Standard Model, say Quinn and other physicists, and they hope to find it by studying CP violation, which shows up as a difference in the lifetimes of the B particles and their antimatter counterparts.

To measure these lifetimes with any reliability, however, these investigators need a machine that can make a million B particles per year—hundreds of times more than current accelerators can muster. That, in turn, requires a collision rate, or luminosity, 10 times higher than ever achieved before. "Each lab is pushing the state-of-the-art in luminosity," says panel head Kowalski. Both propose to do so by mating an existing accelerator with a new one. The two rings will accelerate electrons and positrons, the antimatter counterpart of electrons, in opposite directions and at slightly different energies. When the beams collide, the energy difference will give the B particles spawned in the collision a push away from the collision point, making it easier to track their decay into more stable particles.

In spite of the overall similarities, the designs differ in philosophy. Cornell's is widely considered more daring technologically—something the report is said to confirm. To SLAC director Burton Richter, it also "has some major risks." For one thing, Cornell's smaller rings will generate more synchrotron radiation because they will force the charged particles to move in tighter circles, and that can sap energy from the beam and throw it off course. Second, he says, Cornell is planning to use superconductors rather than the traditional copper in the radio-frequency cavities that will accelerate the charged particles—an untried innovation.

The biggest risk, Richter claims, is a novel plan to collide the beams of particles at an angle instead of head-on, as SLAC plans to do. The object is to fix the collision point precisely; the collision of two beams approaching from exactly opposite directions tends to get smeared out. To avoid that beam-degrading effect, Cornell has devised a way to angle the beams in a technique called "crab crossing," which brings them to a sharp collision point and keeps uncollided particles from traveling on into the other beam. "That's never been tried before," says Richter. Cornell has done some experiments with the technique, he says, but never employed it in a working accelerator.

To SLAC proponents, all that venturesome technology makes Cornell's low price tag alarming. SLAC physicist Michael Riordan charges that the Cornell people plan to build their accelerator on the cheap and tinker with it once it's running. That's the approach, he notes, that got SLAC itself into trouble with the Stanford Linear Collider.

But the head of the Cornell team, physicist Karl Berkelman, argues that their design comes at a lower price not because they are skimping on engineering, but because Cornell is starting with some advantages. For one thing, the existing accelerator at Cornell that would serve as the basis for the B factory is much smaller than its counterpart at SLAC, making it cheaper to build the second ring, says Berkelman. In addition, Cornell has a working detector, known as CLEO, while SLAC must build a new one.

Berkelman also argues that he and his colleagues have done plenty of computer simulations and small-scale experiments to show that their design should work. SLAC's decision to stick with tried-and-true technology, meanwhile, entails risks of its own, he says. SLAC's design forgoes a fancy beam crossing pattern, but as a result the beams run close to each other beyond the intended collision point, something he thinks might spell trouble with the torrential beams needed for the B factory. SLAC also risks excessive heat buildup by doing without superconductors in the accelerating cavities, he claims.

Richter, however, makes an argument that goes beyond the merits of the two proposals and invokes SLAC's history. The community has far more at stake in SLAC, he says, than in the lesser known Cornell lab. "Putting it [the B factory] at SLAC is the best choice for the long-term future of the field.... The government has invested a billion dollars in SLAC—we have been leaders in electron-positron physics," he says. "If you want to preserve the vitality of this lab in the future it makes a great deal of sense to put in a B factory."

But in these lean times, says one source at NSF, Cornell's low bid may be hard to resist. "The report says there is a top-rate lab, with a good record for B physics, that claims it can build [the facility] for $100 million less," says the source. "If it is not selected, someone will face some serious questions."

–Faye Flam

MEETING BRIEFS

Innovative Techniques on Display at Boston Meeting

Boston may be one of the United States' more tradition-laden cities, but a few weeks ago when more than 1800 exhibitors and scientists descended on Beantown for the ScienceInnovations meeting, the ideas they tossed about were anything but old. Here's a small sample of the talks that caught our eye.

Stepping Out With Kinesin

Steve Block, a biophysicist at the Rowland Institute for Science in Cambridge, generally draws a crowd at scientific meetings. His good humor and mixture of scientific data with video clips of tractor beams from "Star Trek: The Next Generation" have helped many an audience delight in the potential of "optical tweezers," a laser-based system that uses light gradients to trap and move objects cell-sized and smaller. At this year's Innovation meeting, however, Block eschewed his normal stump speech to report on what he called "the most exciting thing in science that I've been involved with."

The achievement that's got him so revved up? Block, his Rowland colleagues Karel Svoboda and Christoph Schmidt, and Bruce Schnapp of Harvard Medical School devised a new optical tweezers method that allowed them finally to measure the movement of a single molecule of kinesin, one of the important "motor molecules" that power the movements of the cell's internal structures (*Science*, 26 June 1992, p. 1758). It's only the second time that researchers have been able to document the motion of a single protein. (The first was when patch clamp techniques were used to watch the opening and closing of ion channels.) And it certainly won't be the last time. James Spudich, a cell biologist at Stanford University School of Medicine, says his group has also recently made use of optical tweezers to watch myosin, one of the molecules that power muscle contraction, take strides across actin filaments. Such methods have enormous potential, said Block: "If you want to look at the actions of a single molecule, this is the way to go. It opens up whole new avenues of research."

That would be welcome news to cell biologists. A wide variety of cellular activities, including muscle contraction, the separation of the chromosomes before cells divide, and in kinesin's case, the ferrying of small vesicles containing enzymes and other proteins through cells on tracks called microtubules, depend on the ability of motor molecules to convert the chemical energy stored in attached ATP molecules to movement. But despite years and even decades of study, researchers don't fully understand how motor molecules actually move. Does kinesin, for example, glide smoothly down the microtubules, or move more jerkily? And if the latter, does it take small steps or big ones? The an-

swers to questions like these might help settle such unresolved issues as how much force a kinesin molecule can exert or how efficiently it uses ATP.

The puzzle concerning how kinesin moves so intrigues Block that he calls the search for its solution the Great Step Hunt. Now, by combining optical tweezers with an optical interferometer that measures displacements as small as one angstrom (the diameter of a hydrogen atom), Block believes he has finally snared his quarry. "We have actually been able to see steps directly for the first time," he said. And those steps turn out to be tiny shuffles.

Block and his colleagues work with an artificial system that allows a single molecule of kinesin to strut its stuff. Instead of moving a vesicle, the motor molecule is attached to a microscopic bead. Optical tweezers then place one of these beads near a fixed microtubule, allowing the kinesin to latch on and slowly move the bead down the tubular track. Still, the movements are so small that steps cannot be discerned by direct visual observation, so the group also directs polarized light through the bead. As the bead shifts position, the displacement manifests itself by a change in the polarization of the collected light. The technique is so sensitive that, to tease out any true steps from background noise, Block's group must use the optical tweezers to dampen the bead's thermal motion. Moreover, the experimental system is vulnerable to small vibrations; it operates best after 1:00 A.M., when Cambridge's subway system shuts down.

Those late nights paid off. The Block group's experiments, to be published in *Nature*, show that a single kinesin molecule takes an 8-nanometer step when tethered to its microscopic bead. This is but a tiny stroll compared to the 100-nanometer leaps some investigators had hypothesized. Moreover, the result dovetails nicely with recent research from other labs showing that kinesin molecules naturally sit on microtubules at 8-nanometer intervals, a gap corresponding to the spacing of some of the smaller proteins of which microtubules are formed. Spudich's myosin measurements revealed a comparable step as well; the strides average 11 nanometers. While a few nanometers is definitely a very short distance, the ability to make measurements of this small stride is a giant step forward for the field of motor molecules.

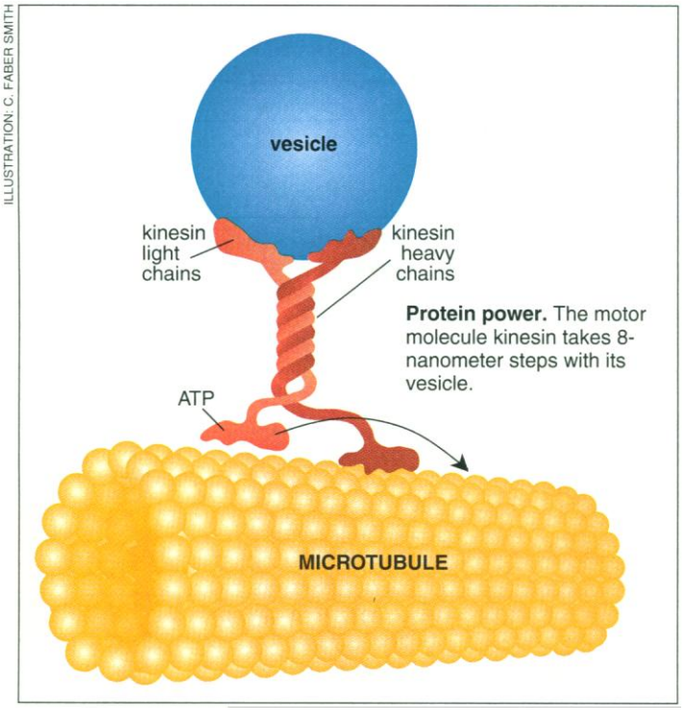

ILLUSTRATION: C. FABER SMITH

Protein power. The motor molecule kinesin takes 8-nanometer steps with its vesicle.

Slicing the Pro Off Proinsulin

Until recently, the islet cells of the mammalian pancreas had a unique ability. They alone in the body have the specialized enzymes and ability to create mature insulin, the protein hormone that's necessary for normal glucose metabolism. Now investigators at Genentech Inc. in South San Francisco, aided by some adept genetic engineering, may provide islet cells with some company by giving almost any type of cell the same talent.

The achievement may be important for diabetes gene therapy in the future, but that wasn't the original motivation for the work, explains molecular biologist Cori Gorman, who recently moved from Genentech to Megabios Corp. in South San Francisco. The Genentech team was simply looking for a more elegant way to maintain genetically engineered cell lines, such as those that make medically valuable proteins like the clot-buster TPA. These cell lines require insulin to grow, and the protein is often supplied by adding blood serum to the cell culture fluids. The catch, however, is that the serum may be contaminated with viruses and other microbes, and, because it has a high protein content, it also complicates the task of purifying the protein products made by the cells. Insulin by itself may be added, but it's expensive. So Gorman and her Genentech colleagues decided to explore a more direct approach: getting the cell lines to provide insulin for themselves.

The problem the researchers had to overcome is that islet cells make insulin as an inactive "prohormone." This proinsulin must then be converted to the mature active form by protease enzymes that clip out the middle portion of the prohormone protein, leaving behind two smaller peptides, called the A and B chains, held together in active insulin by disulfide bonds. The first hint that it might be possible to get other cells to make the active hormone came 3 years ago when, after many years of effort, researchers finally identified the proteases, known as PC1 and PC2, that in islet cells slice up proinsulin (*Science*, 10 May 1991, p. 779).

The Genentech group first thought that all they would have to do to achieve their goal would be to introduce the proinsulin gene into their target cells along with the genes for PC1 and PC2. But success wouldn't come that easily. "It's not simply the presence of these specialized enzymes that allows processing [of proinsulin to insulin] to occur," notes Gorman. In islet cells, the proteases concentrate in special vesicles that protect proinsulin from further degradation as the mature insulin is produced.

Trying to duplicate that condition would be just too complicated, if not impossible, so the Genentech workers took another tack. The hypothesis, recalls Gorman, was that "maybe we could fool the cells into processing proinsulin by modifying proinsulin." She, along with her then colleagues Debrya Groskreutz and Mark Sliwkowski, started altering the proinsulin gene to change some of the amino acids in the prohormone. The strategy worked. By replacing just three amino acids, they created a proinsulin molecule that could be whittled into shape by another protease called furin, which almost all cells make.

There was only one slight problem. Since furin processing does not occur in protected vesicles, the insulin produced was quickly broken down. Searching through the literature on insulin, the Genentech team turned up what they hoped would be a fortunate point mutation that might increase the hormone's stability. So the Genentech team changed one more amino acid in the proinsulin gene, creating a form of the protein that is indeed more resistant to unwanted degradation. And with that, they finally succeeded: Genentech now has insulin-producing kidney cell lines that can grow serum-free.

The success also raises the possibility, Gorman says, of using their modified proinsulin gene for gene therapy of diabetes. Since its product can be converted to active insulin in almost all kinds of cells, it might be possible to correct patients' insulin deficiency by putting the gene into kidney cells, say, or liver cells.

–John Travis