SCIENCE NEWS of the week

New Vehicle for Reliable Gene Transplant

In a novel approach to genetic engineering, scientists have successfully moved genes from one strain of fruit fly into other flies. "We are the first to make a really stable modified strain with a different genetic property," says Gerald Rubin of the Carnegie Institution in Baltimore. In work with Allan Spradling, Rubin employed a natural element of the fruit fly genetic material. It is a transposon, a segment of DNA that naturally moves around within the chromosomes.

"The main reason for all the excitement is that the genes are stably inherited in future generations and correctly expressed," Rubin told SCIENCE NEWS. He contrasts the fruit fly results with recent work on mice using animal viruses as carriers or simply injecting genes without any special carrier (SN: 10/16/82, p. 252). In this work the transplanted genes often are present in the recipient animals, but they are usually not functional. When they are expressed it is only at a small fraction of the normal level and not in the appropriate tissues, for instance a blood protein is made in muscle but not in blood cells.

In early work on the new technique, Spradling and Rubin isolated a movable segment, called the P element. They injected copies of the transposon into fruit fly embryos shortly after fertilization and later found the P element stably incorporated into the chromosomes.

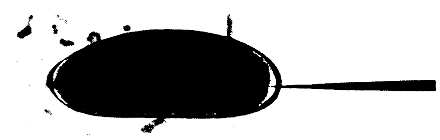
With recombinant DNA techniques in their next experiments the scientists replaced part of the transposon with a gene of their choice. The gene first used in these experiments is one responsible for a fly's red eyes and so is called "rosy." They inserted this gene, in a P element, into embryos that would otherwise have matured into flies with brown eyes, the eye color of flies lacking the rosy gene. As many as half the flies that developed from the treated embryos produced some progeny with red eye color instead of brown. Descendants of these red-eyed offspring also had red eyes. Thus the brown eye color was completely and permanently corrected by the transferred gene. In some cases the gene inserted itself in the fruit fly chromosomes near its natural site. In other cases it took up residence in other chromosomes.

Since the early experiments, the Carnegie scientists and others have transferred five or six genes and have shown them to work properly, Rubin says. The transposon technique has enabled the scientists to bypass a difficulty of previous work: the unpredictable rearrangement of the DNA being transferred. Rubin explains that it is crucial to demonstrate that natural, intact genes work correctly after being transplanted. Then scientists can do experiments to examine how genes are normally regulated and do genetic engineering by altering genes before inserting them into animals.

Although the results of Spradling and Rubin were just published in the Oct. 22 SCIENCE, approximately 70 laboratories are already using the technique with material supplied by the Carnegie scientists. Some of the researchers are trying to use the P element to carry genes into species other than fruit flies. Scientists are trying the technique on mice, plants, frogs and nematodes (microscopic worms), Rubin reports. He and Spradling suggest that even if the P element is not successful in these other species, it should be possible to select similar movable elements native to other organisms and employ them in gene transfer. Transposable elements were first discovered more than 30 years ago in maize by Barbara McClintock, who is now at the Cold Spring Harbor Laboratory.

A special characteristic of transposons gives the scientists control over the movement of genes to make the transplanted genes stable. In their genetic engineering, Spradling and Rubin remove from the natural P element a gene that codes for an enzyme required for the transposon to insert itself into a chromosome. During the initial transfer, they provide this missing gene on another transposon. But in later generations, the enzyme is insufficient for the transplanted gene to move out of the chromosome again. Spradling and Rubin find no limit to the size of gene that can be transferred in a transposon, except perhaps the length of DNA that can be conveniently prepared with recombinant DNA techniques.

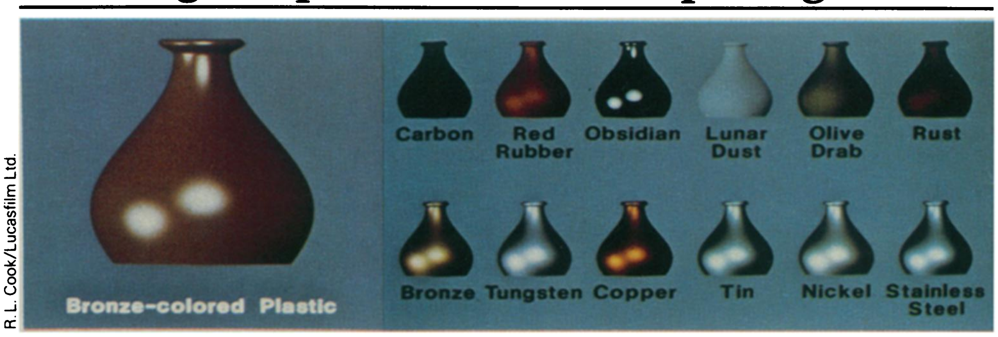
Although Rubin and Spradling are providing investigators with cloned P elements, the Carnegie Institution has filed a patent application. Rubin says he hopes some of the money that may be generated by industrial uses will come back to the place where the technique was developed. *—J. A. Miller*



Carnegie Institution

DNA is injected into the posterior end of a fruit fly embryo 0.5 millimeters long.

Avoiding the 'plastic look' in computer-generated



R. L. Cook/Lucasfilm Ltd.

Computer-graphics developers have made great strides in producing computer-generated images that look realistic. Or almost realistic. A problem plaguing most graphics programs is that computer-synthesized images appear to be made out of plastic. It's all due to "a misunderstanding" about how to model the reflectivity of a computer image's theoretical surface, explains Rob Cook at Lucasfilm Ltd.'s computer-graphics laboratory in San Rafael, Calif. And at Siggraph 82, a computer-graphics conference recently held in Boston, Cook offered a mathematical cure for the graphics industry's plastic-image problem.

In realistically modeling an illuminated object, three types of reflection must be considered: ambient, diffuse and specular. And Cook notes that nonhomogeneous objects — like a waxed apple — "may have different reflectance spectra for each."

The ambient component represents light that is assumed to be uniformly incident from the environment and that is reflected equally in all directions by the object's surface. (It's the type of illumination provided by a bright, overcast sky.) Diffuse and specular components are associated with light from specific sources, such as a lamp or the sun. The diffuse portion involves light scattered equally in all directions, while the specular component represents highlights — light that is concentrated around "the mirror direction" (bouncing off the object at an angle that is equal to, but complementary to, the incoming light, as measured from a reference line perpendicular to the reflecting surface).

In the past, Cook explains, when people computed an object's reflectance components, they assumed ambient and diffuse components were the color of the object and that the specular component was the color of the light source — generally close to white. But, Cook found, "the specular component is usually the color of the material [doing the reflecting], not the color of the light source."

Biological structure, nature of matter are topics of Nobel prizes

The 1982 Nobel prizes in physics and chemistry went to scientists from the United States and Britain, respectively. Aaron Klug of the Medical Research Council Laboratory of Molecular Biology in Cambridge, England, was awarded the chemistry prize "for his development of crystallographic electron microscopy and his elucidation of biologically important nucleic acid-protein complexes." Kenneth G. Wilson of Cornell University won the physics prize for his theoretical work on the behavior of matter.

Klug, who is originally from South Africa, has worked to determine the detailed conformation of what chemists call "large structures" or "macromolecular assemblies." Such aggregates of molecules as simple viruses and cell components are too large for the conventional X-ray diffraction techniques, but still too small to be viewed with a light microscope.

Klug devised methods for applying electron microscopy to such biological structures. "We were forced to develop apparatus and techniques to tackle things that are difficult," Klug told SCIENCE NEWS in an interview in Cambridge last year.


J. A. Miller


Cornell Univ.

Chemistry award goes to Aaron Klug (above) for elucidating biological structures, physics award to Kenneth G. Wilson (right) for work on phase transitions.

Among the techniques developed by Klug is optical diffraction of micrographs to analyze repeating structures in viruses, muscle and flagella. Klug also employed densitometers and digital computers to interpret electron microscopic images. An important process he developed takes a number of electron micrographs, viewing a specimen from different angles, and constructs the complete structure as a three-dimensional contour map.

Klug has applied the image processing and reconstruction techniques to a variety of problems. He is well-known for his detailed analysis of how the tobacco mosaic virus assembles itself. He says this work was most important for its working out of the techniques. "It was a workhorse for methods," Klug says. "No other system is known in such detail."

The simple virus, a strand of nucleic acid encased in a rod of stacked protein units, aggregates from a flat disk of protein units with an RNA loop inserted into its center. Klug and colleagues determined the structure of the disk at a resolution of better than 3 angstroms to get a detailed atomic model. The virus grows by adding disks that interact with the RNA. Klug says, "This is what we're now aiming for with chromatin [the material of chromosomes]—the interaction of structure and chemistry."

In recent work Klug has described the three-dimensional structure of nucleosomes, the bead-like repeated chromosome subunits made up of proteins, called histones, and DNA. The "very surprising" finding was that the DNA chain wraps around clusters of histones. "It's not beads on a string but a string on beads," Klug says. He and co-workers determined that 166 nucleotide pairs of DNA superhelix make a ramp winding two full turns around a core of eight protein subunits. A separate histone on the outside seals off the nucleosome. Klug says, "The structure of the nucleosomes give a hint as to how things work inside the cell."

The 1982 Nobel prize in physics goes to Kenneth G. Wilson of Cornell University for work on the theory of phase transitions in physical systems. Phase transitions are changes in the way some substance is ordered, such as the change from liquid to gas or from paramagnetic state to ferromagnetic state. Most often phase transitions are induced by changes in temperature, but they can also result from changes in other ambient conditions (chemical balance, for example). The work for which Wilson is cited involved discovering a way to calculate what happens in phase transitions in spite of difficulties engendered by widely varying distance scales.

A problem in physics usually involves a distance scale, that is, a degree of refinement of detail, proper to itself. Calculation can ignore other scales. For example, calculating the orbits of the planets involves distances in the millions of kilometers. The person doing this calculation works on that scale without having to worry about changes taking place on the scale of the molecules or atoms in those planets. Conversely, a scientist working on nuclear structure is concerned with a scale of a few fermis; what is happening at the same time on the moon is not of interest.

Phase transitions, however, do not have this simplicity. Scientists trying to follow the changes in important properties of a substance undergoing a phase transition find that those properties undergo complicated fluctuations in which a wide variety of distance scales are involved. This circumstance led to extreme mathematical difficulty. Wilson is credited with putting together a comprehensive and simplified theory that permits the calculation to be done. Phase transitions are most commonly encountered in the physics of solids and liquids, but they play crucial roles in such branches as astrophysics, nuclear physics, particle physics and cosmology.

A native of Waltham, Mass., Wilson was educated at Harvard University and California Institute of Technology. He has been a professor at Cornell since 1971.

—*J. A. Miller, D. E. Thomsen*

color images

The mistake was moot for objects like plastic or a waxed apple, whose surfaces were white. For homogeneous surfaces like metal, the mistake was disastrous. Cook explains why: Wax, or plastic—even colored plastic—is typically composed of a transparent or white substrate whose hue is achieved by embedding particles of colored pigment into it. Therefore, light reflected directly from the surface — a specular reflection — "is only slightly altered in color from the light source," Cook says: It would essentially be white. Only reflections penetrating the surface could be expected to interact with the pigments enough to acquire a colored, uniformly distributed diffuse spectral quality.

With metals, incoming light barely penetrates the surface, so all reflection "essentially occurs at the surface," Cook explains. To model the proper spectral distributions associated with metals, painted surfaces or other materials, Cook recommends consulting tables of standard thermal-radiative properties for values to plug into mathematical formulas described in the paper he co-authored with Kenneth Torrance in the ACM TRANSACTIONS ON GRAPHICS (Vol. 1, No. 1).

The proof is in the seeing. A computer-generated bronze-colored vase (left) was computed using a white specular component, and appears to be made of plastic. Similar vases (right), computed with thermophysical spectral data from standard-reference tables, exhibit more realistic metallic and matte finishes. —*J. Raloff*