test causal effects of differentiated regions on reproductive isolation and coupling, as are larger studies examining numerous taxon pairs. Such experiments could comprise experimental evolution studies in the lab or field transplants in the wild. Moreover, natural history and molecular studies, including those using ancient DNA, are required to establish whether divergence really occurred with gene flow. This is critical because false inference of gene flow could lead to erroneous evidence for coupling, because numerous genetic regions diverge between isolated populations through other processes (*5*). Moreover, genome assembly errors, particularly in regions of low recombination, could lead to a single genetic region being falsely inferred as multiple regions of differentiation. Nonetheless, initial evidence points to coupling as a consideration for understanding speciation. In turn, this suggests that sets of genes might exhibit emergent properties not seen by individual genes, implying the potential for sudden tipping points in the ability for selection to overcome gene flow (*4*).

By combining theory and data, evolutionary biologists are now poised to better understand how new species are created. A large part of this understanding will involve discovering how the effects of genes and phenotypes become coupled to cause a transition from polymorphism or geographic variation within species to genome-wide differences between distinct species. A major outstanding question is the extent to which the microevolutionary process of coupling can explain broader macroevolutionary patterns of biodiversity, as observed in radiations such as those in cichlid fish (*9*, *14*). ■

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GRAPHIC: N. CARY/*SCIENCE* FROM A. WACHOLDER AND A.-R. CARVUNIS

GENETICS

New genes from borrowed parts

Vertebrate genes acquire new capabilities by capturing parasitic genomic elements

By **Aaron Wacholder**[1,2] *and* **Anne-Ruxandra Carvunis**[1,2]

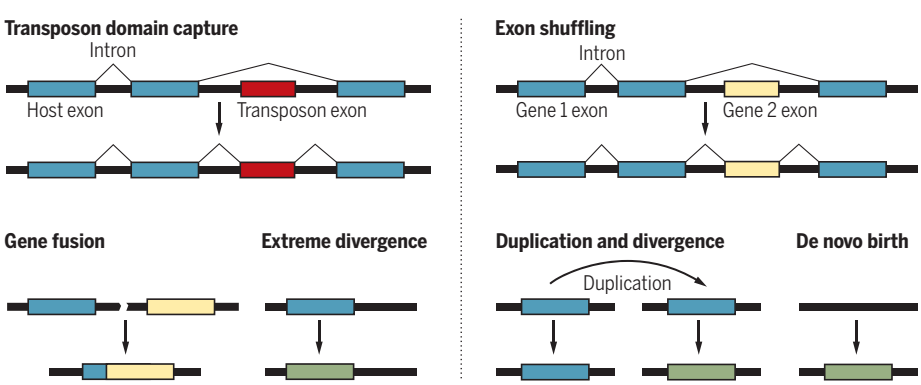
The vast phenotypic diversity of life is in part a consequence of a continual process of genetic innovation. New genes, with distinct structures and capabilities, emerge regularly throughout evolutionary history. Making use of genomics technologies, researchers are beginning to form an understanding of the details of the processes by which new genes arise. On page 797 of this issue, Cosby *et al.* (*1*) provide clarity for one such process. Transposons are parasitic genomic elements that replicate by inserting copies of themselves in the host genome. Cosby *et al.* report how vertebrate genes have captured DNA transposon domains, generating new genes that encode new fusion proteins with distinct domain architectures. Fusion of transposon domains with host genes appears to be frequent, with 94 fusion events identified over tetrapod evolution. Transposon domain capture may be a common source of new genes and molecular innovation across the tree of life.

Cosby *et al.* expand on and generalize previous work that has characterized a small sample of host-transposon fusion proteins (*2*–*4*). For example, the mammalian gene *GTF2IRD2* (GTF2I repeat domain containing 2) (*2*), implicated in the rare genetic disorder Williams-Beuren syndrome, was previously discovered to be a carboxyl-terminal fusion of an ancestral transcription factor with a transposon domain. By using large-scale genomic comparison, Cosby *et al.* were able to reconstruct the general process by which DNA transposon domains are captured by host genes. Some DNA transposon families have been highly successful at replicating within tetrapod genomes, inserting themselves in proximity with numerous host genes. Capture occurs through exon shuffling: An exon from the transposon is spliced into the transcript of a nearby host gene, usually making use of the native splice sites within the transposon. The fusion product emerges initially as an alternative splice isoform to the main prefusion product and then becomes the dominant isoform through DNA sequence changes over evolutionary time.

DNA transposons appear especially well-suited for generating transcription factors through exon-shuffling. DNA transposons encode transposases that must recognize and bind to the transposon itself to replicate it. Cosby *et al.* found that most domains captured from DNA transposons perform this self-recognition role. Thus, the captured DNA-binding domains in

Origins of new protein-coding genes

A gene can acquire new molecular capacities by capturing a domain from a transposon or from a different host gene. Fusion among host genes can similarly assemble preexisting domains into distinct combinations. Alternatively, a gene can evolve new molecular capacities through a series of major sequence changes. This can be facilitated by gene duplication, which creates a copy that can diversify. In de novo gene birth, a fully new gene evolves from a previously noncoding sequence.



the fusion protein will initially bind to copies of the transposon itself. Because these copies are common throughout the genome after a period of successful transposon replication, the transposon family provides both DNA binding capacity to the new fusion protein and an initial set of binding sites throughout the genome. A skeleton of a regulatory subsystem is thus formed immediately, which can be further refined though coevolution of the fusion gene and the corresponding DNA-binding sites of the encoded fusion protein. In support of this model, Cosby *et al.* show that four recently evolved fusion proteins with captured transposon DNA-binding domains repress transcription of genes downstream of the transposon binding site. For example, the bat transcription factor KRABINER, a fusion with the DNA transposon *mariner*, binds both *mariner* and other sites throughout the genome, regulating hundreds of genes.

The study of Cosby *et al.* highlights the key role of transposons as drivers of genetic innovation. In addition to genes that originate as host-transposon fusions, full transposon genes can also be captured by the host. For example, the transposon-derived genes recombination activating gene 1 (*RAG1*) and *RAG2* are of central importance to adaptive immunity, generating antibody diversity through recombination (*5*). Studies have found that hundreds of human genes appear to be derived from transposons, as are an abundance of long noncoding RNAs (lncRNAs) and regulatory sites (*6*). Why is host capture of transposons so common? Although transposons themselves are "selfish" elements that can reproduce at the expense of the host, their replicative success brings with it the spread of raw material for potential innovation throughout the genome. This raw material is not random but is already capable of activities involved in transposon replication. DNA-binding activity encoded by the transposon can be directly incorporated in transcription factors, and transposon-derived genes can make use of translocation activity already present in the transposon ancestor to generate diversity-promoting genomic rearrangements in somatic cells.

Historically, the focus of much research on the generation of new genes has been on gene duplication followed by the diversification of these duplicates into distinct genes (*7*). However, many gene duplicates remain structurally similar to their parents. Cosby *et al.* demonstrate that transposon domain capture is a common mechanism by which entirely new capacities can be obtained in genes that were absent in the host parent, such as DNA-binding capacity. This is not specific to host-transposon interaction. Gene fusion and exon shuffling among host genes can similarly create new combinations of already-existing capacities (*8*). In contrast to this class of new gene-formation mechanisms, in which the innovation consists of rearranging functional domains in new contexts, the phenomenon of de novo gene birth from a nongenic sequence generates completely new domains and genes. Although once thought rare, well-characterized cases of de novo gene birth have now been reported in numerous taxa (*9*). New genes and domains can also arise through extreme divergence, in which a sequence evolves beyond recognition through a series of molecular changes (*10*).

"...transposon domain capture is a common mechanism by which entirely new capacities can be obtained in genes..."

A major open question is the relative contributions of these mechanisms (duplication and divergence, gene rearrangement, de novo birth, and extreme divergence) to gene formation and functional innovation (see the figure). Perhaps even more important will be to determine the distinct contexts in which these mechanisms contribute to innovation and how the mechanism of origin affects the type of molecular, physiological, and evolutionary impacts the newly created genes can have. Therefore, it is of great interest that Cosby *et al.* find that most domain capture events from transposons involve acquisition of DNA-binding domains and associated capabilities. ■

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PHYSICS

A masing ladder

A maser that amplifies emission of periodically modulated quantum states has uses in metrology

By **Ren-Bao Liu**[1,2]

Masers, the precedent and radio-frequency (rf) counterpart of lasers, have many applications in metrology, communication, and spectroscopy. Jiang *et al.* (*1*) demonstrate a new type of maser in which rf radiation is amplified by stimulated emission from transitions between periodically modulated quantum states, called Floquet states (*2*), unlike a conventional maser, which uses transitions between stationary quantum states. The Floquet maser presents a phase-locked frequency comb equally spaced by the modulation frequency. With a modulating signal at a low frequency (1 to 100 mHz) converted to maser emission at high transition frequencies (~10 Hz) of ultranarrow spectral linewidth (<0.3 mHz), the authors overcome the low-frequency noise problem in metrology and show that subpicotesla sensitivity of magnetometry is achievable. Conceivable applications of this work include precision clocks and detection of ultralight dark-matter particles such as axions.

The quantum emitters used are the nuclear spins associated with xenon-129 (^{129}Xe) nuclei, whose quantum states have long lifetimes (~14 s). A static magnetic field splits the quantum states of the nuclear spins into the upper and lower energy levels (see the figure). The periodic modulation of the magnetic field can be viewed as what would result from a magnet mounted onto an oscillator. The spins in the upper or lower levels, which point upward or downward, would be attracted or repulsed by the magnet and in turn offset the oscillator in the opposite direction. In quantum mechanics, the offset oscillator has a ladder of equally spaced energy levels, corresponding to the upper and the lower ladders of Floquet states.

Jiang *et al.* optically pump the ^{129}Xe spins to achieve population inversion (the up-

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