growing shortage of fuel oil and petroleum-based fertilisers is about to strain power production and national infrastructures around the world, wild-fish stocks have already collapsed and the rate of species extinction is climbing throughout the biota, polar ice is melting and the accelerating rise of the world's acidifying seas will soon devour civilisation's most densely populated and productive land.

In short, evolution's sixth mass extinction in the past half-billion years is now well under way and *Homo sapiens*, the primary instigator of this biological holocaust, is high on the list of critically endangered species. Adding the further threat of GM crops in GM-free Australia would appear to warrant a charge of criminal insanity."

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**"In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation."**

Principle 15 of the UN's **Declaration on Environment and Development** (signed by Australia at the UN's Rio conference in 1992)

**"What is baffling is why our regulators have failed and continue to fail to act on the precautionary principle. They tend to rely instead on what we might call the anti-precautionary principle. When a new technology is being proposed, it must be permitted unless it can be shown beyond reasonable doubt that it is dangerous. The burden of proof is not on the innovator; it is on the rest of us."**\*

"Use and Abuse of the Precautionary Principle" Dr. Peter Saunders, Professor of Applied Mathematics at King's College London.

\*The anti-precautionary principle is also known as 'The Argument from Ignorance'.

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1 (*Nature Neuroscience* vol.7 p.847, 2004)

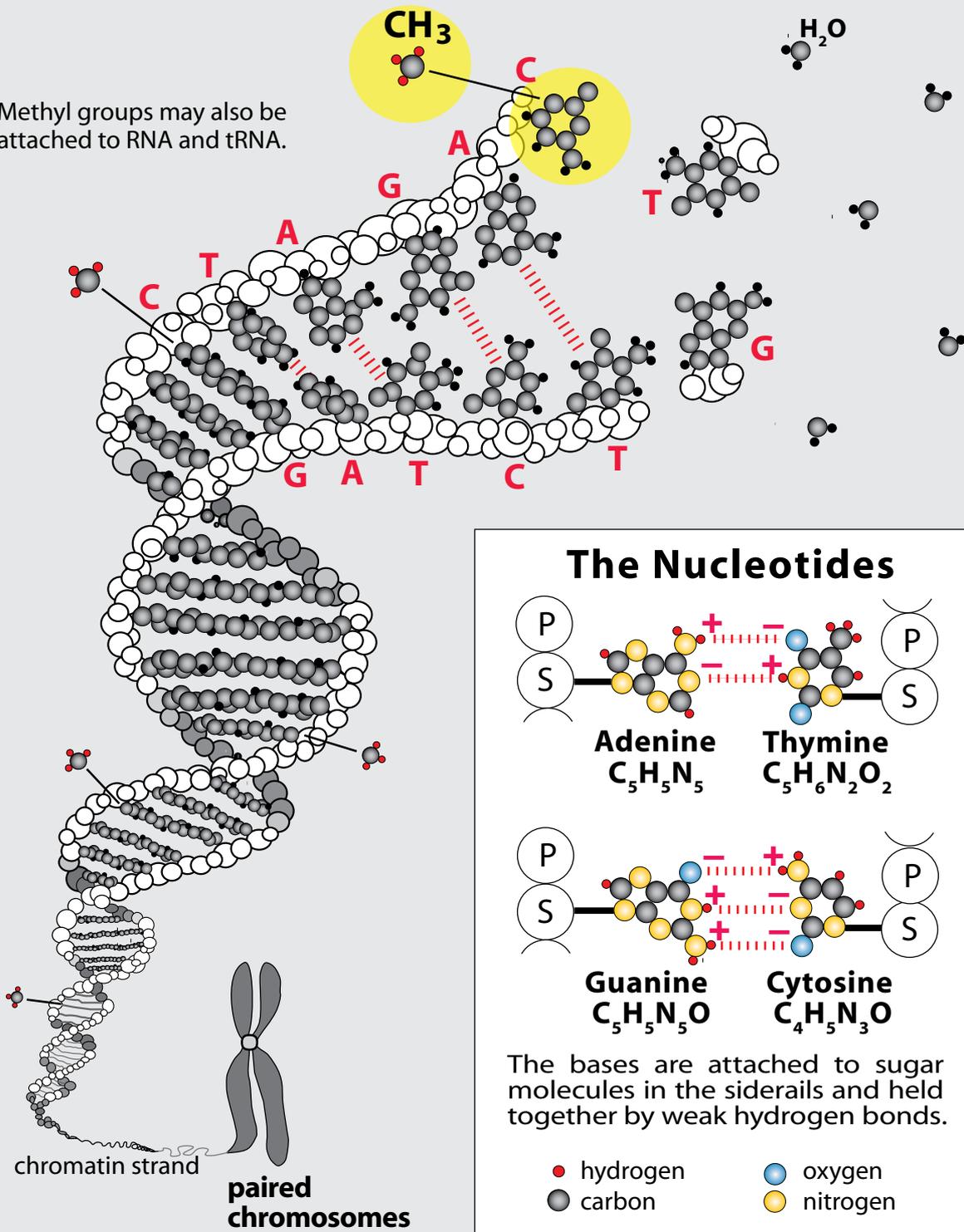
2 (Vandenberg, J. D. "Safety of four entomopathogens for caged adult honeybees" *Econ. Entomol.* 83(3): 756-59, 1990.10-152.)

# DNA Methylation

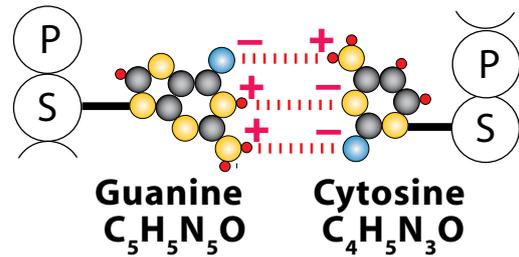
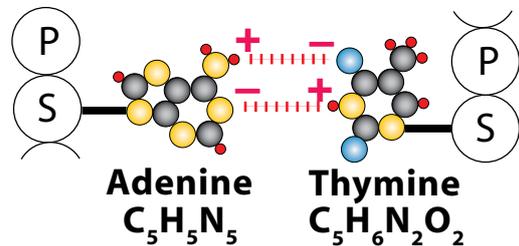
Methyl tags (CH<sub>3</sub>) are most commonly attached to cytosine, but occasionally to adenine and other sites, including the histone 'bollards' about which the strands of chromatin are wrapped.

Adenine (A)  Thymine  
 Guanine (G)  Cytosine  
 hydrogen bond 

Methyl groups may also be attached to RNA and tRNA.



## The Nucleotides



The bases are attached to sugar molecules in the siderails and held together by weak hydrogen bonds.

-  hydrogen
-  carbon
-  oxygen
-  nitrogen

By regulating the folding pattern of DNA's chromatin strands its methyl tags determine which genes can be transcribed and which are 'switched off'. DNA's epigenetic code thereby constitutes a highly flexible gene-management system that is sensitive to external and internal interference initiated by environmental factors.