naling pathway as p110γ. In vitro studies also imply that Rac is downstream of p110γ because activation of the *f*MLP receptor results in cytoskeletal rearrangements in a pathway involving Gβγ, p110γ, the Rac exchange factor vav, and Rac (*16*). However, the study by Li *et al.* (*1*) suggests that Rac activation still occurs in p110γ-deficient cells. The detailed analysis of possible downstream effector systems in p110γ-deficient mice will no doubt further elucidate the mechanisms involved in the regulation of phagocytic cell migration.

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PERSPECTIVES: EVOLUTION

Is Bigger Better in Cricket?

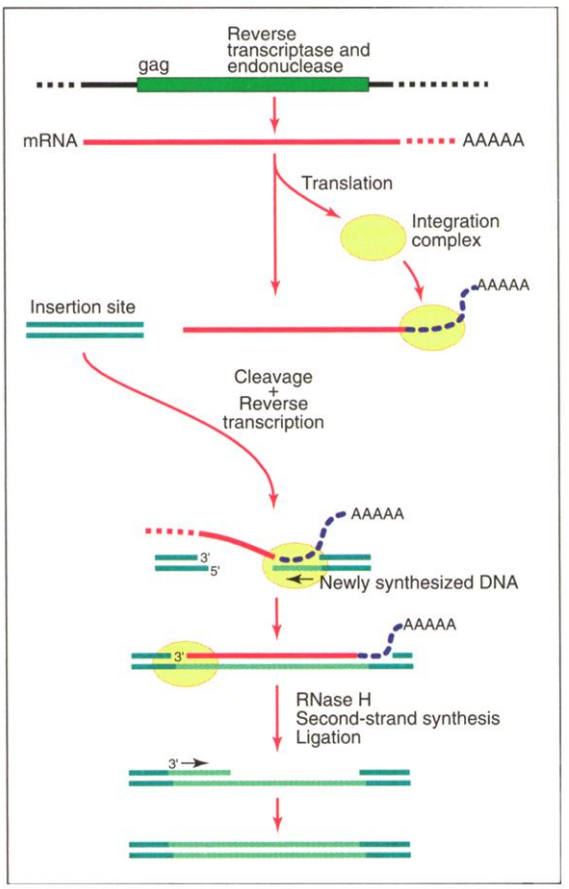
Pierre Capy

The size of an organism's genome—measured by the DNA content (*C* value) of egg and sperm—varies greatly among species (*1*). However, genome size does not correlate with the amount of genetic information that it contains or with the complexity of the organism (assessed by, for example, the number of different cell types) (*2*). This is called the *C*-value paradox and has puzzled biologists for decades. Now on page 1060 of this issue, Petrov *et al.* (*3*) present a possible solution to this paradox. The investigators provide evidence to show that the long-term accumulation of excess noncoding DNA (and thus total genome size) differs among species owing to the differential rates at which this nonessential DNA is eliminated.

Enhanced online at www.sciencemag.org/cgi/content/full/287/5455/985

Among the smallest eukaryotic genomes are those of the yeast *Saccharomyces cerevisiae* [14 megabases (Mb)], the nematode *Caenorhabditis elegans* (100 Mb), and the fruit fly *Drosophila melanogaster* (165 to 180 Mb). Yet, the single-celled amoeba, one of the simplest of eukaryotic creatures, has an enormous genome worthy of a whale (>200,000 Mb) (*3, 4*). Plant genomes vary in size from 50 Mb for angiosperms (flowering plants) to 307,000 Mb for pteridophytes (ferns). In animals, genome sizes range from 49 Mb in sponges to 139,000 Mb in bony fishes (*3, 4*). The smallest vertebrate genome is that of the Japanese pufferfish, *Fugu rubripes* (about 400 Mb) (*4*), whereas that of *Homo sapiens* (about 3000 Mb) is fairly typical of mammals (*5*).

Several mechanisms to explain the *C*-value paradox have been proposed. These include partial or complete duplication of the genome, genetic transposition (mobility of transposable elements), retroprocessed pseudogenes, replication slippage, unequal crossing over, and DNA amplification (*4*). Although larger genomes do not contain more genes than smaller genomes, they do contain more repetitive DNA (that is, sequences present in multiple copies) (*5, 6*). Retrotransposable elements (which move within the genome as RNA intermediates transcribed into DNA by reverse transcriptase) are one of the most abundant classes of repetitive DNA. These so-called retrotransposons are estimated to account for more than 50% of the total genome of maize (*Zea mays*) and the crucifer *Arabidopsis thaliana* (*7*). Of the 280 kb between the *alcohol dehydrogenase* and *u22* genes in maize, about 60% is a jumbled mixture of retrotransposable elements (*8*).



Sneaking in the back door. Mechanism by which a non-LTR retrotransposable element (LINE) moves within the genome. The LINE is transcribed into mRNA (red). A part of this mRNA is translated into proteins involved in the integration complex, which binds to the 3′ end of the mRNA transcript. The target site (blue) is cleaved followed by reverse transcription, with the 3′ end of the target site as the primer. Newly synthesized cDNA is shown in pale green. Ligation of the cDNA occurs at the 5′ end, and the second strand is synthesized using the first cDNA strand as template and the host DNA polymerase. [Redrawn from (*12*)]

From this kind of example, it is clear that genome size may increase because of multiplication of retrotransposable elements, but what is the long-term fate of this extra "junk" DNA? By investigating the fate of non-LTR (long terminal repeat) retrotransposable elements in the cricket *Laupala* and fruit fly *Drosophila*, Petrov and colleagues provide evidence for differing rates of "junk" DNA elimination. In an evolving genome, non-LTR elements are thought to proliferate by amplification of an extremely small number of "master" genes. These genes usually give rise to inactive copies (truncated at the 5′ end) that are incapable of further transposition within the genome (*9*). The defective copies arise because of their mode of transposition through reverse transcription (see the figure), which in most cases stops replication before the 5′ end is reached. These truncated elements, called DOA ("dead on arrival"), can be used as surrogates for pseudogenes in species

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such as *Drosophila* that have few bona fide pseudogenes (*10*).

Petrov *et al.* (*3*) examined multiple sequences of a LINE (long interspersed nuclear element) from 10 species of the Hawaiian cricket, which has a genome size about 11 times that of *Drosophila*. They present a phylogenetic tree of DOA elements. The terminal branches of this tree show evidence of relaxed selection in the form of equal numbers of changes in all three codon positions across the coding region. (In coding regions of functional genes, the substitution rate of nucleotides in the third position of the codon is generally higher than in the first and second positions; in pseudogenes all codon positions have similar substitution rates.) Their key finding is that in *Laupala* the average rate of deletion per substituted nucleotide in the LINE is significantly lower, and the average size of deletions significantly smaller, than in *Drosophila*. This translates into a rate of DNA loss for the cricket that is 40-fold slower than that for the fruit fly. Consistent with its markedly bigger genome, the pattern of deletions in *Laupala* is more similar to that in mammals than to that in *Drosophila*, even though *Laupala* is an insect.

It will be interesting to see how widely the inverse correlation between deletion spectrum and genome size holds up across diverse taxa. In mammals there is already a suggestion that the deletion spectrum (as estimated from processed pseudogenes) may differ according to genome size (*11*). By using degenerate PCR primers to identify a non-LTR element in *Laupala*, Petrov *et al.* (*3*) provide an experimental approach that should be applicable to almost any group of organisms. At a deeper level, why should creatures such as *Drosophila* and *Laupala* show such differences in tolerance or permissiveness toward excess DNA? Do these variations reflect intrinsic differences in the mechanisms of DNA replication or other genomic processes, or is this an adaptive trait or just plain chance? More information of the type provided by Petrov *et al.* as well as data from genome sequencing of diverse model organisms, should be useful in addressing these and related questions.

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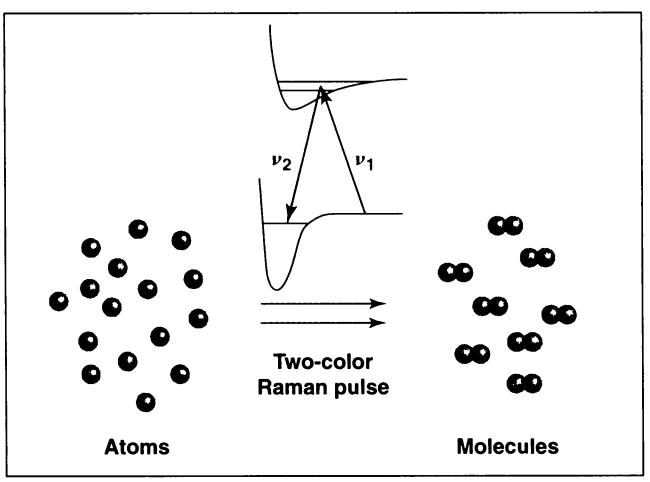
PERSPECTIVES: ULTRACOLD MATTER

Molecules at Rest

C. J. Williams and P. S. Julienne

In this issue (*1*), a group from the University of Texas reports producing rubidium dimers that are essentially at rest, by assembling them from ultracold Rb atoms in an atomic Bose-Einstein condensate (BEC). The report (see page 1016) contains several important accomplishments: the first observation of molecule formation in a BEC, an ultraprecise measurement of a molecular binding energy, and the first measurement of the interaction energy between a condensate and a molecule.

The development of cold or monoenergetic sources of matter has led to revolutionary breakthroughs in fundamental science and applications alike. Nowhere is this more obvious than in the use of lasers as light sources. Monoenergetic sources of atoms, neutrons, electrons, and ions have also provided new tools with wide-ranging applications in physics, chemistry, and biology. More recently, the production of cold, trapped neutral atoms, after a decade of progress in laser and evaporative cooling that reduced temperatures from 1 K to 1 nK, led to the observation of Bose-Einstein condensation of dilute atomic gases (*2*). An atom laser (*3*)—a coherent matter wave analogous to the photon laser—has now also been demonstrated. Cold, neutral trapped atoms and BECs are proving to be powerful tools for extending our understanding of atomic physics and of the collective properties of quantum fluids and are finding applications in precision atomic clocks and gyroscopes and in atom lithography.



Stimulated Raman production of molecules from an atomic Bose-Einstein condensate. The graph shows the ground and excited state potential energy curves for a pair of atoms. Two atoms in their ground state are optically coupled by lasers of frequency ν_1 and ν_2 to a bound dimer vibrational level with a binding energy of $h(\nu_1 - \nu_2)$. In the experiment, the frequency difference was controlled to much better than 1 kHz. Neither laser was resonant with an excited state vibrational level, and loss of coherence by excited state spontaneous radiative decay was therefore not a problem. The left and right pictures indicate a complete coherent interconversion between atomic and molecular forms of the condensate. Wynar *et al.* (*1*) only converted a fraction of atoms to molecules.

Unlike atoms, molecules have complicated internal vibrational and rotational structure and are therefore poor candidates for laser cooling. Although molecules are routinely cooled internally to a few kelvin with the use of supersonic expansions, they still have high translational velocities. Recently, several approaches have been developed for producing and detecting translationally cold molecules (*4*). At Harvard, Doyle's group (*5*) has developed an approach to trap cold molecules using a magnetic trap in a cryogenic helium refrigerator. The resulting molecules are not only translationally but also vibrationally and rotationally cold. With this method, 10^8 CaH molecules have been trapped at 400 mK. Meijer's group at Nijmegen (*6*) has used deceleration of neutral dipolar molecules using time-varying inhomogeneous fields to decelerate CO molecules to around 15 K. Further reductions in temperature are expected with this general tech-

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