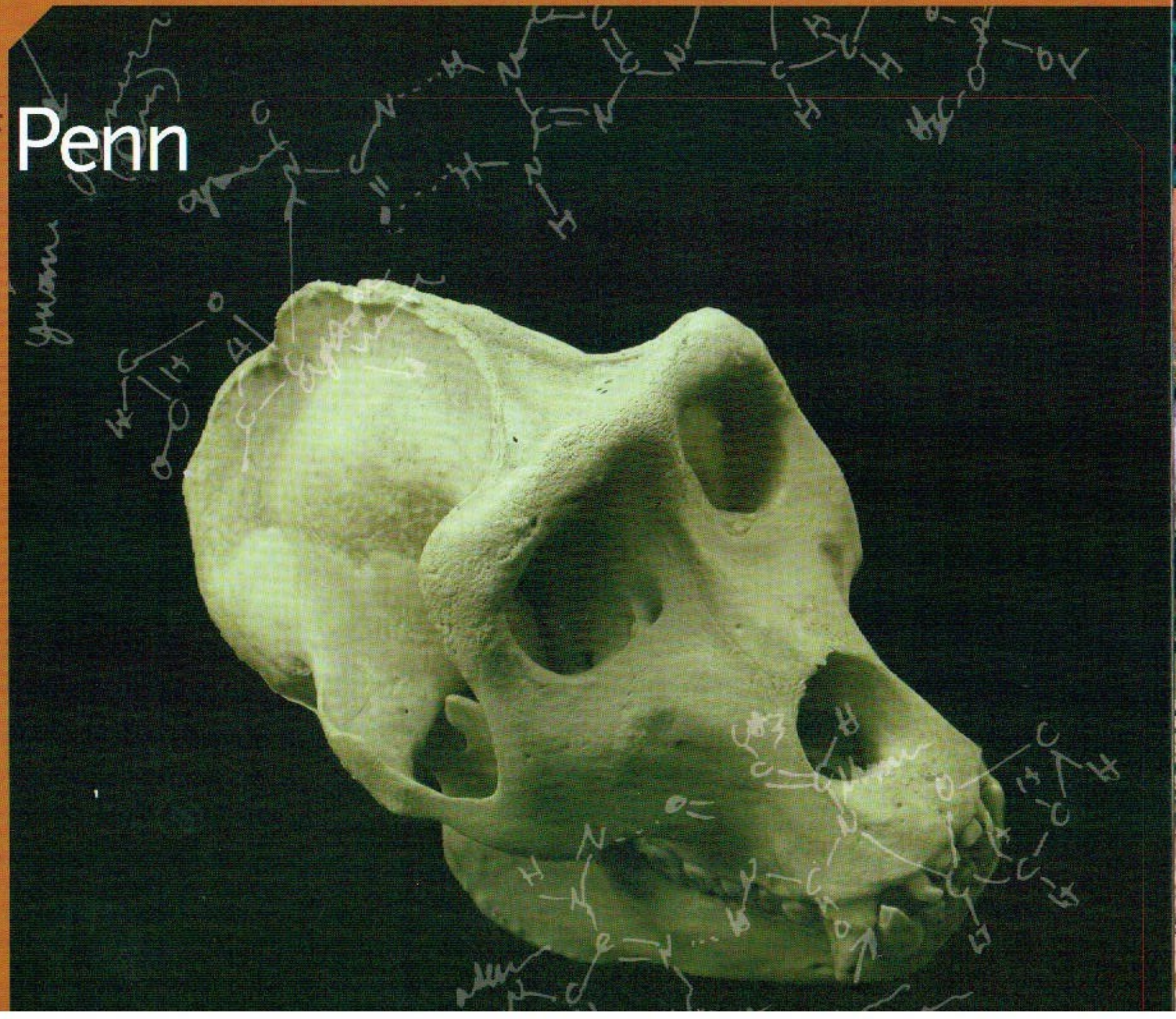
HEALTH | NATURAL SCIENCE | TECHNOLOGY | SOCIETY | BUSINESS

Research *at* Penn

Advances in Knowledge from the University of Pennsylvania



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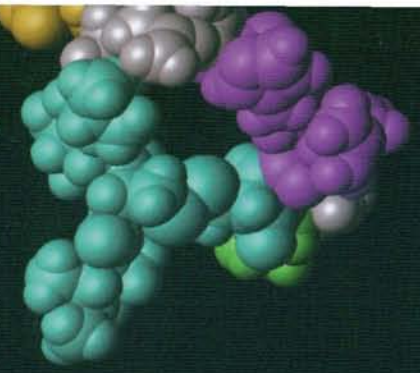


Computer Takes Guesswork out of Refining Drugs

TECHNOLOGY

COMPUTER SCIENCE

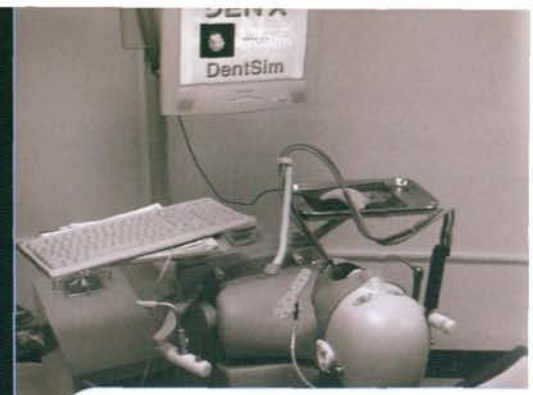
IT'S ONE THING TO CREATE A NEW MEDICATION, BUT QUITE ANOTHER TO PERFECT IT. FOR PROTEIN-BASED DRUGS, REFINEMENT OFTEN FOLLOWS THE TRIAL-AND-ERROR APPROACH—CHANGING ONE AMINO ACID AT A TIME to see if it makes the protein more stable or makes it bind to its target with a higher degree of accuracy.

In an effort to refine the protein fragment, or peptide, called Compstatin, researchers at the University of Pennsylvania demonstrated the work of honing potential drugs can be reduced by taking an "in silico"—or, "by the computer"—approach instead of relying on traditional lab work. Compstatin, discovered in 1996 by Penn professor John D. Lambris, shows promise in preventing complement-mediated tissue damage in several diseases.

With funding from the National Institutes of Health, Lambris worked with colleagues at Princeton University and the University of California, Riverside, to develop a modeling system that would calculate all the possible configurations of Compstatin that occur if you substitute one or more links in the peptide's chain of amino acids at a time. The computer modeling and optimization process quickly created a version of Compstatin many times more efficient than the original peptide.

Using a network of 80 Linux-based computers, the modeling program selected and ranked sequences for a particular fold of a virtual peptide. Once the computers made their predictions, the best of the new peptides were subsequently synthesized and experimentally validated in the Lambris laboratory.

"It would have taken us years to synthesize and screen the 80 quadrillion possible peptide sequences that the protein design program considered," says Lambris. "In the end, combining the 'in silico' approach and rational design we came up with an analogue of Compstatin—created by altering three amino acids—that is 220 times more effective than the original peptide."



Dental Student High-Tec

IN PENN'S DENTSIM LAB, STUDENTS LEAN OVER TEETH MODELS IN THE MOUTHS OF PLASTIC MANNEQUINS AS INFRARED ATTACHMENTS TRANSMIT THEIR DRILLING technique onto a mounted computer screen. The computer displays a virtual image of the tooth and indicates the ideal drilling position. If students drill too deeply, the computer responds with an audible "ping."

This is the newest technology in dental training, and it's also proving to be the most effective. Research at the University of Pennsylvania School of Dental Medicine shows that the cutting-edge computerized technique known as DentSim is enabling future dentists to sharpen their skills faster.

With funding from computer manufacturer DenX and Penn's University Research Foundation, Judith Buchanan, associate dean of academic affairs and associate professor of community oral