of the Harvard-Smithsonian Center for Astrophysics argues that comets with nuclei in the 10-kilometer range, such as Halley's, are likely to be exceptions. Although observers have spotted a few of these outsized comets, he notes, they are more likely to be noticed than their smaller brethren, making them seem more common than they are. Since Shoemaker-Levy did nothing to distinguish itself before it broke up—it can't be found in images taken beforehand—it probably is small, says Marsden, that is, 1 to 2 kilometers in diameter. "It's going to be tough to see much," he concludes. "I don't think there's going to be a very large explosion."

Traces left by other comet impacts also suggest that the fragments will be small, Melosh says. He and Paul Schenk of the Lunar and Planetary Institute in Houston pointed out last fall that 13 linear chains of craters stretching up to 600 kilometers across the Jovian moon Callisto record the impacts of comets disrupted when they passed too close to Jupiter. The sizes of the original comets, as reflected in the lengths of the crater chains, vary widely, but the sizes of most of the craters tend to cluster around 10 to 15 kilometers, implying fragments with a fairly uniform size of around half a kilometer. Melosh and Schenk conclude that whatever a comet's size, it is likely to break up into these relatively small pieces, which they think may be comets' primordial building blocks. "The evidence is," says Melosh, "that when you shake a comet, it comes apart in pieces of about a half kilometer in diameter."

Although size is most important in determining whether there will be anything to see when the fragments slam into Jupiter, other factors will also come into play. Unfortunately, they are just as uncertain. The fragments would gain extra punch if they contain a high proportion of rocky "dirt," while their blows would be weakened if they consist of a fluffy aggregation of ice and dust. But comet experts can only guess at the density of the comet-stuff. Nor can theorists predict just how the fragments will behave during the impacts. Computer simulations have yet to agree on how deeply a 1-kilometer sphere of ice would penetrate, whether the impacter would ultimately explode, and how high the fireball might rise.

Perhaps the best advice for the observers who will be turning their telescopes toward Jupiter comes from Melosh: "I've been telling them it's best to cast as wide a net as possible. Theoreticians are often wrong, especially in predicting things."

–Richard A. Kerr

BIOCHEMISTRY

Finding Molecular Needles-in-a-Haystack

If you took a gram of protein and mixed it evenly in Lake Michigan, you might think it would be lost forever. But chemists Manfred Eigen and Rudolf Rigler claim that, given a sample of lake water, they could find one of the far-flung protein molecules within an hour and fish it out. While retrieving lost molecules from lakes may not sound useful, the chemists say they could also apply their single-molecule trapping scheme in the laboratory to find a single choice molecule lost among countless others: the one antibody in billions that binds tightest to its target, say, or the one enzyme that cuts another molecule most efficiently.

In last week's *Proceedings of the National Academy of Sciences*, Eigen, a Nobel Prize–winning chemist at the Max Planck Institute for Biophysical Chemistry in Göttingen, Germany, and Rigler, of Sweden's Karolinska Institute, describe their scheme, which combines fluorescent labeling with finely focused lasers and electromagnetic traps. Techniques such as the polymerase chain reaction already make it possible to home in on single molecules of DNA and RNA and amplify them, but Eigen and Rigler say their system can sort a wider variety of molecules for some desired property. Biochemist Richard Lerner, director of the Scripps Research Institute in La Jolla, envisions using it to mine useful but dilute compounds from the body, a strategy he thinks has "massive discovery potential." And Eigen and Rigler think it may prove most valuable in sorting though the billions of different molecules produced by so-called evolutionary biotechnology.

To identify a target molecule, Eigen and Rigler take advantage of specially designed dyes that fluoresce when illuminated with a laser. When linked to the desired molecule's target, the dye provides a way to home in on the unknown molecule itself. Ordinarily the fluorescence from a single molecule would be lost in background light resulting from the interplay of the lasers with the surrounding medium. In the late 1980s, however, Eigen and Rigler realized that the smaller the sample volume becomes, the less background they have to contend with, so they decided to scrutinize just a tiny volume—less than the volume of a single bacterium.

Using specially focused lasers, they created a tiny "light cavity," which can be kept stationary or scanned around the sample to hunt down the target. Small amounts of background light still trickle from the cavity into the light-sensitive detectors, but mathematical techniques enable the researchers to distinguish the steady fluorescent light of a single target molecule from the broken chirps of background. In 1991, says Rigler, the team demonstrated the detection of a single molecule of fluorescent dye.

Other researchers have matched that feat; chemist Richard Keller and his colleagues at the Los Alamos National Laboratory, for example, found a way to home in on single fluorescing molecules by shining a laser on a stream of sample flowing through a capillary tube. But Eigen and Rigler have now taken single-molecule hunting a step further, by adding a trap that is triggered when the molecule of choice is detected. As long as the target molecule has an electric charge—and most biomolecules do—the trap's electric field can separate it from other molecules that carry different charges, including leftover fluorescent dye. The trapping can thus eliminate false positives caused by unbound dye molecules. And because the electrodes are tiny pipettes, says Rigler, the apparatus can vacuum up the desired molecule.

Eigen and Rigler successfully tested their trap last year by snaring a single molecule of the nucleic acid base uracil. This ability to detect and trap individual bases, Rigler thinks, could be parlayed into a strategy for rapid DNA sequencing. Researchers would take apart an unknown sequence base by base, then identify and remove each base as it moved through the trap. Lerner, meanwhile, thinks the trapping ability might make it possible to identify and extract powerful trace substances in the human body, such as steroids and prostaglandins. "I think this is going to open the way for natural products chemistry in man," he says.

Besides harvesting compounds produced by evolution in nature, Eigen and Rigler add, their system could sift the products of an artificial version of evolution. By randomly altering the gene for, say, an antibody, then expressing it, researchers in evolutionary biotechnology can easily generate 10^{13} new versions of the antibody. To find the ones that bind most tightly to their target molecule, researchers mix the antibodies with the target, then alter conditions such as temperature or pH until only the most tenacious antibodies remain bound.

With current technology, it can take several sorting steps to narrow the field. Eigen and Rigler think that by homing in on the fluorescence from a single bound antibody, their system could go directly to the very best antibody of all—the one in billions that stays bound when all others dissociate. Once trapped, the antibody could be analyzed by spectroscopy. Rigler says they are now testing their ability to sift through 10^{11} variants, and they are working their way up to 10^{13}. That's almost as good as fishing a molecule out of Lake Michigan, and a lot more useful.

–Faye Flam