might be a specific need for the retention of all sequence patterns during germ-line differentiation and meiosis.

These varied aspects of organisation and activity suggest, albeit tenuously, that there is some overall selective marshalling of arbitrary sets of sequences which give some specific and common form to closely related genomes. Although the sequences concerned may not intrinsically define a specific function, selection may act on the phenotypic effects arising from the mere presence or position of the sequences within a genome.

When we enter the depths of the higher genome we should not abandon all hope of arriving at an understanding of the manner in which some sequences might affect the biology of organisms in completely novel and somewhat unconventional ways. It was imaginatively suggested by Goldschmidt in 1940[27] that saltatory steps in chromosome repatterning lead to abrupt changes in phenotype, some of which ('hopeful monsters') might have a degree of success in particular environments. It may be that the rapid changes in sequence organisation (in particular of the germ-line) can give rise to interesting discontinuities in morphology or developmental timing in such a process of speciation[28]. Evidence is accumulating that speciation is rarely the result of a gradual and large accumulation of adaptive allelic differences, but that it is episodic and rapid followed by long periods of morphological and genetic constancy, (aptly reviewed in detail by Stanley.[29]) The accidental and sudden accumulation of extraneous DNA sequences might lead to the inception of a process whose subsequent constancy reflects the much slower rate of diminution and loss of these elements, (among other things). □

# Occam's razor

*from Temple F. Smith*

DOOLITTLE and Sapienza argue that since the evolution of properties such as transposability ensure sequence survival, no other selective or functional properties are required to explain the existence of much of this 'extra DNA'. Orgel and Crick argue, in addition, that for the eukaryote no phenotypic selective pressures of sufficient strength are known to forbid the internal genomic evolution of these nonviral parasitic DNAs. These arguments are at their base a variant on Occam's razor, and have an analogue in the axiom of high energy physics: what (state transition) is not forbidden is mandatory. These apparent solid arguments are supported by considerable data: the large variation in total DNA content among organisms of equal complexity, if not always of close taxonomic association; and, the recent work on the yeast Ty-1 element (Cameron, Loh & Davis *Cell* **16**, 739; 1979) which is strongly suggestive of just such a parasitic sequence.

No rigorous calculations, however, have been made of phenotypic selections on such extra DNAs. The coordinate evolution required between parasitic sequences and the enzymes manipulating nucleic acids, particularly those with sequence specificity, requires more detailed analysis. There is a need for careful statistical analysis on transposables as to their probability of disrupting functional sequences or on the stability of non-functional repeats generated via such mechanisms as consecutive uneven cross-overs. There are also other curious statistics which must be investigated in connection with these ideas. For example, the entire GC content of the vertebrates appears constrained by the genetic code (Smith *Math. Biosci.* **4**, 1979; 1969) to a very narrow region about 42% while invertebrates are less constrained and prokaryotes not at all. This, at first glance, seems in direct contradiction to the expectation of the 'Selfish DNA' hypothesis.

For many evolutionary biologists, there is another problem inherent in these discussions on selfish DNA. It is epistemological in nature, as the presented theory appears nearly irrefutable. If a phenotypic constraint or function is found for any given sequence, it is either removed from consideration under the theory or it is argued that its function was a later adaptation exploiting the already existing parasitic sequence. Similar considerations have, of course, plagued the theory of evolution from its inception. Yet the important question is not to prove the potential for neutral parasitic sequences (of that there seems little doubt) but rather to predict by the 'selfish hypothesis', under known phenotypic gene level selection pressures, the distribution and other statistical characteristics of particular genetic sequences. The more constraining the predictions, the more seriously we must take the theory. □

# Selfish DNA in 'Petite' mutants

*from R. A. Reid*

DIRECT experimental evidence of DNA arising in eukaryotes by non-phenotypic selection is furnished by 'petite' mutations of the mitochondrial DNA of *Saccharomyces cerevisiae*. These mutants are promising systems for investigating the questions raised by Orgel and Crick[1] on the molecular mechanisms involved in the appearance and maintenance of seemingly superfluous DNA and the selective disadvantages of carrying such DNA. In brief, suppressive 'petite' mutants have defective mitochondria that cannot respire because of the deletion of large segments of mit DNA. Typically, these deletions, which probably arise through site-specific illegitimate recombination events[2], are accompanied by amplification of the non-deleted DNA so that the total amount of DNA in defective mitochondria is very similar to that of the wild type[3]. This amplification confers no obvious advantages; the resulting mit genome appears to be irrelevant to the immediate needs of the cell which, being deprived of functional mitochondria, uses energy from sugar glycolysis for growth. In other words spontaneous or artificially induced 'petite' mutations constitute systems where selfish DNA is created before our eyes and confirm that strategies exist for increasing the probability of survival of DNA that does not contribute to organismic phenotypic fitness.

Yeast mit DNA is probably more closely allied to eukaryotic nuclear DNA than to prokaryotic DNA as it contains highly reiterated short sequences and introns[4,5]. Therefore its small genome size (26 $\mu$) and the ease with which amplification can be induced and identified make it an attractive system for testing models of how middle repetitive and highly reiterated sequences can arise in eukaryotes without phenotypic selection. Progress has already been made in defining the nucleotide sequences that delimit the repeat units of recently arisen and old petite mutants relative to their wild type parental strains[6]. The mit DNA of 'petites' can amount to over 10% of the total cell DNA. Far from contributing to fitness this implies a selective disadvantage of about $10^{-2}$ if some reasonable assumptions are made about the energy costs, and suggests that under substrate limiting conditions the redundant mit DNA could be substantially eliminated within some thousands of generations. Theoretically it would seem easier for a yeast strain under metabolic stress to rid itself of irrelevant DNA in redundant mitochondria than to carve out selfish DNA already integrated into the nuclear genome, and quite different mechanisms may apply. Nevertheless, detailed long-term studies of the evolution of the mit DNA of new 'petites' grown under defined selective pressures should at least illuminate the proposition that the DNA loads of extant cells represent compromises between the expansionist tendencies of selfish DNA and the restraining forces of selective disadvantage. □

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