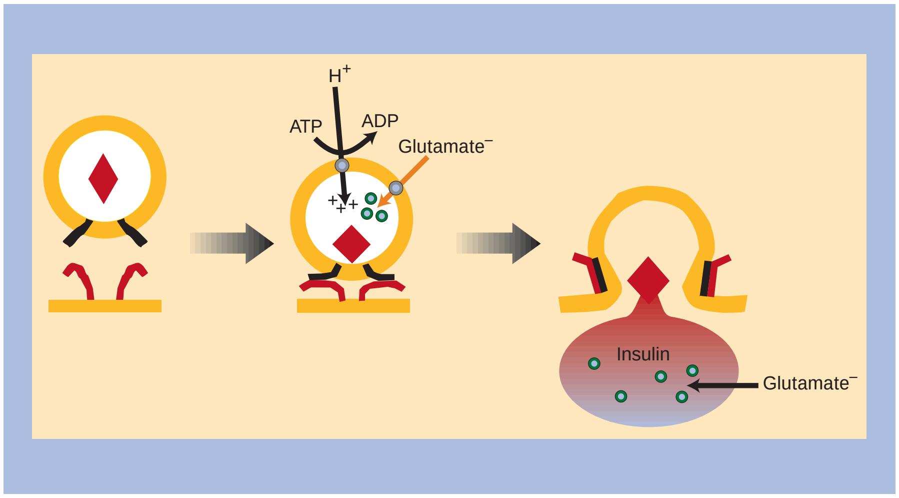

Figure 2 **Model to account for the effects of glutamate on granule priming, based, in part, on the results of Maechler and Wollheim[1]. The granular membrane contains v-SNAREs (black), whereas the plasma membrane contains t-SNAREs (red). The two membranes come together, and granule priming requires intragranular acidification. Glutamate uptake reduces the granular membrane potential, facilitating the pumping of H^+ ions into the granule.**

the activity of this proton pump can be envisaged as driving negatively charged glutamate into the secretory granules (although we still do not know how uptake of glutamate facilitates release). The identity of the glutamate-uptake mechanism in the β-cell is also not known, but pharmacological studies indicate that it is related to the mechanism documented in synaptic vesicles[7]. Maechler and Wollheim propose that glutamate acts by reducing the granular membrane potential, in which case it would act as a negative counter-ion, allowing a larger pH gradient to develop across the granular membrane (Fig. 2). In the absence of such a counter-ion, the large granular membrane potential that developed on proton pumping (positive inside) would quickly prevent further uptake of H^+ and, thus, acidification.

It seems wasteful of the β-cell to use glutamate in a process where it could easily be replaced by chloride or any other cytosolic anion. One possibility is that, once priming has been completed, glutamate also has an extracellular function similar to that in the central nervous system. Interestingly, ionotropic glutamate receptors have been documented in all types of endocrine cell in the pancreatic islet[8]. This points to the exciting possibility that glutamate coordinates the complex interplay between the different types of islet cell and their secretory products.

With the paper by Maechler and Wollheim, researchers should finally be able to get a firm grip on biphasic insulin secretion and its metabolic regulation. Secretion involves similar mechanisms in different cell types. So the functions that the authors have documented in the β-cell — namely, the role of glutamate and a low intragranular pH in the priming of secretory granules — may have counterparts in other secretory cells. Bafilomycin (an inhibitor of the vesicular H^+-ATPase) has, in fact, been reported[9] to abolish a late phase of glutamate release in neurons. In this context, it may be significant that vacuole acidification is required for the pairing of the SNARE proteins in yeast[10]. If this also applies to the SNAREs involved in the fusion between the granules and plasma membrane, then it is easy to see how granule acidification promotes secretion. The traditional view that a low intragranular pH is required for hormone processing and uptake may represent only one side of the coin. And as the coin is now tossed, we may discover that intragranular acidification is also essential for exocytosis itself. ■

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Nuclear physics

Taking serious risks seriously

Sheldon L. Glashow and Richard Wilson

Risk management is not a new idea: miners once used caged canaries as methane detectors. But modern technologies have made worldwide catastrophes imaginable — disasters so dreadful that we demand proof-in-principle that they cannot happen. Failures at nuclear reactors and chemical plants (such as Union Carbide in Bhopal, India) can kill or endanger many thousands of people. So the old protocol for risk avoidance — try it once; if it turns out to be dangerous don't do it again — is no longer acceptable. For example, scientists working on the Manhattan Project seriously considered whether a nuclear explosion could release enough energy to ignite the Earth's atmosphere. Their theories said no, and history has proved them right. But do we know enough about genetic engineering to proceed safely, or could someone unwittingly (or even deliberately) create a plague worse than the Black Death? For now, it's the physicists who are under the spotlight. The worry is that a new particle accelerator could trigger an irreversible process that would destroy our planet. It is a fair concern: one that must be raised, and one that has been answered decisively by scientists in the United States[1] and in Europe[2].

This latest doomsday vision relates to a unique facility now being completed at Brookhaven National Laboratory (Fig. 1). At the Relativistic Heavy Ion Collider (RHIC), beams of highly charged gold or lead atoms (the heavy ions) travelling at relativistic speeds (99.95% of light speed) will speed in opposite directions around circular racetracks before colliding. RHIC is truly an atom smasher: nucleus–nucleus impacts, taking place thousands of times per second, will each produce thousands of secondary particles. These incredibly complex 'events' will be recorded by sophisticated detectors and analysed at supercomputers or farmed out to a world consortium of smaller computers. RHIC will study matter at densities and temperatures never seen in the laboratory. On a small scale, it will reproduce the extreme conditions that reigned in the early Universe, conditions under which the constituents of ordinary matter are expected to be liberated as a quark–gluon plasma. Physicists have long speculated about this state of matter, but RHIC may soon let them glimpse it.

Meanwhile, the media and a concerned public demand to know whether these experiments could have unforeseen adverse consequences. The root of their anxiety may

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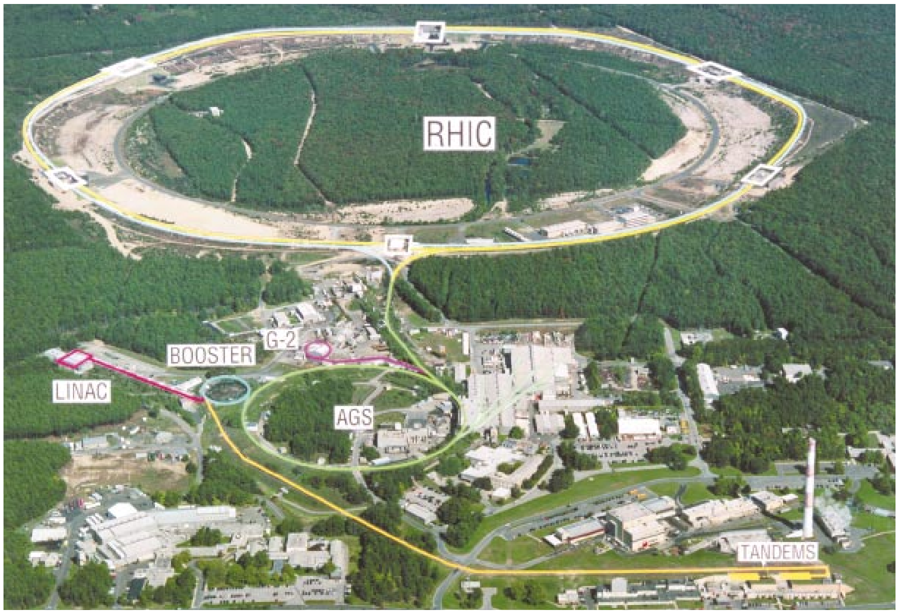

Figure 1 **Would RHIC wreck the world? Fears that the Relativistic Heavy Ion Collider at Brookhaven in the United States could trigger an unforeseen disaster have been allayed by new calculations[1,2] that show the risk of a worldwide catastrophe to be truly negligible.**

have been a comment by theorist Frank Wilczek in the July issue of *Scientific American*[3], which was picked up by a British newspaper. Later that month, the director of Brookhaven got together a panel of independent experts (including Wilczek) to investigate the reality behind the headlines. The report from Buzna *et al.*[1] identifies three conceivable disaster scenarios at RHIC: in which experiments produce 'black holes' that could gradually consume the Earth; a 'vacuum instability' that could expand catastrophically in all directions at the speed of light; or 'strangelets' — a stable kind of 'strange matter' — that would grow to incorporate ordinary matter, perhaps transforming the entire Earth into its form.

The first two issues have been raised, and dismissed, each time a new particle accelerator opens. Using similar arguments, Buzna *et al.* were able to conclude that neither poses any threat at RHIC. There is no chance at all that RHIC could manufacture a black hole or a gravitational singularity. Even if the RHIC (or its higher-energy successors) could create a black hole, it would be so tiny that it would evaporate instantly. Previous studies also argue against a vacuum instability, but cannot quite rule it out. In the natural world, relativistic heavy ions in the form of cosmic rays have been making RHIC-like collisions with one another in space for aeons (more, in fact, than will ever take place at RHIC). These distant collisions do not make RHIC experiments any less useful because they cannot be directly studied, but one fact is clear: cosmic-ray collisions in space have not led to the creation of a new vacuum, so we can breathe easily.

The third possibility is a new concern raised by the fact that RHIC accelerates heavy ions rather than individual elementary particles, and must be considered more carefully. This was done by Buzna *et al.*[1] and also by Dar *et al.*[2] at CERN in Geneva. Both groups include theorists who were among the first to speculate that lumps of strange matter called strangelets — which contain many strange quarks as well as the usual up and down quarks that make up atomic nuclei — might be more stable than ordinary matter. If strangelets exist (which is conceivable), and if they form reasonably stable lumps (which is unlikely), and if they are negatively charged (although the theory strongly favours positive charges), and if tiny strangelets can be created at RHIC (which is exceedingly unlikely), then there just might be a problem. A newborn strangelet could engulf atomic nuclei, growing relentlessly and ultimately consuming the Earth. The word 'unlikely', however many times it is repeated, just isn't enough to assuage our fears of this total disaster.

Once again, Mother Nature's own experiments with energetic cosmic rays have much to teach us. These natural processes produce collisions similar to those to be studied at RHIC, and in much greater numbers. Using different, but decisive, cosmic-ray arguments, the two groups[1,2] make a compelling case that RHIC will not produce dangerous strangelets. Buzna *et al.* use the Moon as their canary. Lacking a protective atmosphere, with a surface rich in mid-sized atoms such as iron, it is a plausible target on which incident cosmic rays of iron (or larger) nuclei with RHIC energies could produce strangelets. Yet countless collisions over billions of years have left the Moon intact. In contrast, Dar *et al.* consider heavy-ion collisions in space that are virtually identical to those at RHIC. Strangelets produced in this way would be swept up into stars where they could instigate supernova explosions or create ultra-bright stars (such as have never been seen). The low rate of supernovae — a few per millennium per galaxy — also makes this extremely unlikely.

Both of these groups, using worst-case arguments and sound empirical data, find the chances of a catastrophe at RHIC to be truly negligible: "Cosmic ray collisions provide ample reassurance that we are safe from a strangelet-initiated catastrophe at RHIC"[1], and "Beyond reasonable doubt, heavy-ion experiments at RHIC will not endanger our planet"[2]. Amen. Even though the risks were always minimal, it is reassuring to know that someone has bothered to calculate them. Now, the only conceivable disaster at RHIC would be a costly failure to detect the fabled quark–gluon plasma. ■

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Neurobiology

The topography of memory

Howard Eichenbaum

For more than 40 years neuroscientists have explored the cerebral cortex with microelectrodes, recording the electrical activity of single neurons while 'tickling' them with different stimuli. Early investigators found that the cortical areas responsible for initial processing of sensory information yielded their secrets relatively easily[1,2] — for each area, a small set of simple sensory features that activate the neurons could be identified. Many of these features have since been found to have a systematic anatomical organization; they are mapped onto the surface of the cortex, and the topographies for different sensory features are interleaved within each cortical area.

Since those early successes, the feature-coding properties of other cortical areas,