Yichen Lu at the Virus Research Institute in Cambridge, Massachusetts, who has constructed different SIV-HIV hybrid viruses, called SHIVs, that differ in their ability to infect Langerhans' cells in test-tube studies. In Lu's experiments, monkeys given an intravaginal dose of the SHIV that favors Langerhans' cells were easily infected, while the ones given the SHIV that was nontropic for Langerhans' completely resisted infection.

Essex used this data as a springboard to hypothesize that there are two distinct HIV-1 epidemics. In developed countries, he argued, subtype B predominates and is spread primarily through blood and homosexual sex. In contrast, developing countries are experiencing "epidemic 2," which is driven by the other subtypes being spread primarily through vaginal sex (see table). "If other HIV-1 subtypes take hold in Western Europe or the U.S., we must predict a more significant heterosexual epidemic than we now see in the West," said Essex.

By and large, the response to Essex's presentation was enthusiastic. "I think he's on to something," said epidemiologist Sten Vermund of the University of Alabama, Birmingham. "I think it's highly plausible that E clade HIV could differ in its infectivity." John Mascola of the Walter Reed Army Institute of Research (WRAIR)—which first isolated subtype E—also found the talk provocative. "It's potentially extremely important," said Mascola. "Any single piece [of Essex's argument] is not compelling, but when he puts it together it makes a reasonably compelling case."

Still, some researchers had serious reservations about Essex's conclusions. Ann Duerr of the U.S. Centers for Disease Control and Prevention (CDC), in collaboration with Vinai Suriyanon and colleagues at Chiang Mai University, have been studying transmission rates between "discordant" couples—where only one is initially HIV-infected—in Chiang Mai. Although nearly 90% of these infections are subtype E, their work has shown that the rate of transmission is nearly identical to the rate found in a U.S. study that looked at discordant couples infected with subtype B. "The data I have on hand don't support [Essex's] conclusion," said Duerr, who cautions that they have not done a direct comparison of transmission rates of the two subtypes in their cohort.

Another wrinkle to Essex's theory, as William Heyward of the World Health Organization pointed out, is that subtype B is predominant in the Caribbean, Central America, and Brazil, and these regions all have primarily heterosexual epidemics. Essex countered that this discrepancy may be because anal intercourse is more common in these countries, although he offered no data to support that contention.

WRAIR's Donald Burke, who heads the U.S. military's AIDS program, said his group is now gearing up to do assays of different subtypes' ability to infect different cell types. Until the hypothesis gains more support, says CDC epidemiologist Timothy Mastro, who is based in Bangkok and heads the HIV/AIDS Collaboration, "the data are too thin to say it's true." But he notes: "The fact that there is this remarkable separation [of subtypes] is hard to explain."

–Jon Cohen

TWO HIV-1 EPIDEMICS

Category	Epidemic 1	Epidemic 2
Location	West (U.S., Europe)	South (Africa, S.E. Asia)
Cause	HIV-1B	HIV-1C, -E, -D, -A
Number infected	~1.5 million	15–20 million
Epidemic status	Plateau or decreasing	Increasing
Exposure route	Blood, rectal bleeding	Vaginal intercourse
Exposure cell	Monocyte, lymphocyte	Langerhans' cell

SOURCE: MAX ESSEX

ENDANGERED SPECIES

Minimum Population Grows Larger

When it comes to saving endangered species, Noah's ark offers little practical guidance. As population geneticists have long known, a single breeding pair can't provide enough genetic variability to allow a small population of their progeny to survive an array of environmental onslaughts or an accumulation of deleterious traits. But just how large a population must be to ensure long-term survival has been a matter of some debate. Back in the early 1980s, researchers estimated that at least 500 randomly mating individuals would be required. New studies of the genetics of small populations offer a much more sobering estimate: They suggest that a species must number 10,000 or more to maintain its evolutionary viability.

That's grim news for modern-day Noahs. Recovery goals for many endangered species are in the hundreds, so the new figures imply that current efforts—even if successful for years or decades—won't prevent extinctions hundreds of generations from now. "The implications are that in the very long run, our recovery plans may allow genetic damage to accumulate. Well down the road, we could lose what we've been trying to save," says Robert Lacy, conservation geneticist at the Chicago Zoological Society.

When researchers originally estimated the population size needed for long-term survival, they focused primarily on variation in quantitative, polygenic traits, which are determined by the effects of many different genes; height in humans is a common example. Such genetic variation, which arises by mutation, is important because it is the raw material of evolution. Over many generations, natural selection will favor the few beneficial mutations that allow species to adapt to changes in climate, pests, food, or other environmental factors. In the 1980s, researchers concluded that 500 randomly mating individuals (comprising what geneticists call an effective population) could supply enough variability.

"Well down the road, we could lose what we've been trying to save."
—Robert Lacy

Now population geneticist Russell Lande of the University of Oregon, Eugene, argues that these calculations underestimated the critical population size because they failed to consider the effect that these mutations have on the fitness of organisms. Lande's analysis, published in the August issue of *Conservation Biology*, is based on recent work in which other researchers, particularly geneticists Maria López and Carlos López-Fanjul of Complutense University in Madrid, studied mutations in quantitative traits such as the number of bristles on the abdomen of the fruit fly *Drosophila melanogaster*. The Madrid workers found that the most extreme mutations—those causing dramatic changes in bristle numbers—often had lethal side effects and so had no chance of spreading in the population.

Only mutations with little effect on fly survival and reproduction, the so-called quasi-neutral mutations, could be maintained in the population. But these mutations typically had much smaller effects on the trait, causing only about 10% of the total genetic variation in bristle number. To produce the same amount of variation from quasi-neutral mutations—rather than from all mutations as done in the original calculation—requires 10 times as many individuals, says Lande. This implies that the effective population size needed to preserve a species' evolutionary potential is 5000, not 500. Because the vagaries of mating make a population's effective size much smaller than its actual size, real-world numbers would be even higher—at least 10,000 and often even more, says Lande.

"What Lande has done is partition out the quasi-neutral mutations—the only ones potentially useful for evolution—from all new mutations. The resulting mutational input is lower than expected, so you need a much bigger population," explains geneticist Philip Hedrick of Arizona State University in Tempe.

That conclusion is further buttressed by studies in which Lande and his Oregon colleague Michael Lynch, who was working independently on similar questions, explored another genetic danger faced by small populations: an extinction spiral Lynch has christened "mutational meltdown." In this process, mildly deleterious mutations—whose effects are too small for them to be purged by natural selection—accumulate and become fixed in small populations. Their cumulative impact eventually leads to extinction.

In papers in this month's issue of *American Naturalist* and in press at *Evolution*, Lynch and colleagues John Conery, also at Oregon, and Reinhard Bürger of the University of Vienna use genetic models, computer simulations, and empirical data on mutation frequency to calculate that on time scales of 100 generations, effective populations smaller than 100 individuals are at risk. Lande, using a different genetic model, gets even higher numbers, estimating that an effective population of 1000 is needed to avoid mutational meltdown.

Although their estimates aren't identical, Lynch and Lande agree that when the effects of both genetic perils are considered, the old numbers need to be revised upward, to effective populations on the order of thousands rather than hundreds. Actual populations would be even higher. "The main point is that 500 is too low," says Lynch, who says that a "genetically safe" real-world population would be about 10,000.

All these new estimates are much larger than the populations of most endangered species. On average, only about 1000 individuals remain when an animal species makes the endangered list—and only about 120 individuals of plants—according to a 1993 study by the Environmental Defense Fund. The somber implication for those trying to save endangered species: They're going to need a much bigger ark.

–Elizabeth Culotta

PHYSICS

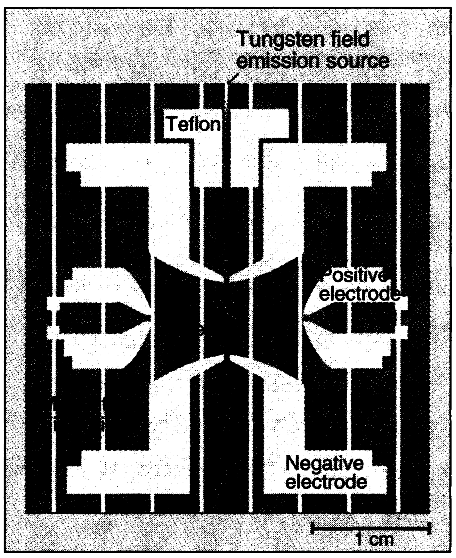
Electron Ball Probes 'House of Mirrors'

All theories strive for accuracy, but none succeeds more spectacularly than quantum electrodynamics. QED's predictions of how particles behave in electric and magnetic fields have held up to within a few parts per billion in some of its most demanding tests, which scrutinize the behavior of a single electron in an electromagnetic trap. Success has made experimentalists greedy for still more accuracy, however. They want to see whether tiny discrepancies between QED's predictions and their measurements result from flaws in the theory or in the experiments—and that means accounting for tiny perturbations introduced by the traps themselves. In an upcoming issue of *Physical Review Letters*, a group at the University of Washington reports a way to do just that, by first creating a superelectron that magnifies those perturbations, then scaling the perturbations down to a single electron.

The group's recipe for a superelectron is simple: Just confine a thousand electrons in the region of the trap ordinarily occupied by one. As a result, all of the electron's properties are multiplied, including one that has been the bane of experimenters: the tendency of the negatively charged electron to induce "image charges" in nearby conductors, which in turn subtly influence the electron's behavior. These image charges, says Richard Mittleman, one of the experimenters, cause a trap to behave like a "house of mirrors." They confuse the search for the slight deviations from QED that might point to a better theory, or perhaps suggest that the electron is not an indivisible particle.

But Mittleman and Washington colleagues Hans Dehmelt and Sander Kim found that an electron ball can amplify the house-of-mirrors effect. As a result, says Dan Dubin of the University of California, San Diego (UCSD), "you see the effect directly instead of having to evaluate it [theoretically]." And that should open the door to more accurate tests of QED with single electrons.

To create the electron ball, the team fired a beam of electrons into a standard electromagnetic trap, a device that can confine electrons along magnetic field lines capped with negatively charged end plates. The energetic beam knocked clouds of slower electrons from residual gas atoms in the trap.



Electrons by the kilo. A ball of 1000 electrons probes the effects of "image charges" on measurements in an optical trap.

These electrons eventually condensed into a ball less than 200 microns across.

Electrons caught in such a trap orbit the magnetic field lines at a rate known as the cyclotron frequency. For a single trapped electron, the ratio of this cyclotron frequency to the rate at which each electron's direction of "spin" precesses, or wobbles, gives a measure of the electron's intrinsic charge and magnetism and how it interacts with the fleeting "virtual" particles that populate free space, according to QED. That's where the house-of-mirrors effect comes in. For the comparison with theory, "you want to measure the properties of an isolated electron in empty space," says Dehmelt, but the image charges cause an unpredictable slowing or speeding up of the cyclotron motion.

Because a 1000-electron ball has the same charge-to-mass ratio as a single electron, its cyclotron frequency—in this case, 164 billion hertz—should also be the same, except for a stronger contribution from image charges. To tease out those effects, the team went on to trap smaller balls, containing hundreds fewer electrons. They saw the frequency increase by about 5 hertz for each electron removed. The increase implies that the image effect, at the same magnetic field strength, should slow a single electron by 5 hertz.

"It's a very nice experiment," says UCSD's Dubin, and it should help remove the largest remaining uncertainty in the single-electron tests. Others, such as Gerald Gabrielse of Harvard University, who has performed related measurements, want to see more data before they're convinced. "It would be nice to show that the [shift] is different at different magnetic field strengths," as theory predicts, he says.

The Washington team plans to go even further than Gabrielse suggests. Taking their cue from another theoretical prediction, they hope to find the precise field strengths at which "the whole frequency shift disappears," says Dehmelt. Then, by running single-electron tests of QED at those field strengths, Dehmelt hopes to feed yet another order of magnitude to the most ravenous obsession with accuracy in physics.

–James Glanz