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NEWS AND VIEWS

Meeting review: the origin of novel features

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Major innovations such as floral organs and the amniotic egg define the nodes of the tree of life. But what processes occurring along the branches between nodes allow novel traits to arise? The substantial progress achieved by recent research in understanding how novel features originate and evolve was considered at a minisymposium on 'The Origin of Novel Features' held at Indiana University, Bloomington, last 6–8 October 2006. This student-organized meeting was the fifth in a series sponsored by the NSF Integrative Graduate Education and Research Traineeship (IGERT) grant in Evolution, Development, and Genomics shared by Indiana University, Bloomington, and University of Oregon, Eugene. Below, I synthesize the diverse ideas and findings presented at the meeting while characterizing potential paths evolution can and does take when novelties arise. These perspectives will also be related to several major questions and themes that re-emerged throughout the minisymposium.

What, if anything, is a novelty?

Is any modification sufficiently different to be considered a novelty rather than simply a variation on a theme? As defined by Rudolf Raff (Indiana University, Bloomington), a novelty must transcend the present range of variation of homologous structures or produce new nonhomologous structures. Mary Jane West-Eberhard (Smithsonian Tropical Research Institute) phrased her definition in terms of developmental networks: novelties arise when new switch points leading to new network branches evolve.

Massimo Pigliucci (State University of New York, Stony Brook) noted that definitions of novelty in the literature come from three perspectives: history, function, and structure. He argued that while history is a source of contingency, it is not a constraint; constraints are solely structural or functional. Given these considerations, Pigliucci and Patrick Phillips (University of Oregon, Eugene) both emphasized that novelties are best understood as the phenotypic products that result from novel interactions of genetics, development, and ecological selection and that open new zones for adaptive diversification. Meeting the expectations of this process-focused characterization requires an integrative research programme probing the how, from what, and why of any particular novelty.

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How do novelties arise?

Genetic context and environmental conditions must both be favourable for a novel feature to evolve. This deceptively simple statement conceals rich complications in the timing, order, and likelihood of events in the evolutionary process caused by contingency and constraint. Each segment below discusses how results presented at the meeting bear on several genetic and environmental means of generating new phenotypic variation and the interaction of these forces with natural selection.

Genetic initiation: an environment awaits mutations of higher fitness

In this classic picture of adaptation, mutation introduces variation, and selection fixes the fittest variants in an environment. When multiple mutational steps are necessary, time and the order of substitution must be considered. Phillips observed that rapid evolution is possible when few novel mutations with direct effects cause large phenotypic changes. In contrast, novelties involving interactions between multiple mutations will arise at intermediate or very long timescales, as the likelihood of multiple mutations co-occurring is proportional to some power of the mutation rate. Since recombination breaks up co-adapted combinations, tight linkage facilitates fixation of novelties requiring coordinately evolving mutations.

Seeing evolution in action at these longer intervals is a major challenge. However, Richard Lenski (Michigan State University) described results from his study of experimental evolution in *Escherichia coli* that approaches such stretches of time (30 000 generations and growing!) albeit in the laboratory context. For instance, even in a simple and constant environment, stable de novo polymorphisms arise (Rozen

et al. 2005). Multiple independent replicate lines, the ability to preserve and resurrect ancestral states, and quick genome sequencing are major advantages of this prospective approach. As novelties arise, Lenski's system has the potential to identify their molecular basis, trace the timeline and order of contributing substitutions, measure their fitness advantages, and ask whether constraints exist that prevented independent lines from evolving similarly.

Answering these questions of process is much more difficult for historical instances of innovation. Nevertheless, Joseph Thornton (University of Oregon, Eugene) has done so by bringing past forms into the present through ancestral gene resurrection. Thornton's group phylogenetically reconstructs ancestral gene sequences of vertebrate hormone receptors, determines which nucleotide changes occurred in which lineages, and then synthesizes progressively more derived sequences and tests their biochemical function following transformation into cell lines. This approach allowed identification of the key mutations leading to the loss of aldosterone sensitivity in the cortisol receptor following duplication from an ancestral receptor capable of binding both hormones (Bridgham *et al*. 2006). A pair of substitutions is sufficient to eliminate ancestral aldosterone sensitivity without impairing cortisol sensitivity. In isolation, one mutation of this pair completely abolishes binding of both hormones while the other still permits receptor function. Since the phenotype requires an epistatic interaction of two mutations and given the asymmetric effects of each mutation individually, the order in which these two substitutions must have occurred is clear.

David Stern (Princeton University) also reported involvement of multiple mutations in the same gene in his talk on trichome evolution in *Drosophila*. Notably, this common finding comes from a system involving a different form of mutational input (*cis*-regulatory region evolution) and evolving on a much shorter timescale.

Standing variation: mutations await an environment or genetic background that alters the fitness landscape

Both Paul Brakefield (Leiden University) and Lynda Delph (Indiana University, Bloomington) presented artificial selection studies demonstrating that selection on standing genetic variation within populations can produce large changes in phenotype. Indeed, artificial selection on multiple traits simultaneously can generate combinations of features not observed in nature. For instance, Brakefield and colleagues' concurrent selection studies on eyespots in *Bicyclus anynana* led to combinations of eyespot sizes not represented anywhere in the *Bicyclus* clade (Brakefield & Roskam 2006). A key lesson from such studies is that given an environment with the appropriate selection regime, standing variation responds substantially, even if opposed by genetic correlations.

These changes are quantitative, tinkering with the size, shape, and colour of features already present and elaborated. Does standing variation contribute to qualitatively new features? If so, how? Standing variation's most important role may occur following colonization of a new environment or the fixation of a major mutation affecting a trait or its environmental sensitivity. Previously cryptic or deleterious variants may have different phenotypic and fitness effects in the new context that facilitate initiation, elaboration, or refinement of the new phenotype.

Alternatively, introgression of variation from other populations or species can serve as a valuable source of standing variation that contributes meaningfully to the origin of novelties. For example, phylogenetic analyses presented by Bruce Lahn (University of Chicago) suggest that hybridization with an archaic *Homo* lineage may have introduced critical variation at the *microcephalin* locus contributing to adaptive brain size expansion in the modern human lineage (Evans *et al*. 2006). While introgression's role may just be as a means to further sample independent evolutionary experiments, it is also possible that these adaptive alleles were unachievable within a given population because negative gene-by-gene or gene-by-environment interactions blocked necessary mutational paths.

Nancy Moran (University of Arizona, Tucson) highlighted the importance of the genomic form of adaptive introgression: endosymbiosis. Major innovations in the history of life have involved the engulfment and maintenance of one or more whole organisms within another species, and Moran presented several cases representing different key phases in evolving endosymbiotic relationships. Interactions may begin facultatively with symbionts being transmitted among host individuals like pathogens. More specialized endosymbionts are obligately maternally inherited and, consequently, often codiversify with their hosts (Takiya *et al*. 2006). At the extreme, endosymbionts can transition into organelles; Moran cited the psyllid symbiont *Carsonella rudii* as an example of an organism in such a shift (Nakabachi *et al*. 2006).

Phenotypic initiation: a new environment changes phenotypic and fitness landscapes

West-Eberhard (2003) asserted that environmentally induced phenotypic changes are the basis for much adaptive innovation. Ancestral polyphenisms rather than ancestral genetic polymorphisms are the starting material for the origin of novel features in this situation. Alterations in the course of development caused by environmental conditions produce alternative forms, physiological responses, or behaviours. Provided repeat induction over multiple generations, these novel features may serve as both catalysts and substrates for evolutionary change as selection may rapidly fix standing genetic variation affecting the material

basis and regulation of these environmentally induced novelties.

How does development influence the origin of novelty?

While having the appropriate selective environment is a critical prerequisite for the origin of novelty, development may also limit what is possible or favour certain evolutionary outcomes over others. However, disentangling which of these sources of constraint and bias is cause or effect is not straightforward. The difficulty of reaching particular regions of phenotypic space may be a consequence of absolute developmental limits. Then again, genetic correlations and the amount of additive genetic variance along particular phenotypic axes may be legacies of natural selection.

The biochemistry and structure of regulatory relationships in gene networks may preferentially favour involvement of certain types of mutations or genes in the origin of novelty. Gunter Wagner (Yale University) argued that novelties are more likely to arise when new protein–transcription factor interactions evolve than when transcription factor binding sites evolve. He reasoned that a single mutation affecting a protein's interaction with a transcription factor may have a much larger effect on transcriptional output than a point mutation in a binding site.

While many have said that downstream components of a network are more often sources of change as they generally have fewer pleiotropic effects, Stern argued that network structure has another effect. Stern proposed that genes acting as major network switches, those that integrate multiple developmental and environmental signals and that regulate expression or stability of many target effectors, are crucial for evolving novel features. His group's work on *shavenbaby*, a gene involved in multiple independent instances of trichome evolution in *Drosophila*, provides one line of empirical support for this assertion (Sucena *et al*. 2003). Concordant findings described by Thomas Kocher (University of New Hampshire, Durham) and Arhat Abzhanov (Harvard University) implicating *Bmp4*'s involvement in adaptive radiations of both cichlid jaws and finch beaks provide additional evidence for Stern's contention that major regulatory switches are primary targets for evolutionary innovation (Abzhanov *et al*. 2004; Albertson *et al*. 2005).

Promising directions

In addition to these broader lessons concerning the intricacies of various evolutionary paths to novelty, the 'Origin of Novel Features' minisymposium saw several exciting new findings regarding the developmental mechanisms underpinning individual novelties. For instance, Armin Moczek (Indiana University, Bloomington) discussed how his laboratory's application of RNAi in the horns of dung beetles of the genus *Onthophagus* has successfully found instances of both conservation and change in the functions of the co-opted appendage development genes that pattern these novel structures. Along similar lines, combining a candidate gene approach with a less biased search using cDNA microarrays, Abzhanov has successfully implicated involvement of two orthogonally acting signalling pathways in generating the adaptive radiation of beak shape in Darwin's finches (Abzhanov *et al*. 2006). In time, exciting advances will also come from genome sequences of multiple haplochromine cichlids, another classic example of adaptive radiation and parallel evolution (Danley & Kocher 2001).

Studying these mechanisms not only reveals causative substitutions underlying novel features but also provides insight into how evolution both recycles and innovates to generate novelty. Furthermore, this knowledge helps resolve how aspects of development that integrate or modularize the phenotype constrain or promote innovation. With the continued development of genomic and manipulative tools for nonmodel systems, micro evolutionary approaches to macro evolutionary problems hold great promise for furthering our understanding of how novelties arise.

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