PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

The Influence of Bone Cells on the Formation, and Mineralization, of Bone Matrix

Janet Vaughan

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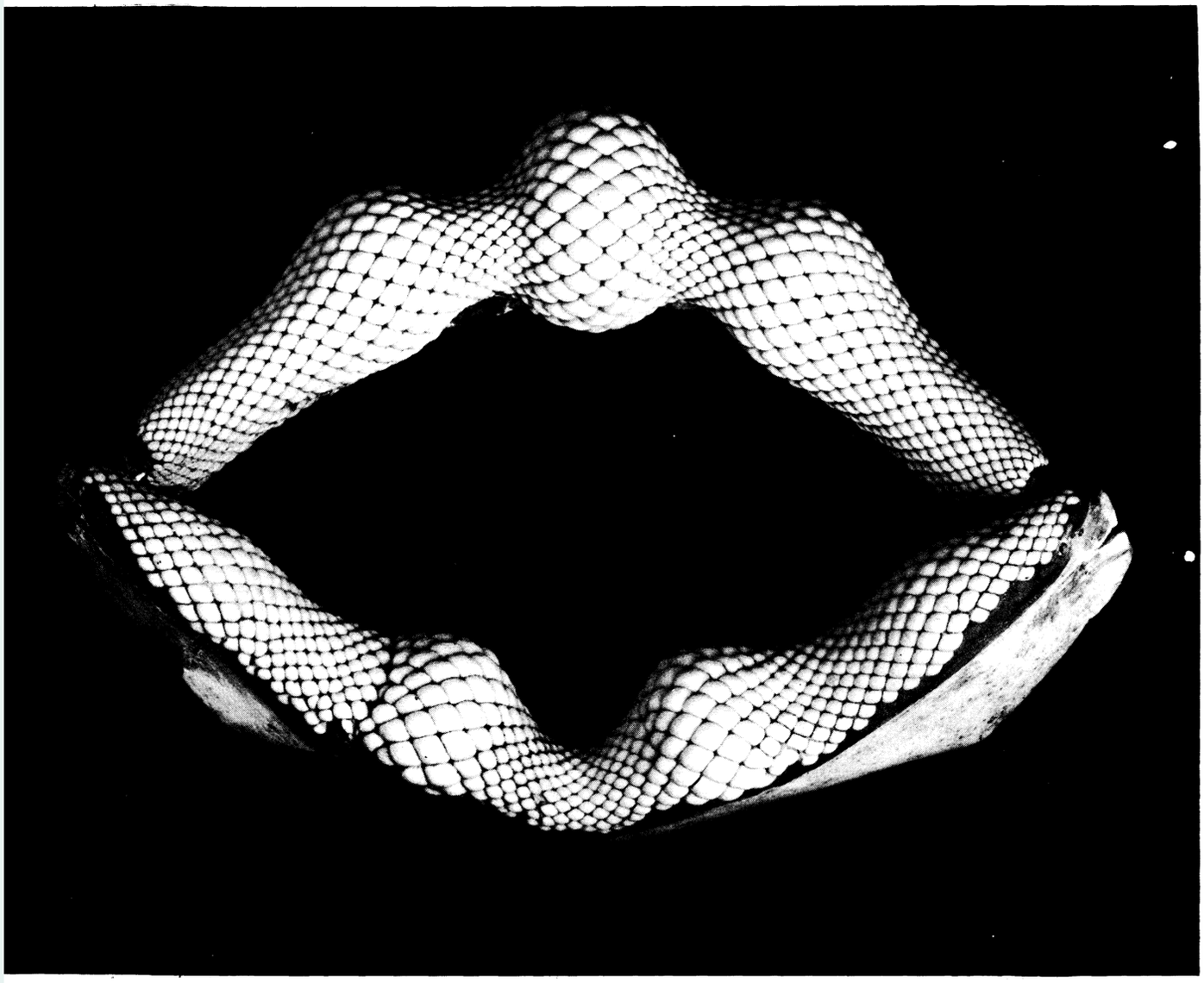

CALCIUM PHOSPHATES

Rhynchobatus ancylostomus; Guitar fish (ray). The teeth of fish show great variety of form and structure. In sharks and rays there is a succession of teeth; new ones form on the buccal surface of the jaws and, as they migrate outwards, they increase in size and thickness. Finally, they are cast off and replaced by succeeding teeth. The teeth in this specimen are used for crushing prey.

Cementin, enamel and dentine may all be constituents of fish teeth. Of these, dentine, in all its different varieties, is the most important. It is a calcium hydroxy phosphate.

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The influence of bone cells on the formation, and mineralization, of bone matrix

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The Western World today faces a new and alarming epidemic–osteoporosis, i.e. a loss of bone mass affecting the elderly (Lane & Vigorita 1983). It has taken us by surprise. We do not understand its cause and therefore we have at present no cure. The osteoporosis may be so severe that our bones fracture for no good reason. In youth and early adult life we successfully mineralize the organic matrix of our skeletons. Inevitably as we pass from middle to old age we may suffer a loss of bone mass that affects both mineral and matrix. This skeletal deterioration varies in severity in different individuals. There is no satisfactory explanation of why it occurs and what the underlying mechanisms involved are; nor is it known what can be done to prevent or cure it. Hospital organization here in England is disorganized because beds are occupied by elderly people with broken bones (Dix 1983). Chemists and biologists face a double challenge. First, why and how does the matrix of the bone mineralize? Secondly, why, with increasing age, is there a deterioration both in matrix and in mineralization?

In considering these problems the part played by bone cells must not be forgotten. These cells are concerned, not only with the formation, maintenance and calcification of matrix but they are also involved in association with the kidney and intestines in the complex mechanism of mineral homeostasis. The bone cells are therefore exposed to many demands and contributing mechanisms that affect both mineral and matrix. The contribution the bone cells make to the structure of matrix and its mineralization must be recognized if we are to understand the matrix deterioration and failure of mineralization such as occurs in osteoporosis.

The two important bone cells are the osteoblast, which synthesizes type 1 collagen molecules (Epstein & Munderloh 1975) to form the major component of the expanded fibrillar structure of the matrix (Neuman 1980), and the osteoclast, which resorbs the mineralized matrix (Loutit & Nisbet 1982). The function of the osteocyte, buried in the matrix, is far from well defined (Smith 1983).

If the osteoblast is stimulated to lay down matrix on one side of a bone trabeculae, for instance by parathyroid hormone, the osteoclasts at once start to resorb bone on the other side. This is often attributed to a 'coupling mechanism'. Some workers indeed claim to have isolated and characterized 'a coupling factor' in organ culture that links the activity of these two cell types (Howard *et al.* 1981).

In addition to collagen the osteoblast is also responsible for the synthesis of some of the non-collagenous proteins of the matrix. Though they constitute only about 10% of the matrix they are extremely important (Triffitt 1980). These proteins are largely glycoproteins. One of these, bone sialoproteins, has been studied extensively (Herring 1979). It has been shown to have strong binding properties for actinide elements as well as for calcium (Chipperfield & Taylor 1974). It is not found in non-calcifying tissues such as tendon (Herring 1976), which suggests it is specific to bone (Triffitt 1980). Other non-collagenous proteins are also specific to bone matrix rather than sequestered from the bone fluid or blood plasma as are the plasma

proteins, α_2HS glycoprotein and albumin (Ashton *et al.* 1976). The function of osteocalcin, a protein that contains γ-carboxyglutamic acid, in bone formation is uncertain; it is thought to be important in maintenance and resorption (Price *et al.* 1980, 1981). Osteonectin is another bone specific protein, presumably derived from the osteoblast. It is able to bind mineral to matrix, i.e. hydroxyapatite crystals to collagen, and may well be involved in the continuous attachment of such crystal to collagen fibres (Termine 1981, 1983). Failure on the part of the osteoblast to synthesize some of these bone-specific non-collagenous proteins may well contribute to the deterioration of matrix and subsequent deficient mineralization in old age.

In culture the osteoblast produces local growth factors that regulate bone growth and development (Canalis *et al.* 1980). These have not been characterized and how they function is not clear. Bone morphogenic protein is thought to be a small peptide that is isolated from decalcified bone matrix. It is capable of inducing active bone formation when placed in connective tissue. It is presumed to have been formed initially by osteoblasts and then to have been secreted and stored in the matrix (Urist *et al.* 1979). The part this morphogen plays in normal bone physiology is not at present clear.

This brief account describing some of the varied but important constituents of bone matrix originating from bone cells indicates the close relation that exists between cellular activity and mineral deposition, even though the latter occurs in an extracellular site.

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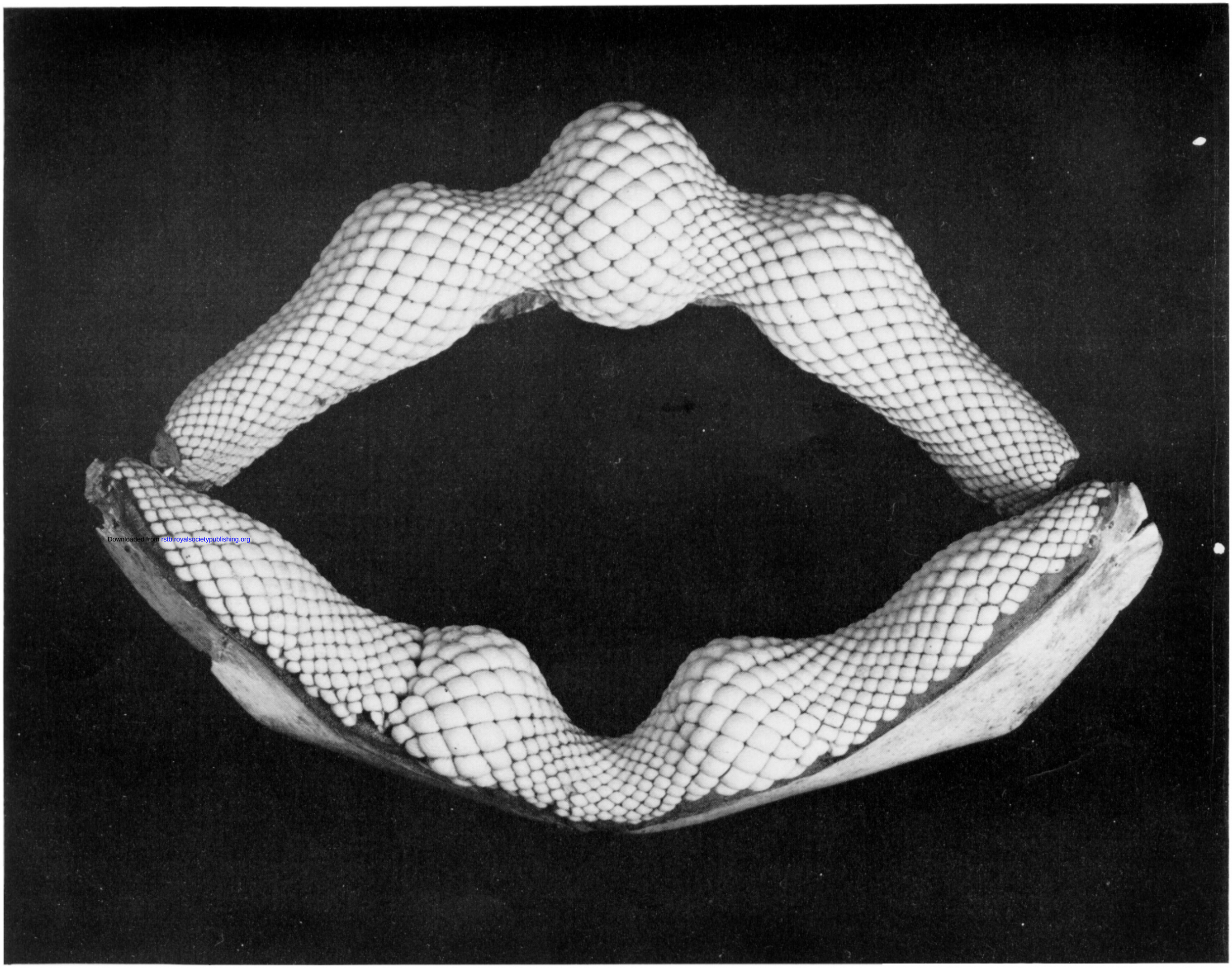

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