with a pupil 2.4 mm in diameter. All three avian functions are substantially superior to estimates of maximum human performance (*8, 14*). When measured by identical methods, human optics at best cut off at approximately 60 cycle/deg (*8*); the eagle cutoff at 120 cycle/deg (Fig. 2) is twice the human value and may yet improve at smaller pupil diameters.

How superhuman might an eagle's visual acuity be? From published sections of heads of diurnal rapacious birds (*5*) I estimate the ratio of the width of the skull just posterior to the lateral canthus, to the axial length of the eyeball, to be 2 : 1. I have measured that skull width on four preserved specimens of *Dryotriorchis spectabilis* and obtained a mean of 48 mm, which corresponds to an eyeball length of about 24 mm. For the eye of a Golden Eagle 29 mm long, Rochon-Duvigneaud estimated a focal length of 19 mm (*10*). When this is scaled down, the African Serpent Eagle will have a focal length of 15.5 mm, compared to the human's 17 mm (*15*). The theoretical resolving power of the retinal mosaic is proportional to the square root of receptor density; from hawk data (*1*) the ratio to human (*2*) foveal resolution is then 2.6 : 1. After correction for optical magnification, this becomes approximately 2.4 : 1. It is impossible to characterize a transfer function by a single number, but on the basis of cutoff frequencies the eagle to human ratio is 2 : 1. It seems fair to conclude that the visual system of the eagle under test may be capable of from 2.0 to 2.4 times human resolution. On the basis of size the Golden Eagle *Aquila chrysaetos* might reach 2.4 to 2.9 times, and the Martial Eagle *Spizaetus bellicosus*, which is reported to have an eye 36 mm long (*4*), might reach 3.0 to 3.6 times human visual acuity.

In evaluating avian visual performance, certain other factors should be kept in mind. If examined in ordinary (probably tungsten) light, many diurnal birds are somewhat hyperopic (*5, 16*). When chromatic aberration is taken into account, this refraction will allow birds to accommodate to distant objects in blue light, something an emmetropic human eye cannot do (*17*). Avian ability to detect objects against the sky should therefore be enhanced. Secondly, the small size of eagle cones with respect to the wavelengths of visible light (*1, 4–6*) means that they are inefficient absorbers of radiant energy. Consequently, the photopic visual performance of eagles must fall off very rapidly as luminance decreases.

ROBERT SHLAER*
Center for Visual Science,
University of Rochester,
Rochester, New York 14627, and
Department of Theoretical Biology,
University of Chicago,
Chicago, Illinois 60637

References and Notes

1. A. Rochon-Duvigneaud, *Ann. Ocul.* **156**, 717 (1919).
2. G. A. Osterberg, *Acta Ophthalmol. Suppl. No. 6* (1935).
3. A. Rochon-Duvigneaud, *Ann. Ocul.* **156**, 376 (1919).
4. ———, *Recherches sur l'Oeil et la Vision chez les Vertébrés* (Barneoud, Laval, 1933).
5. ———, *Les Yeux et la Vision des Vertébrés* (Masson, Paris, 1943).
6. S. L. Polyak, *The Retina* (Univ. of Chicago Press, Chicago, 1941); *The Vertebrate Visual System* (Univ. of Chicago Press, Chicago, 1957).
7. G. L. Walls, *The Vertebrate Eye* (Cranbrook Institute of Science, Bloomfield Hills, Mich., 1942).
8. F. W. Campbell and R. W. Gubisch, *J. Physiol.* **186**, 558 (1966).
9. S. Shlaer, *J. Gen. Physiol.* **21**, 165 (1937).
10. A. Rochon-Duvigneaud, *Bull. Soc. Sci. Natur. Maroc* **8**, 160 (1928).
11. L. Brown and D. Amadon, *Eagles, Hawks and Falcons of the World* (McGraw-Hill, New York, 1968), vol. 1; M. L. Grossman and J. Hamlet, *Birds of Prey of the World* (Potter, New York, 1964).
12. G. Black and E. H. Linfoot, *Proc. Roy. Soc. Ser. A.* **239**, 522 (1957).
13. For incoherent monochromatic illumination the transfer function of a diffraction limited optical system having a circular aperture is given by:

$$T(u) = \frac{1}{\pi}\left[-\sin\left(2\cos^{-1}\frac{u\lambda}{d}\right) + 2\cos^{-1}\frac{u\lambda}{d}\right]$$

where u is spatial frequency in cycles per radian, λ is the wavelength of the light, and d is the diameter of the entrance pupil.
14. F. W. Campbell and D. G. Green, *J. Physiol.* **181**, 576 (1965).
15. H. L. F. von Helmholtz, *Treatise on Physiological Optics*, J. P. C. Southall, Ed. (Optical Society of America, Washington, D.C., 1924), vol. 1.
16. W. F. Hamilton and J. L. Goldstein, *J. Comp. Psychol.* **15**, 193 (1933).
17. S. Shlaer, E. L. Smith, A. M. Chase, *J. Gen. Physiol.* **25**, 553 (1942).
18. I thank F. W. Campbell and J. G. Robson, whose apparatus I used, R. M. Boynton for his support and encouragement, and E. L. Blake of the Field Museum of Natural History in Chicago for making available the preserved specimens. C. R. Ingling, M. L. Myers, and L. G. Standing provided help when it was most needed. The research was supported by NIH grant NB 00624 to R. M. Boynton.
* Present address: Neurosurgical Research Laboratory, Chicago Wesley Memorial Hospital, 212 East Superior Street, Chicago, Illinois 60611.

18 November 1971

Replamineform: A New Process for Preparing Porous Ceramic, Metal, and Polymer Prosthetic Materials

Abstract. *The replamineform process (meaning replicated life forms) is a technique for duplicating the microstructure of carbonate skeletal components in ceramic, metal, or polymer materials. The special pore structures of marine invertebrate skeletal materials such as echinoid spines and corals, which are difficult or impossible to create artificially, can thus be copied in useful materials. Of immediate interest is the possibility of using these replicated microstructures in the fabrication of orthopedic prosthetic devices. By means of this technique, prosthetic materials having a controlled pore microstructure for optimum strength and tissue ingrowth may be obtained.*

The replacement of damaged body tissue with foreign materials has been an appealing possibility. Sterilized animal bone is seemingly an obvious substitute for human bone, but its use as an implant has been abandoned because of problems with residual organic matter that elicits immunological reactions. Another possible means of repair of fractured bone or damaged joints is the fabrication of prosthetic implants from materials compatible with body tissue and having acceptable mechanical properties. Screws, pins, nails, and other items fashioned from highly polished metal alloys such as Vitallium, for example, have been widely used, but these implants often cause inflammation and excessive development of fibrous tissue. Corrosion of metal and lack of long-term mechanical attachment are further disadvantages, although attempts to increase the degree of tissue attachment by sintering a layer of metal spheres to the outer surface of the Vitallium have been reported (*1*). Sintered titanium fiber composites have also been evaluated (*2*). Other potential prosthetic materials include phosphate bonded alumina (*3*), and porous ceramics (*4*). The difficulty in controlling pore size, and more important, the size of the interconnections between adjacent pores, has been a major limitation in the production of porous ceramics (*4*). We now describe

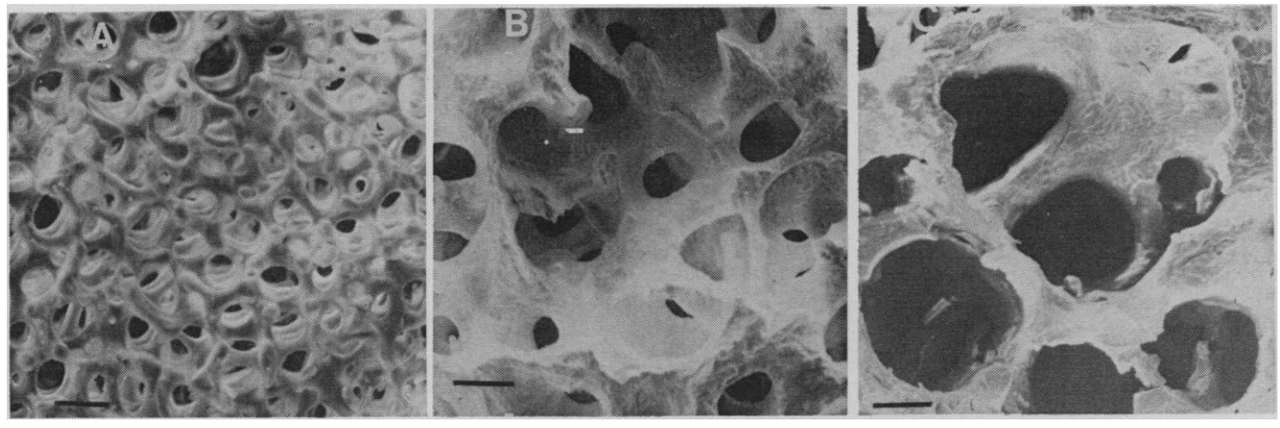

Fig. 1. Scanning electron micrographs of skeletal materials. (A) Echinoid spine calcite (scale, 400 μm); (B) *Porites* skeletal aragonite (scale, 20 μm); and (C) human bone (scale, 20 μm).

a new technique for the fabrication of metal, organic polymer, and ceramic prosthetic materials having a controlled pore microstructure for optimum strength and tissue ingrowth.

Experimental studies indicate that pore connections between 100 and 200 μm are necessary for the development of haversian systems and the anastomosing blood supply which is essential for bone nourishment. Minimum pore sizes for the ingrowth of osteoid cells and fibrous tissue are 40 to 100 μm and 5 to 15 μm, respectively (*4*). Although uniform pore size and permeability are difficult to obtain artificially, such materials are common in nature. Most echinoderm skeletons, for example, are characterized by a pronounced three-dimensional, fenestrate structure, which Donnay and Pawson (*5*) describe as a periodic minimal surface. Such a surface divides space into two interpenetrating regions, each of which is a single, multiply connected domain. According to Donnay and Pawson, the surface, which is the interface between the solid calcite phase and the organic matter component, provides maximum contact for crystal growth. This microstructure appears to be unique to the echinoderms.

The microstructure of calcite echinoid spines can be precisely replicated in the form of epoxy resin and sodium silicate, as has been shown in this laboratory (*6*). The ratio of pore volume to the volume of the solid is approximately 1, and cross-sectional diameters of both the pore and solid phases are about the same size, ranging from 10 to 50 μm among species (*7*). Although the echinoderm skeletal structure with fully interconnected voids would appear ideal for implant materials on the basis of permeability and porosity requirements, the size of the pores is generally too small to permit other than fibrous tissue ingrowth (*4*).

Further investigaton of naturally porous skeletal materials indicates that a considerable variety of microstructures might serve as the basis for the production of implant materials by structural replication. Among the most promising is the common scleractinian, reef-building, colonial coral *Porites*, whose skeleton is constructed of radiating clusters of acicular aragonite crystals (sclerodermites) (*8*). The small (less than 2 mm) corallites, which are closely united without coenosteum, have both perforate skeletal walls and septa with perforations.

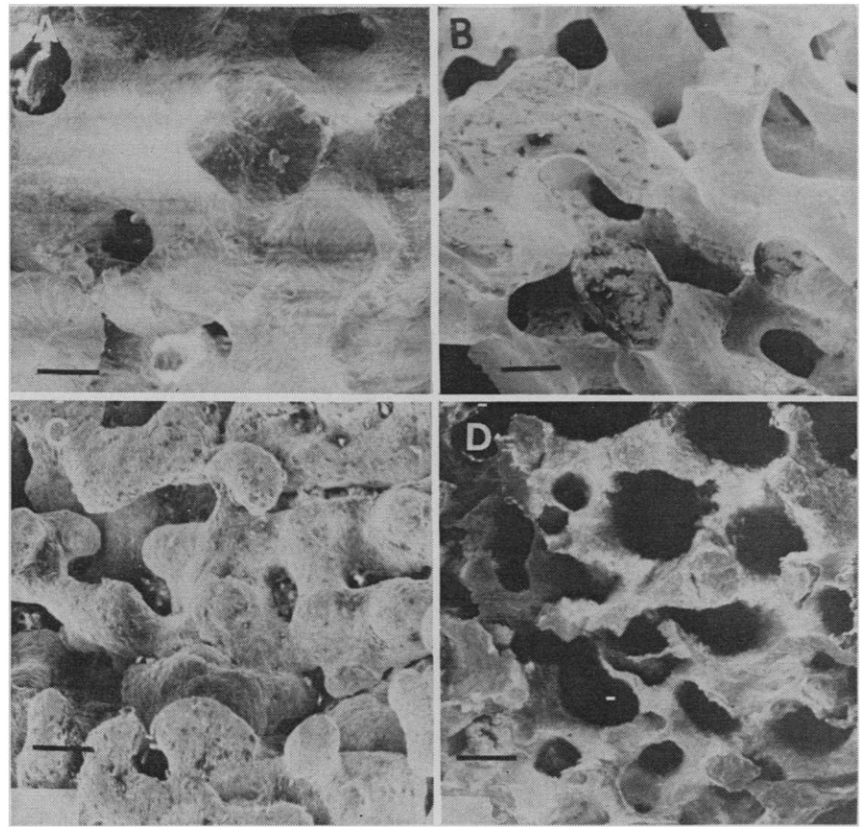

Fig. 2. Replamineform copies of *Porites* in (A) methacrylate (scale, 200 μm); (B) tin (scale, 400 μm); (C) Tichonium (scale, 400 μm); and (D) alumina (scale, 400 μm).

Representative photomicrographs of three animal skeletons with somewhat analogous microstructure are shown for comparison in Fig. 1: Except for greater orientation of the pores in Fig. 1, A and B, the gross microstructural features of the three materials are similar. In human bone, the pore volume ranges from about 95 percent in regions of low calcification to as low as 10 percent in the most heavily calcified areas.

It appears possible to select from the animal kingdom a microstructure most suitable for a particular application and then to reproduce that structure in ceramic, metal alloy, or polymer materials. The disadvantages in using skeletal materials directly include the low strength and high solubility of calcite and aragonite and, in the case of the hydroxyapatite bone of humans and vertebrates, the difficulty in completely removing residual organic matter which elicits immunological reactions.

The first step in the replamineform process (meaning replicated life forms or structures) is the removal of most of the organic matter contained in the source material by immersion in a 5 percent solution of sodium hypochlorite for up to 30 hours. After the soft tissues have been oxidized, the sample is rinsed in deionized water and dried at 90°C. A stream of compressed air may be used to aid in expelling liquified organic constituents. If the specimen to be replicated is echinoderm calcite or scleractinian coral aragonite, it can be easily preformed by machining to any desired geometry—for example, cylinders, screws, nuts, bolts, and pins. For methacrylate replicas, negative copies of the structure are obtained by vacuum impregnation and subsequent polymerization of methacrylate, followed by leaching of the original calcite or aragonite with 5 to 20 percent HCl. To yield positive copies, the source material is first vacuum-impregnated with wax. The $CaCO_3$ is then removed with dilute HCl, and the wax negative is vacuum-impregnated with methacrylate. After polymerization of the methacrylate, the wax is removed by melting.

Natural microstructures can also be replicated in metal alloys such as Tichonium and Vitallium. In the case of Tichonium, the echinoderm or coral skeleton is first vacuum-impregnated with wax, and the calcite or aragonite is removed with HCl. The wax negative is then vacuum-impregnated with refractory material such as cristobalite investment (*9*), and the metal is cast by means of standard centrifugal casting techniques. The result is an exact negative reproduction of the original structure in metal. For very large specimens, vacuum casting would be desirable. Positive replicas in metal require manipulation of the intermediate copies, so that the sample invested with Kerr cristobalite is a wax positive. Kerr ivory inlay casting (regular) (*9*) was used in these preparations to assure complete removal of the wax and to preserve detail in the replications. Sintered alumina copies are prepared by vacuum impregnating the wax negative with a thixotropic slurry of 5-μm particles of α-alumina. The alumina is rendered fluid by vibratory action to facilitate the filling of the pores in the wax negative. After the wax is burned off at 400°C, the alumina is sintered at 1650°C in an air atmosphere. Replamineform copies of the structure of *Porites* in methacrylate, tin, Tichonium, and alumina (α-Al_2O_3) are shown in Fig. 2.

The implications of this process are many. The special geometric characteristics of a particular microstructure, which are difficult or impossible to create artificially, could be utilized simply by copying the substance of the source material into one having the chemical, physical, and mechanical properties necessary for a given application. New avenues might also be opened in the production of composite materials. Artificial limbs might be permanently attached by means of an implant device consisting of a central Vitallium rod (for strength) coated with porous ceramic for firm attachment of living tissue. Furthermore, source materials for replication are readily obtainable in large quantity. The genus *Porites*, for example, is one of the most successful of the reef-building corals, having a worldwide distribution in the coral reef zone. The colonies grow rapidly, with massive forms often exceeding 1 m in diameter.

R. A. WHITE
School of Medicine, State University of New York, Upstate Medical Center, Syracuse 13210

JON N. WEBER
E. W. WHITE
Materials Research Laboratory, Pennsylvania State University, University Park 16802

References and Notes

1. R. P. Welsh, R. M. Pillar, I. Macnab, *J. Bone Joint Surg.* **53-A**, 963 (1971).
2. J. Galante, W. Rostoker, R. Lueck, R. D. Roy, *ibid.*, p. 101.
3. S. N. Bhaskar, D. E. Cutright, M. J. Knapp, J. D. Beasley, B. Perez, T. D. Driskell, *Oral Surg.* **31** (2), 282 (1971).
4. S. F. Hulbert, F. A. Young, R. S. Mathews, J. J. Klawitter, C. D. Talbert, F. H. Stelling, *J. Biomed. Mater. Res.* **4**, 433 (1970).
5. G. Donnay and D. L. Pawson, *Science* **166**, 1147 (1969).
6. J. N. Weber, E. W. White, J. Lebiedzik, *Nature* **233**, 337 (1971).
7. J. N. Weber, R. T. Greer, B. Voight, E. W. White, R. Roy, *J. Ultrastruct. Res.* **26**, 355 (1969); J. N. Weber, *Amer. J. Sci.* **267**, 537 (1969).
8. J. W. Wells, in *Treatise on Invertebrate Paleontology*, Part F, *Coelenterata*, R. C. Moore, Ed. (Geological Society of America, Washington, D.C., 1956), p. 328.
9. Commercial product supplied by Kerr Manufacturing Co., Romulus, Mich.
10. We thank Drs. R. T. Chiroff and R. Greer for invaluable discussion concerning medical applications. Dr. W. A. Barrickman, provided a centrifugal casting apparatus and casting supplies used for the tin casting, and W. Hughes assisted in the casting of Tichonium. J.N.W. has been partially supported by NSF grant GA-31217.

5 January 1972

Noradrenaline Nerve Terminals in Human Cerebral Cortices: First Histochemical Evidence

Abstract. *The cerebral and cerebellar cortices of man are richly provided with varicose noradrenaline nerve terminals, which are visualized by fluorescence histochemistry of brain smears obtained by a new technique. The density of such nerves in human cortices equals that of the rat. The method permits simple and rapid analysis of noradrenergic nerves of the human cortex during routine neurosurgical operations.*

There is evidence for a cellular localization of the three monoamines—dopamine, noradrenaline (NA), and 5-hydroxytryptamine—within specific neuron systems of the brains of laboratory animals (*1*). The distribution of the bodies and terminals of monoamine nerve cells is known in detail for the rat, and the presence of these cells has been documented also in other species (*2*). The functional significance of the various monoamine neuron systems, for instance their involvement in the mechanisms of action of psychotropic drugs, is under study, yet the appearance and distribution of these neurons in the human brain has not been demonstrated. In this report we describe the