in the disk was not large enough for the accumulation process to produce planets, this planetesimal disk would have been preserved to the present day. This would certainly be the case for the Kuiper belt: because of its less dense mass distribution and large distance from the Sun, the accretion process in the belt would have ended when object sizes were no bigger than Pluto. However, in contrast to the present estimate for the Kuiper-belt mass, this accretion theory would require there to be around 10 Earth masses in the Kuiper-belt region, to allow the formation of objects as big as those presently seen in the belt.

The paucity of mass in the Kuiper belt is not the only enigma. Lying at such great distances from the rest of the Solar System, and experiencing no great perturbations from other large bodies, Kuiper-belt objects were expected to have orbits that were nearly circular and located close to the average plane of the Solar System. In fact, the orbits are quite eccentric, and are inclined out of the Solar System plane (Fig. 1). Planetary scientists have wondered how these orbits could have been so dynamically excited. My own idea[3] is that these objects formed much closer to the Sun and were then propelled outwards by a mechanism involving close gravitational encounters with the outward-migrating, primordial Neptune. Other work[4] shows that, if there had originally been a large mass beyond Neptune's present position, this planet would have moved much further out than it is today (effectively, into the Kuiper-belt region).

Thus, the puzzle seemed to be nearly solved. On the one hand, the original planetesimal disk would be truncated near Neptune's present position (Fig. 1), and was massive enough to form the large bodies now observed in the Kuiper belt; on the other hand, some objects would have been transported to the belt from this dense inner planetesimal disk by a mechanism that induced high-inclination orbits through close encounters with Neptune[3]. However, there was one piece that didn't fit. In addition to the Kuiper-belt objects in high-inclination orbits, there is a roughly equal number of objects at low inclination. These could not have been pushed out by the same mechanism.

Levison and Morbidelli[2] propose a solution. Their premise is based on another enigma — the fact that the Kuiper belt is considered to have an outer edge at about 7×10^9 km from the Sun (equivalent to 48 AU, or astronomical units). This distance is significant: at this point, the orbital periods of Kuiper-belt objects are twice that of Neptune, a feature known as the '1:2 mean motion resonance'. As Neptune migrated outwards through the primordial Solar System, it pushed out some of the objects in this resonance trap[5,6]. This mechanism would naturally create orbit eccentricities, causing the resonant objects to approach close to Neptune and the other major planets, such that they would eventually be ejected from the Solar System after a final gravitational encounter with Jupiter.

Levison and Morbidelli argue, however, that the influence of other, so-called secular resonances, inside the 1:2 resonance, would have kept the eccentricities and inclinations of some resonant objects low. A secular resonance is also based on commensurability of periods — not of the periods of the objects' motion around the Sun, but instead of the motion of the orbits themselves around the Sun. Such resonances are powerful, and can induce large variations in orbital eccentricities and inclinations, either raising or lowering them. According to Levison and Morbidelli's simulations, a small fraction of the resonance-trapped objects, once released through the rather jumpy migration of Neptune, would eventually be left in fairly low-inclination orbits in the Kuiper belt, owing to the influence of secular resonances. A few other objects remaining in the 1:2 resonance would set up the outer edge of the Solar System as it is today.

Of course, this new set of ideas raises further questions. The main one is, how could the primordial Solar System be formed in a truncated disk? The few observations made of other planetary systems as they are forming indicate that they have radially expanded disks. Is the Solar System then a rare case? Regardless of the answer, what conditions could cause this truncation of a developing planetary system? This, I believe, will be a major topic in planetary science for years to come. ■

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Comparative genomics

Two worms are better than one

Mark Blaxter

The genome of the microscopic worm *Caenorhabditis briggsae* has been sequenced, and shows some remarkable differences from the genome of the better known — and physically similar — *C. elegans*.

In the early 1960s, when biologist Sydney Brenner was searching for a new model organism with which to study animal development and neurobiology, he screened a wide range of invertebrate species and chose the nematode *Caenorhabditis elegans* because it is easy to culture and transparent at all stages of its life cycle[1]. This small worm is now famous, not least for being the first animal to have its whole genome sequenced[2]. A close relative of *C. elegans* also passed by Brenner's microscope, and narrowly missed this accolade. This creature, *C. briggsae*, is physically very similar to *C. elegans* (it takes an expert to distinguish them), and the two have near-identical biology, even down to the minutiae of developmental processes. Surprisingly, however, their genomes are not so similar, as the sequencing of the *C. briggsae* genome to around 98% completion, reported in *Public Library of Science Biology*, now reveals[3]. Comparing the two species offers a new view of the patterns and processes that have shaped genomes, and raises many questions for the future.

From the first draft of the *C. elegans* genome[2], it was predicted that this microscopic worm has more than 19,000 protein-coding genes and 1,000 RNA-encoding genes. With the completion of the sequence to the last base pair (all 100,258,171 of them[4]) in late 2002, these numbers have grown respectively to around 21,000 and 3,000. There is still vigorous debate as to how many of these genes are actually functional[5], but what is clear is that the complexity of the *C. elegans* gene set contrasts markedly with the organism's morphological simplicity. For comparison, the more physically complicated fruitfly *Drosophila melanogaster* has only around 15,000 protein-coding genes[6], and humans have some 40,000 (refs 7, 8).

The *C. briggsae* sequence reported by Stein *et al.*[3], with its 19,500 protein-coding genes, provides comparative confirmation of most of the *C. elegans* gene set and, surprisingly, suggests that there may be another 1,300 *C. elegans* genes to add to the list. Stein *et al.* also propose more than 4,800 changes to current *C. elegans* gene predictions, such as the existence of new exons (the coding parts of genes, as opposed to their intervening, non-coding regions). These refinements will be crucial in exploiting this nematode as a model system. There are also some fascinating differences between the two species (why, for instance, does *C. elegans* have more than 700 chemoreceptor genes when *C. briggsae* gets by on just 430?), and many genes unique to each (about 800 per species).

Two other pairs of related genomes have been sequenced: humans[7,8] and mice[9] last

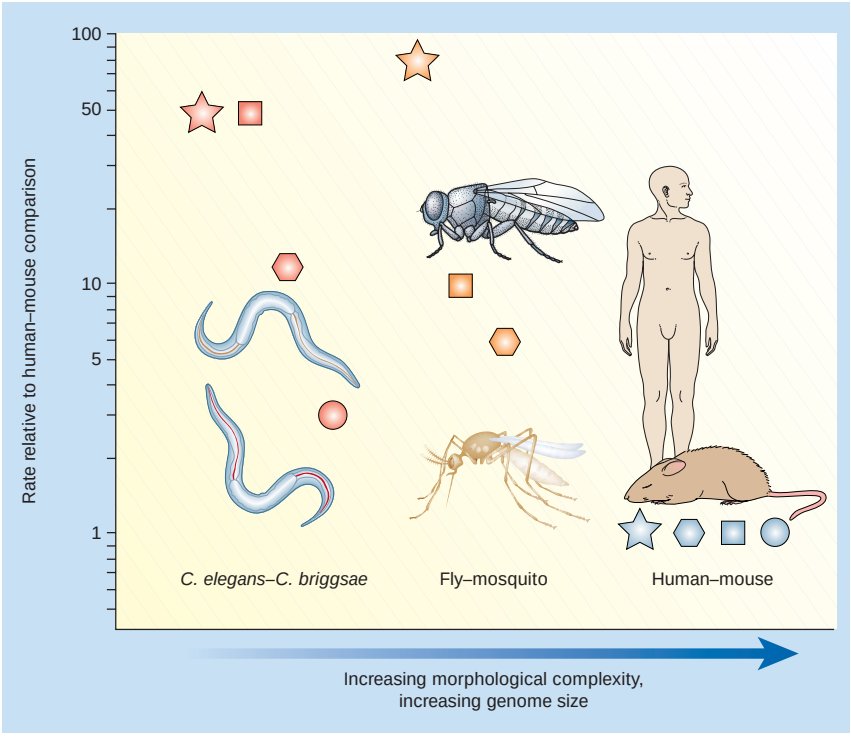

Figure 1 **Rapid genome change and physical conservation in nematodes. Stein *et al.*[3] have sequenced the genome of *Caenorhabditis briggsae*, and their comparison of its genome with that of *C. elegans* reveals rates of genomic change that stand in stark contrast to the lack of major morphological change that has occurred since the two species shared a common ancestor, around 100 million years ago. Humans and mice have undergone much more morphological evolution since they parted 85 million years ago, but have relatively more stable genomes. Flies and mosquitoes, separated by 250 million years, have an intermediate rate of change. The units on the *y*-axis are rates relative to the human–mouse divergence rates. Stars represent the rate of loss and gain of introns (non-coding gene regions); squares, the rate of genome reorganization; circles, the rate of 'silent' base-pair changes (not calculated for the fly–mosquito pair); hexagons, the number of blocks of genes whose order is conserved. The scale on the *x*-axis is arbitrary.**

shared a common ancestor about 85 million years ago, and mosquitoes[10] and fruitflies[6] diverged around 250 million years ago. When did *C. briggsae* and *C. elegans* split? Judging from their morphology, one might think it was relatively recently, but the sequences tell a different story. Using equivalent genes from mosquitoes, humans and the two nematodes, Stein *et al.* estimate that the worms diverged between 80 million and 110 million years ago.

Do patterns of genome change help to describe the range of physical disparity between these various species pairs? The answer is a resounding no: the physically most similar pair, the nematodes, shows the most differences in terms of rate of genome evolution (Fig. 1). For instance, there are about three times more synonymous substitutions ('silent' base-pair changes that do not affect encoded proteins) between the two nematodes than there are between mice and humans. And changes in genome organization have occurred around 50 times as often.

Similarly, since the nematodes diverged, there have been about 0.5 changes in gene structure — that is, in the pattern and spacing of exons — per gene. Since the divergence of mice and humans, there have been fewer than 0.01 changes in gene structure per gene[9]. Given all these changes, one question for the future is why the nematodes still look so similar. Stein *et al.* give a hint of an answer: they identify 1.3 million base-pair-level sequence matches between the two genomes, only a third of which correspond to coding portions of genes. The remaining sequence matches may represent conserved control elements that coordinate gene expression to produce physically similar organisms.

Another interesting finding comes from a look at the pattern of gene evolution along chromosomes. In *C. elegans*, the 'arms' of the chromosomes were found to be rich in repeated sequences and genes that have no similarity to those of other organisms, and undergo frequent genetic exchange[2]. By contrast, the centres of the chromosomes had few repeats and contained more genes that are also found in other animals. Comparison with *C. briggsae* reinforces this model: genes on the arms are significantly more different to genes in other organisms than are those in the centres, and gene order is less likely to have been preserved on the arms. This is strikingly reminiscent of the linear chromosomes of streptomycete bacteria, where exotic functions, such as antibiotic synthesis, are encoded on the arms and housekeeping genes are encoded in the centre. In *C. elegans*, gene-knockout studies have identified blocks of genes from the same chromosome that are expressed in the same tissues or stages of the life cycle[11]. How these blocks are maintained in the face of randomizing genome reorganization remains unknown.

Rapid change is not the rule, however. Despite having undergone more than 4,000 chromosomal breakages since they parted[3], *C. briggsae* and *C. elegans* have the same number of chromosomes: most rearrangements occur within chromosomes rather than between different ones. This pattern may be generally true of nematodes, as comparisons with the distantly related human parasite *Brugia malayi* also suggest a preponderance of intrachromosomal rearrangements[12]. Moreover, the nematode group to which *C. elegans* and *C. briggsae* belong, the Rhabditida, has a remarkable constancy of chromosome number, with six or seven chromosomes being the norm[13]. So another question for the future is how this set number of chromosomes is maintained.

The publication of the *C. briggsae* genome sequence will undoubtedly spur many workers to use this species in comparative work, and a programme of identifying 'true' genes (rather than 'predicted' ones) by mutating them is already under way[14]. A third nematode genome, that of *B. malayi*, should be added soon[15], and plans are also afoot to fill out the caenorhabditid tree with genome sequences of related species, such as that of *C. remanei*, approximately equally related to the two with sequenced genomes. These additional genomes will nourish comparative genomics, and bolster *C. elegans*' position as an invaluable model organism. ■

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