ments on the ends of chromosomes; centromeres, which serve as attachment points for the protein fibers that pull duplicate sister chromosomes (chromatids) apart during cell division; and origins of replication, DNA segments where the double helix can unwind and begin to copy itself. "YACs showed us that this type of thing could be done in yeast, but there was no guarantee that it could be done in human cells, because human chromosomes are much more complex," says molecular biologist Gil Van Bokkelen, president of Athersys and a co-author of the *Nature Genetics* paper with Case Western researchers John Harrington, Robert Mays, Karen Gustashaw, and senior author Huntington Willard.

The members of the Ohio team believe that they succeeded because they decided to add non–protein-coding "satellite DNA," repeated sequences of five to 171 base pairs found near mammalian centromeres, to their HAC recipe. Some researchers regard the satellite sequences as nonfunctional "junk DNA," but from earlier studies, Willard's team had concluded that the alpha type of satellite is actually the centromere's main component.

In the current work, the researchers first devised a way to build long strings of alpha satellite DNA. They then inserted the satellite arrays into cultured human tumor cells, together with DNA fragments from telomeres and plain "genomic" DNA, including origins of replication. Some of the satellite arrays combined with DNA fragments, forming microchromosomes 6 million to 10 million base pairs long. These apparently replicated when the tumor cells divided, because 6 months later, the progeny cells still contained HACS.

To use HACs to uncover more about how real chromosomes work, experimenters will need a more reliable method than the current vehicles—lipid bubbles called "lipofectins"—to get HACs or their ingredients into cells. But with refinements, Willard says, HACs could help settle just what centromeres are made of and a host of other questions in molecular biology and biomedical research.

In addition, any gene sandwiched between the synthesized satellite arrays and telomeres would, in theory, behave like a gene on a regular chromosome, because it would be accessible to enzymes, transcription factors, and the other machinery of gene expression and replication. Thus, HACs could give biologists a new way to study gene activity in human cells and gene-therapy researchers a new way to transfer needed genes into patients' cells. "YACs really aren't good for that—they are not stable in human cells," says Louis Kunkel, a leading muscular dystrophy researcher at Children's Hospital in Boston. "This is a neat alternative."

–Wade Roush

PHYSICS

New Proof Hides Cosmic Embarrassment

Stephen Hawking is betting his shirt again. Earlier this year, the Cambridge University astrophysicist conceded one wager about the hypothetical ruptures in the laws of nature called singularities. This time, Hawking has a better chance of winning, according to a new theorem by Princeton University's Demetrios Christodoulou to be published in the *Annals of Mathematics*.

The original bet, made in 1991 between Hawking and two physicists at the California Institute of Technology—Kip Thorne and John Preskill—concerned whether "naked" singularities could ever form in the universe. Singularities, points of infinite density formed when matter or field energy collapses, are hypothesized to exist within black holes, which "clothe" them, but Preskill and Thorne argued that under just the right circumstances, they might also form on their own. Hawking insisted that they cannot.

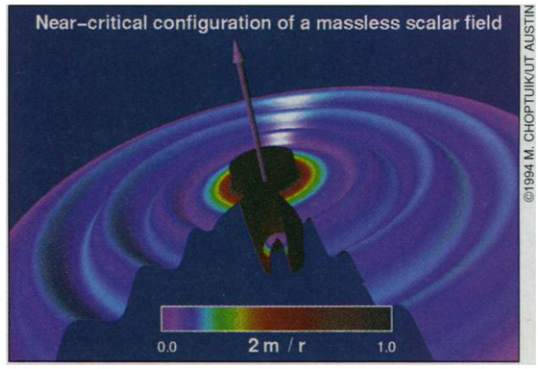
This may sound like a recondite dispute among specialists, but it strikes at the heart of what cosmologists think they know about the fabric of space and time. "I would consider it the most significant question that can be posed entirely within the confines of classical, general relativity," says Robert Wald, a cosmologist at the University of Chicago. Because Einstein's mathematical description of space-time breaks down at singularities, they would in effect throw the universe into unpredictability if they could be observed and their effects felt. "It's ignorance where ignorance really matters," says Christodoulou.

In the 1970s, Oxford University's Roger Penrose had offered some reassurance with his "cosmic censorship" conjecture, which said that singularities could never be directly observed because they would always be shrouded in black holes, from which even light can't escape. Hawking has drawn on the conjecture in some of his best known work, but Preskill says that "it would not be that surprising or terrifying to me if [cosmic censorship] weren't true." Thorne agreed, leading to the 1991 bet.

"Unfortunately, I wasn't careful enough about the wording of the bet," Hawking said during a symposium on black holes in Chicago last December (*Science*, 24 January, p. 476). The wording didn't exclude naked singularities born in circumstances likely to be extremely rare in nature—for example, conditions precisely poised between black-hole formation and a less drastic collapse. Such naked singularities are allowed theoretically, according to earlier work by Christodoulou and computer calculations by Matthew Choptuik of the Center for Relativity at the University of Texas, Austin.

"Kip and I started pressing Stephen that, well, he should pay up," says Preskill. A story in the 12 February *New York Times* reported that Hawking had finally decided to settle the wager, which required the loser to hand over clothing embroidered "with a suitable concessionary message." Hawking's chosen message, printed on a T-shirt: "Nature abhors a naked singularity."

"We said, 'This is a concession? It sounds like fighting words,'" recalls Preskill. But Christodoulou's new theorem lends support for Hawking's not-so-concessionary posture, by proving mathematically—without the approximations of the earlier computer calculations—that infinitesimal changes to the special, naked singularity–forming collapses will produce black holes instead. The proof assumes that the matter or energy collapses spherically, so it doesn't rule out the possibility of naked singularities born in more complicated geometries. But for spherical collapses, it shows that Christodoulou and Choptuik's earlier solutions "were very much of the character of a pencil standing on end," says Wald. "In nature, you're never going to find pencils standing on their ends." In light of his new theorem, says Christodoulou, "I don't think [Hawking] should have paid up."



Censored. Collapsing shells of field energy (ripples) form a singularity cloaked within a black hole.

Now, the original participants have laid a new wager. The bet is the same, except that it is now limited to naked singularities that might develop from "generic"—meaning not unstable or impossibly rare—initial conditions. And this time, says Preskill, the clothing must be embroidered with a "truly" concessionary message. Although Christodoulou's proof says nothing about nonspherical collapses, Hawking says he isn't worried: "The world is safe from naked singularities, at least in classical general relativity."

–James Glanz