

sample homogeneity, so it can be argued that no significant amount of secondary organic matter has affected the isotopic composition of the primary photosynthetic product.

Analyses of the  $^{13}\text{C}/^{12}\text{C}$  of individual acritarchs, coupled with calculated magnitudes of  $\epsilon_p$  depending on the  $\text{CO}_2$  levels of the growth medium and volume/surface-ratio estimates of the original algal forms, suggest that, around 1,400 million years ago,  $\text{CO}_2$  levels were at least 10 times and possibly more than 200 times higher than at present. The results agree broadly with studies<sup>8</sup> on the iron mineralogy of 'weathering profiles' (palaeosols), estimated at 2,750 million years old, which placed a minimum value for  $\text{CO}_2$  of about 100 times those of today. But is this enough  $\text{CO}_2$  to have kept the Proterozoic in a suitable greenhouse state?

Models of solar evolution<sup>9</sup> indicate that the Sun was only about 88% of its present luminosity at the time of deposition of the Ruyang Group. A typical solution to why there was no planetary freeze throughout the Archaean and Proterozoic is to invoke the existence of  $\text{CO}_2$  levels on the early Earth of around 1,000 times present levels<sup>10</sup>. Such a  $\text{CO}_2$ -rich atmosphere can be qualitatively justified by theoretical feedback mechanisms that link increased volcanism and decreased continental weathering resulting in mineral dissolution in liquid water, and thereby to higher atmospheric  $\text{CO}_2$  concentrations.

The new results<sup>2</sup> appear to be close to the limits required in atmospheric models to overcome diminished solar luminosity<sup>11</sup>. Other workers have proposed that a combination of gases, probably including a large contribution from methane produced by living organisms, kept the early Earth from being permanently frozen over<sup>12</sup>. But once free oxygen became a major atmospheric constituent between 2,300 million and 2,100 million years ago, it shortened the

photochemical lifetime of methane, diminishing its greenhouse influence. All in all, it would seem that the imposition of high, steady-state concentrations of  $\text{CO}_2$  is consistent with the temperature record of a mostly ice-free Proterozoic.

Studies of the early Earth are dogged by the meagre evidence available: discontinuities punctuate the entire sweep of the ancient rock record. But they can be tackled by intertwining strands of evidence from, for instance, geochemistry, geophysics, 'fossil morphometrics' and analyses of the molecular phylogenetic relationships between living organisms. 'Geobiology' is an innovative and inspiring venture in the Earth sciences<sup>13</sup>, and by linking metabolism to  $\text{CO}_2$  concentrations, Kaufman and Xiao have provided a promising way of improving our understanding. The way forward is to pursue independent proxy measures of atmospheric  $\text{CO}_2$  levels, and the isotopic payload of fossil microbes may prove an excellent source of such measures. ■

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## Viral genetics

# Deadly partnerships

Steven A. Frank

Pairs of viral genomes work together to destroy their hosts more quickly. How this might occur remains unknown, but study of the phenomenon should provide insight into how genetic systems evolve.

Early in the history of life, different copies of replicating nucleic acids must have existed near each other. Some of these genomes probably parasitized their neighbours by becoming shorter, dropping essential information and using proteins encoded by the full-length molecules. The shorter parasitic genomes might have replicated faster and out-competed their fully endowed neighbours. Other pairs probably complemented each other to mutual benefit,

favouring some method for the pair to disperse together. Viral systems provide our best window back through time, allowing us to glimpse how multi-copy genetic systems might have evolved. There are many known examples of shortened viral genomes exploiting functional partners<sup>1</sup>, but writing in the *Proceedings of the Royal Society*, López-Ferber and colleagues<sup>2</sup> now show that defective viral genomes are not always parasitic. They provide evidence that shortened



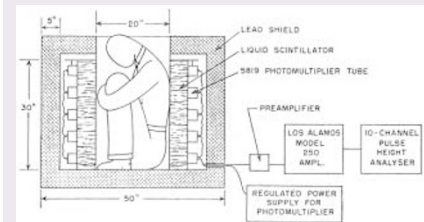
## 100 YEARS AGO

From the study of rays of measurable wavelengths we have lately sailed under the guidance of M. Henri Becquerel into another region where it is doubtful whether all the rays conform to the undulatory theory. In fact some of the rays are believed to be charged particles of matter, charged, that is to say, with electricity. Beyond doubt they are possessed of very extraordinary properties, inasmuch as they are able to penetrate the clothing, celluloid, gutta percha, glass, and various metals. They are, moreover, endowed with a no less remarkable physiological action, producing blisters and ulcerations in the flesh which are difficult to heal... From this we can quite understand that there is no exaggeration in the statement attributed to the discoverer, Prof. Curie, ... that he would not care to trust himself in a room with a kilogram of pure radium, because it would doubtless destroy his eyesight, burn all the skin off his body, and probably kill him.

From *Nature* 17 September 1903.

## 50 YEARS AGO

In the course of developing equipment for other problems, we have made some measurements of the total radioactivity content of several humans and a dog, using a technique which may have other applications in biophysics... (See Fig. 1). A dog of approximately 35 lb. weight was anaesthetized and counted in the small insert. A solution containing 0.1  $\mu\text{C}$ . radium



in equilibrium with its decay products was injected into the femoral vein, and (five min. after injection) the dog was again 'counted'... The large insert was used for the measurements on humans, who were able by doubling up to be entirely within the insert... In the absence of the radium group, the potassium content of the body can be measured with good accuracy, and it is quite conceivable that application of these techniques could yield important results in the study of the role of potassium in the metabolic process. F. Reines, C. L. Cowan *et al.* From *Nature* 19 September 1953.

genomes can work with full-length partners to mutual benefit.

López-Ferber *et al.* investigated how efficiently mixed-genome infections by an insect virus called nucleopolyhedrovirus killed its larval host — in this case, the fall armyworm. First, the authors measured the dose of pure, full-length viral genomes required to kill the larvae. Host mortality is a reasonable measure of viral success because it enables transmission to new hosts — after nucleopolyhedrovirus has replicated to high densities inside the larva, it switches on genes that liquefy the insect and release the viruses to the environment.

After obtaining a baseline measure of viral success for pure, full-length nucleopolyhedrovirus genomes, the authors measured the success of mixed populations of full-length and shortened genomes. They obtained these mixtures in two ways. First, they extracted viral DNA from natural populations of virus, in which about 20–30% of the genomes contain deletions. Surprisingly, they found that this mixed viral DNA was 2.55 times as effective at killing armyworm larvae as were pure full-length genomes. In other words, it took 2.55 times the infectious dose of full-length genomes to produce the same mortality as the mixed population.

To test the pathogenicity of mixed populations in a second, more controlled way, López-Ferber *et al.* investigated a common type of shortened genome found in natural populations. This deletion genotype could not successfully infect the host by itself, but it could succeed when in a mixed infection. The authors created five mixtures containing 10%, 25%, 50%, 75% and 90% of the shortened genome combined with the full-length genome. The most pathogenic combination contained 25% of the shortened genome and it was 2.91-fold as effective at killing as pure full-length genomes. So the maximum pathogenicity in controlled experiments occurred with about the same ratio of short to full-length genomes as is found in natural nucleopolyhedrovirus populations.

Surprisingly, these experiments demonstrate a mutually beneficial interaction between short and full-length genomes. López-Ferber *et al.* do not provide a mechanistic explanation for this phenomenon, but it is worth considering a few hypotheses because the real interest in this story is what can be learned in general about viral population genetics. To understand how this particular case might lead to a deeper insight, we must first look more closely at the biological details<sup>3</sup>.

The nucleopolyhedrovirus has an interesting method of packaging its genomes for transmission between hosts (Fig. 1). Unusually, several viral genomes are packaged together in membranous envelopes derived from larval cells. The multi-genome virus envelopes embed themselves in larger,

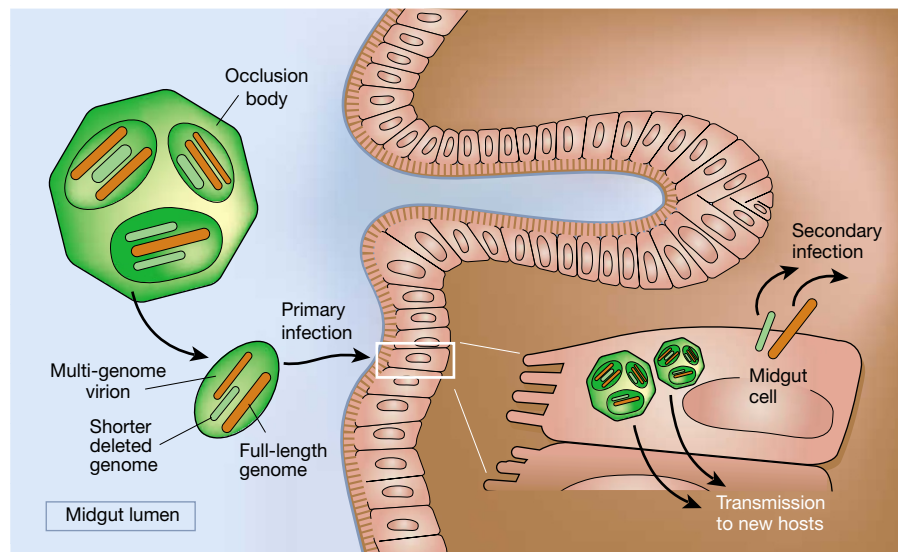


Figure 1 The nucleopolyhedrovirus life cycle. Infection begins when a larva eats a proteinaceous occlusion body, containing many virus envelopes. Each envelope contains a mixture of viral genomes, some of which can contain deletions. The occlusion body dissolves in the larval gut, releasing the enveloped viruses, which establish a primary infection in the midgut cells. The infected midgut cell first produces single viral genomes that bud from the cell surface and infect other cells — it is estimated that around four virus genomes invade each cell during this secondary infection<sup>6</sup>. As viral multiplication continues within the infected cell, occlusion bodies form. After many host cells have been infected, the virus turns on genes that liquefy the host, releasing occlusion bodies, which are eaten by new hosts.

proteinaceous structures called occlusion bodies, which are released when the larva is liquefied. When other larvae ingest the occlusion bodies, they dissolve in the gut to release the virus envelopes and the infection cycle begins again.

The particular shortened genotype investigated by López-Ferber *et al.* lacked a gene called *pif*. The protein, PIF, encoded by this gene enables the virus envelopes to invade the midgut cells — the site of primary infection<sup>2,4</sup>. If envelopes containing shortened genomes are injected directly into a larva, infection proceeds normally but the new virus envelopes produced do not contain PIF. As a result they cannot invade midgut cells in new larvae to start another cycle of infection.

Lack of the *pif* gene explains why a shortened genome needs a full-length partner, but it does not explain why the full-length genome does better with a shortened partner. One hypothesis is that paired genomes can complement defects in partners<sup>5</sup> — certain genes carried by full-length genomes might harbour potentially deleterious mutations that are masked by the normal code carried by its partner. Such complementation is not restricted to combinations of full-length and shortened viral genomes: it is a general explanation for why multiple copies of genomes are often packaged together. Complementation must have arisen with the earliest genetic systems and it continues today in many organisms — even our own genomes have two copies.

A second hypothesis to explain how long

and short genomes might interact to mutual benefit is that the shortened genome encodes a useful trait not carried by the full-length genome. Because the shortened genome must always partner a full genome that has the normal code, the short genome is free to accumulate mutations that lead to new benefits. For example, it might evolve a function that enables mixed infections to kill alternative host species more effectively.

Exactly how the example of mutualism described by López-Ferber *et al.*<sup>2</sup> arose remains to be seen. But their results suggest that insect viruses such as nucleopolyhedrovirus could be effective, general models to study how complementation might promote the packaging together of several viral genomes and how these genomes might then diverge to take on mutually beneficial traits. So, beyond destroying their hosts more efficiently, mixed nucleopolyhedrovirus infections might teach us how genetic systems evolve.

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