A Collection of the Published Works of

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Doctor of Science

Submitted to the Faculty of Science

University of Adelaide

1958

C O N T E N T S

PREFACE

The published works collected in this volume are a record of the original research carried out by me, working either alone or with collaborators. It is the object of this Preface to give a brief account of the main lines of this work, to indicate generally the original findings and to point out my indebtedness to others.

The broad theme uniting most of the work is the problem of the structure and synthesis of biological fibres, such as hair and silk. The techniques employed have been largely physical or physico-chemical in character and particular use has been made of the electron microscope. My colleagues and I were among the pioneers of the application of this instrument to fibres and later, with the development of appropriate techniques, also to the tissues which form these fibres.

Research of this kind may be classified as biophysics, but it cannot be dissociated from chemistry, biochemistry and histology. It seeks to relate the physical and chemical behaviour of the fibres to their structure and to derive this structure ultimately from the activities of the living cell.

The early electron microscopy of fibres (30-35)* was based on methods which aimed at breaking down the fibrous material into fine fragments by mechanical, chemical or enzymatic means. This was necessary because the beam of electrons used in present day microscopes is able to penetrate only very thin layers of matter. Fibres tend to break into finer and finer fibrils in a structurally significant manner and thus lend themselves to this treatment. The work of my colleagues and myself contributed towards the recognition, in hair, wool, silk and muscle, of definite fibrous units, microfibrils or protofibrils, of an order of magnitude between that of the single, long, molecular chain and the finest fibrils visible in the light microscope. (18, 22, 30-35).

My interest has been centred largely on the keratinised fibres of which wool is the most convenient example. The fine structure of this material has been very fully worked out and described in a series of papers (28-60). The need to integrate these structural findings with chemical, optical and X-ray diffraction data led to a study of methods of dissolving and regenerating keratin

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* The numbers refer to the entries in the Classified Bibliography (1-67) or in the Supplementary Bibliography (68-77).

in a fibrous form (17, 36, 43) and to an examination of the development of orientation by X-rays and polarisation optics in the growing hair root (37, 30).

The existence of components, having different degrees of stability which influence the properties of the fibre, was revealed by attempts to dissolve wool (43, 47). Very resistant membranes were discovered both on the surface of hairs (35, 40, 41, 42, 46, 47) and in their interior (42, 46, 47). These resistant membranes were shown to be derived from the original cell membranes of the growing hair and to have been subjected during keratinisation to a chemical modification rendering them insoluble in most solvents (47, 57, 58, 59).

The fibrous keratin within the cortical cells was also found to exhibit different degrees of hardness or keratinisation (47). In wool fibres, in particular, it was shown by me and by others that the distribution of the hard and soft keratin was related to the crimp(or wave) of the fibre (48). The wool fibre in a sense consists of two hemi-cylinders, the ortho- and paracortex (47), of unequal hardness and chemical stability, twisted together to form a double helix, the pitch of which is in phase with the crimp wave of the fibre. The twisted,

bicomponent rodlet, so formed, contributes importantly to the properties of wool as a textile fibre (47, 48, 49, 50, 51, 52).

When methods of cutting suitably thin sections (ca250-500A) for electron microscopy were developed the new technique was applied to the keratinised tissues, which because of their hardness offer special difficulties, and our earlier conclusions were confirmed (54).

I also made a similar study of the structure of silk (21, 22) and discovered the spontaneous formation of fibrils in an extract of the silk gland of the silk worm suggesting that fibre formation was an aggregation of particles. (21, 22, 27). A consideration of these results and of others led to the hypothesis that an important step in the biosynthesis of these fibres was the formation, by linear aggregation of particles, of a fine fibril, of the order of 50-200A in diameter, which formed the unit from which the larger formations were constructed (23, 68). The often complex formations having a fibrous fine texture were regarded as "fabrics" woven from these elementary fine fibrils under the influence of special orienting influences, such as viscous flow or packing against an organising surface. The spinning of silk (21), the formation of fibrous insulin (24) and the shedding of the peritrophic membrane of

certain insects (19) were studied as further examples of fibre formation.

Work on the synthesis of biological fibres received a great stimulus when it became possible to study in the electron microscope thin sections of the tissues where the fibres are formed. In these germinal cells the early steps in synthesis are to be found and their study should lead at the one time to a better knowledge of the structure of the fibre itself and also to the methods of vital synthesis. We have made a close study of the growth of human hair based on these new methods (57, 58, 59). Similar studies of the silk glands of the silkworm and of certain other insect glands, noted for their fibrous secretions, followed (73, 75).

These studies have shown that the fine structure of cells, which are synthesising and secreting a fibrous protein, is essentially similar to those which form a soluble protein such as an enzyme. There is a great elaboration of cytoplasmic membranes, with which are associated small, dense particles (or molecules) known to contain ribonucleic acid. This system, when disintegrated by breaking the cells, gives rise to the microsomes also shown by independent biochemical techniques to be involved in protein synthesis.

Our work on the hair follicle and the skin has

helped to show that the ribonucleoprotein particles are necessary for keratin formation, but that the membranes are not. Since keratin remains intracellular and is not secreted, this would seem to imply that the membrane system or "reticulum" is associated with extracellular secretion rather than the primary synthesis of the protein.

Our interest in the specialised cell membranes of hair and wool led us to pay attention to their development in the hair follicle and from there to the question of their more general rôle in tissue formation and morphogenesis (65, 67). It is clear that cell membranes must stick to each other if the cells are to remain associated in an organised group and undergo differentiation, and this consideration has led to an examination of intercellular adhesion during embryogenesis and in certain simplified cell systems such as tissue cultures and social amoebae (67).

Cancer cells, which exhibit abnormal mobility, also display certain abnormalities of surface adhesion and the microscopy of their surface membranes forms an important part of my present work (67).

As can be seen from the Bibliographies I am now engaged in a number of researches which have in part developed from my earlier work on fibres, but which

concern more fundamental aspects of Biology. The nature of this work may be judged from my recent publications or from the summaries included in the Supplementary Bibliography. It will not be described here since it does not properly form a part of my Subject "The Structure and Formation of Fibrous Biological Materials."

A Note on Sources of Material

Most of the articles collected here will be found to contain an introduction in which specific reference is made to previous work on the subject in question and to the manner in which the original work, to be described, is indebted to and derives from it. The summaries accompanying each article contain statements of the original conclusions drawn from the experimental work.