Energy in Sofia, Bulgaria.

Bulgarian and U.S. officials are still hoping to discover exactly where the sample came from and whether a larger cache exists that the smuggler and his associates were hoping to sell on the black market. But that will require more political cooperation. Although scientists at the original reactor could certainly identify the sample, there is not enough publicly available information to make a conclusive match. "Unless the responsible country is forthcoming, there is not going to be a resolution" to the question of the sample's origin, Wimer says.

In the absence of such cooperation, several meeting participants suggested that the development of a database of known nuclear and other radioactive sources, perhaps coordinated by IAEA, could help trace seized materials. Although secrecy could thwart the development of a comprehensive database, says Lothar Koch of the European Commission's Institute for Transuranium Elements in Karlsruhe, IAEA or another organization could at minimum seek to convince countries to identify matches if presented with details of a suspicious sample.

Stronger links between the scientific community and law enforcement are another vital line of defense against nuclear trafficking. In another case described at the meeting, a bus at the Presevo border crossing between Macedonia and Yugoslavia triggered a recently installed radiation detector. A search revealed a suspicious container with Chinese lettering. Later analysis revealed that it contained highly radioactive cobalt-60. The border guards evacuated the bus, but then they allowed everyone to go—missing the chance to determine who might have been exposed to potentially dangerous levels of radiation from the cobalt-60, not to mention allowing the smuggler to escape.

"The scientific problems are important," Strezov said at the meeting's closing session, "but more important are law enforcement personnel. They are on the front line." Well-trained police and laws with teeth are just as important as high-tech analyses for preventing the stuff of nuclear nightmares.

–GRETCHEN VOGEL

EVOLUTIONARY BIOLOGY

Evo-Devo Enthusiasts Get Down to Details

Researchers seek out variation among individuals to help them understand development's role in evolution

Some researchers are turning Theodosius Dobzhansky's famous quote, "in biology, nothing makes sense except in light of evolution," on its ear. Evolution, it turns out, makes no sense except in light of biology—developmental biology, to be precise. Ever since Darwin formalized the idea that species change through time in response to their environments, researchers have been debating how this happens. Does evolution proceed in leaps, possibly through sudden, major genetic changes? Or do new organisms arise slowly, through the gradual accumulation of more subtle genetic perturbations?

Today many researchers from a field that melds evolutionary and developmental biology—evo-devo—are turning their attention away from dramatic evolutionary events and toward seemingly mundane ones. They hope their work will eventually help explain how subtle genetic changes can sometimes make evolution appear to skip ahead, possibly even reconciling the positions of those who champion large-scale changes with the positions of those who pay heed to more minor variations. Their studies of butterfly eyespots, nematode sex determination, and cavefish eyes, for example, are yielding insights into how the same mechanisms might underlie both types of evolution.

Evo-devo work hasn't always had such a mechanistic bent. When developmental biologists began delving into evolution more than a decade ago, they tended to focus on the big picture: so-called macroevolution. The early emphasis was to survey a broad range of organisms, chasing down developmental genes common to them all. That such genes existed was a startling revelation, suggesting that organisms' body plans were more highly conserved across species than people suspected.

For a while, researchers were taken with trying to figure out how such similar genes could underpin the development of wildly different creatures. But that approach has proven limited. "You can collect lists of conserved genes, but once you get those lists, it's very hard to get at the mechanisms [of evolution]," explains William Jeffery, an evolutionary developmental biologist at the University of Maryland, College Park. "Macroevolution is really at a dead end." The lists gave no insight into how, in the end, organisms with the same genes came to be so different. And given the evolutionary distance between, say, a fruit fly and a shark, "there isn't really an experimental manipulation to let you get at what the genes are actually doing," says Rudolf Raff, an evolutionary developmental biologist at Indiana University, Bloomington (IUB).

The solution, say Jeffery and others, is to focus on genetically based developmental differences between closely related species, or even among individuals of the same species. This is the stuff of microevolutionists, who care most about how individuals vary naturally within a population and how environmental forces affect this variation.

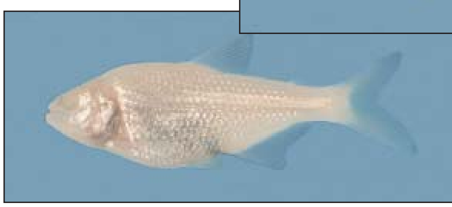
In adopting a microevolutionary approach, these evo-devo researchers are placing themselves smack in the middle of the ongoing debate about how evolution proceeds. The fundamental question, Maryland's Eric Haag points out, is whether the mutations that result in real novelty are the same mutations that happen day to day or

Spotting genetic diversity. Butterfly eyespots have the normally hidden potential to shrink or expand in just a few generations.

CREDIT: ANTONIA MONTEIRO/UNIVERSITY AT BUFFALO are the ones that occur only rarely, on a geological time scale.

Taking this new approach will not be easy for biologists coming from the development side of evo-devo. To those who study how single cells grow into full-fledged organisms, variety within a species is more nuisance than spice of life. They traditionally study organisms with very consistent developmental trajectories to make sense of the process. But because variation is the stuff of evolution, "what developmental biologists consider noise, the [microevolutionists] consider gold," says Raff.

Now Raff and others with developmental backgrounds are beginning to pan for that gold, too. "We think a case can be made that this is the only way that we are going to be able to unravel the actual mechanisms by which developmental pathways diverge," says IUB's Michael Lynch. Sometimes their prospecting yields small differences within the same developmental gene in different individuals. More often variation is turning out to be caused by differences in the way those genes are regulated.



Sensory seesaw. In cavefish, the regulation of one gene tips development to favor either eyes or bigger jaws and teeth.

These efforts might help reconcile the microevolutionary and macroevolutionary mindsets: Small variations in genes involved in development might be springboards to both macroevolutionary and microevolutionary changes. Rare, major genetic events might sometimes occur, but they aren't necessary; minor genetic changes can elicit speciation events that are decidedly less glamorous but in many ways as dramatic as those favored by macroevolutionists.

Genetically wide-eyed

Antonia Monteiro has begun to document how minor genetic changes in butterflies can cause evolution to speed ahead. An evolutionary developmental biologist at the University at Buffalo, New York, she has been breeding butterflies to promote "evolution" in eyespots, dark patches on the wings that distract predators. In one experiment, she began with 800 *Bicyclus anynana* and from their progeny bred the 40 males and 100 females with the biggest spots.

The study simulated a situation in which large eyespots provide an advantage and therefore are favored by natural selection. She reversed the process in other experiments, picking out those with the smallest eyespots. Her goal was to see how much variation was already built into the butterflies' genetic repertoires.

In September at the annual Integrative Graduate Education and Research Traineeship Symposium in Bloomington, Indiana, Monteiro reported that she saw a dramatic shift in the range of eyespot sizes in just six generations. "[We] started changing what the population as a whole looks like," she reported. Some individuals even evolved eyespot patterns not seen in any members of earlier generations: For example, in selecting for ever smaller eyespots, her colleagues came up with butterflies with no eyespots at all. In nature, "if there was [similar] selection, one species can change into another in a very short amount of time," she concludes. The accumulation of minor, hidden variations enables relatively large evolutionary changes, she says.

To home in on the cause of eyespot shrinkage, Monteiro began experimenting with embryos, carrying out some "very nice manipulations," says Jeffery. In this way she has been able to look at the basis of the variation in eyespot size. For example, she transplanted a small piece of tissue from one pupa's wing into a hole cut into the pupal wing of a butterfly destined to have a different-sized spot. The experiments showed that cells called the central signaling cells proved important: "If we put these cells into a [small-eyespot] line, they produce a very large spot," she says.

Like microevolutionists, Monteiro is hot on the trail of the genes behind these cells' powers, working from the few already implicated in eyespot development to the full genetic complement. She also plans to follow these genes throughout development and track down those that interact with them to help determine an eyespot's appearance. She wants to find which pathway within the genetic hierarchy—wherein one gene turns on a second gene, and so on—is more likely to vary and therefore make possible the evolution of a trait. "Is [the source of variation] in a gene high up in a developmental cascade or in a lower downstream target?" she asks. She still has a long way to go, but with these plans, "her work hits the strict definition of microevolution of development right on the head," Haag notes.

Worm by worm

Scott Baird, an evolutionary developmental geneticist at Wright State University in Dayton, Ohio, has also joined the growing group of investigators studying microevolution. Instead of looking at a single component of development, such as eyespot size, he studies the destinies of certain larval cells, charting where they go and how they divide. His subjects are relatives of *Caenorhabditis elegans*, the nematode whose development has been tracked cell by cell and whose genome is now sequenced.

C. elegans is a developmental biologist's dream come true. Its development is very consistent: Each embryonic cell has a specific destiny and gives rise to the same numbers and kinds of cells—the same cell lineage—in each individual. As a result, "until recently, nematodes were famously thought to be morphologically invariant," explains Armand Leroi, an evolutionary biologist at Imperial College in London.

But the more Leroi, Baird, and others study worm species that are closely related to *C. elegans*, the less consistency they see. In 1999, Leroi's examination of 13 of these relatives showed that their cell lineages were quite variable. Then Marie-Anne Felix, a developmental biologist at the Jacques Monod Institute in Jussieu, France,

Image not available for online use.

Image not available for online use.

Variation unveiled. The study of tail rays (*top*) of nematode worms (*above*) shows strain-to-strain differences in development.

CREDITS: (FISH) YOSHIYUKI YAMAMOTO AND WILLIAM JEFFERY/UNIVERSITY OF MARYLAND; (NEMATODES, TOP TO BOTTOM) S. E. BAIRD, *NEMATOLOGY* **3**, 373 (2001); S. E. BAIRD, *GENETICS* **161**, 1349 (2002) looked at the development of the vulva, a female sexual organ. She found that even there, where consistency would seem to be paramount to ensure proper mating, cell lineages that build the vulva varied quite a bit even within a species. As might be expected, such variation becomes even more pronounced between species.

Felix has since tracked down several genes that underlie this variation. "Variation is there," Baird says, "not necessarily hidden, but underutilized." The variation doesn't seem to interfere with the worms' development and doesn't seem to lead to speciation, at least not at this point in time. But that might not always be the case, says Jeffery: "Variations in a reproductive organ could in principle be a cause of reproductive isolation and subsequent speciation."

Baird unearthed variation of a different sort in his studies of sex determination in worms. He hybridized two *C. elegans* cousins, breeding different strains of the hermaphroditic *C. briggsae* with different strains of *C. remanei*, which has male and female members. To his surprise, the reproductive system in the offspring varied depending on the strains used. One mating might yield males and hermaphrodites; another, all hermaphrodites.

It seems that the sequences of the genes involved vary slightly, Baird has determined. That difference doesn't seem to matter when it comes to intraspecies matings. But it can cause havoc during hybridization. Baird observed that slight incompatibilities between the two species' genomes disrupted the normal determination of the sex of the offspring. "We are currently trying to map the genes responsible for that variation, and then [we] want to look at [base changes] to try to see what differences are affecting the interactions," Baird explains. Studying hybrids, he is uncovering variation in the sex-determining pathways that might otherwise go undetected. That hidden reservoir of individual differences might allow the species to adjust to environmental changes, he speculates.

Eyes at a price

Even as Baird and others track down the genes that make nematodes vary, Maryland's Jeffery has a gene in hand from his microevolutionary studies of a cavefish species found in Mexico. He has been looking at two populations of *Astyanax mexicanus*. One group lives underground and lacks functional eyes; the other lives at the surface and sees quite well. In exploring the genetic and developmental basis of this difference, he found a tradeoff: The blind cavefish had bigger jaws and more teeth than the surface ones. These traits, it turns out, are tied to the set of genes that also determine the development of eyes.

This led Jeffery to think that eyes disappeared only because the bigger teeth and jaws proved so advantageous in this new environment. When he began looking for how this evolution occurred, he discovered that it didn't take major genetic changes to tip development in favor of one phenotype or the other. Instead, he and his colleagues found that a slight alteration in where a gene called *sonic hedgehog* was active in the developing head caused eyes to form or not form (*Science*, 23 June 2000, p. 2119). "A fairly small change was able to give a fairly large phenotypic result," he points out.

These efforts exemplify the power of studying evolution on an ever finer scale. Evolutionary researchers such as Lynch hope their developmental colleagues will be inspired to go a step further in incorporating microevolutionary ideas into their thinking. "Often what is compared is just the end [physical and physiological appearance] rather than the actual developmental pathway that led to its production," he laments. He would like to see a more sophisticated approach in which researchers figure out the interplay between genetics and development, keeping in mind that changing either one too much or too fast will lead to organisms incapable of procreating. He also points out that factors such as the size of the population in which the variation develops and the number of genes that influence a changing trait need to be considered. Nonetheless, recent efforts signal that "people are starting to get on the same page about what needs to be done," he says. That should help make sense of the interplay between the micro and macro sides of evolution.

–ELIZABETH PENNISI

MEETING SOCIETY OF VERTEBRATE PALEONTOLOGY

A Bonanza of Bones

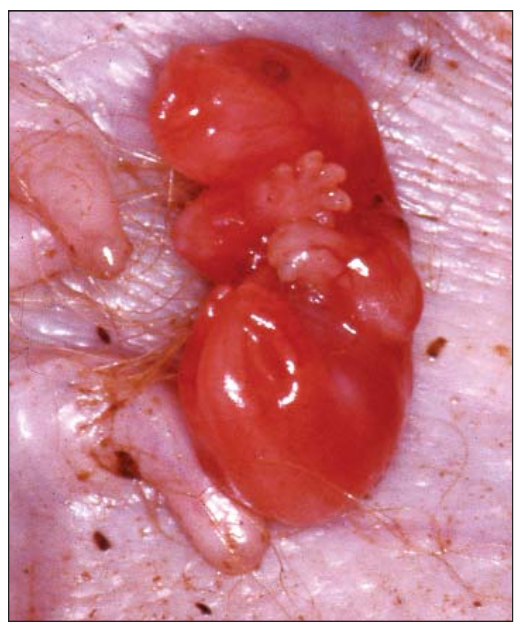
NORMAN, OKLAHOMA—Paleontologists came sweepin' down the plain to the 62nd annual meeting of the Society for Vertebrate Paleontology. From 9 to 12 October, some 1000 attendees heard about new ideas and specimens that spanned the taxonomic gamut.

Marsupial Shoulder Restraint

Placental mammals have evolved shoulder girdles capable of such diverse activities as powered flight, deep-water diving, and playing racquetball. Their marsupial cousins, on the other hand, never came up with forelimbs with these kinds of exotic shapes. Why? The standard answer is that the evolution of their shoulders has been hamstrung by a unique demand of marsupial reproduction: After birth, marsupials must make a life-or-death crawl to a teat in their mother's pouch, where they continue to develop.

Now Karen Sears, a graduate student at the University of Chicago, has tested this long-standing hypothesis for the first time and confirmed it. The results are "insightful and so extremely important for understanding the pattern of marsupial evolution," says Farish Jenkins, a vertebrate paleontologist at Harvard University.

In preparation for their crawl, fetal marsupials develop the bones of the shoulders and forelimbs much faster than the rest of their skeleton. They even temporarily fuse the shoulder blade and collarbone to get more power for the climb. Because important muscles attach to the shoulder blade, or scapula, its shape could have a large influence on how the shoulder girdle and forelimb develop. To check whether adults really are limited in their anatomy, Sears first measured the shape of these bones in 97 families of placental mammals and 21 families of marsupials.



All thumbs. Marsupial diversity is limited because newborns like this wallaby must develop large arms to crawl to a teat.

CREDIT: GEOFF SHAW/UNIVERSITY OF MELBOURNE, AUSTRALIA