



Structure and Function of Cells

COLIN R HOPKINS

STRUCTURE AND FUNCTION OF CELLS

*A text for students in medicine
and science*

COLIN R HOPKINS BSc PhD

*Professor, Department of Histology and
Cell Biology, The Medical School,
Liverpool University*

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PREFACE

Over the last decade the rapid, almost explosive growth in our understanding of structure-related function has served to emphasize the central role that cell biology has to play in the education of students in medicine and science. With its recent progress, cell biology has now developed sufficiently to provide a focus in which the surrounding, related areas of interest in biology can be integrated with those in which attention is directed towards the molecular level. The biology of the cell is thus beginning to be taught as a unifying topic in its own right rather than as an appendage to courses in morphology or biochemistry. The purpose of this text is to convey this view to students taking preliminary courses in basic medical science.

The book is intended primarily for students who have a background of school biology and who are taking concurrent courses in biochemistry and physiology. As a brief, contemporary assessment of the field, it should also provide a useful basis for later courses in pharmacology, histopathology, immunology and experimental medicine in general. However, although the approach is clearly directed at the eukaryotic system as typified by the cells of mammalian tissues, it will be read without difficulty by students in life science who lack a strong medical bias. It is with these students in mind that a glossary has been included.

As this book may be the only exposure a student has to the topic of cell biology, I have, in writing it, tried to make the text accessible to first-year university students whilst maintaining something of the momentum and excitement that pervades the subject at the present time. For this reason the more established aspects have often been treated in a condensed and abbreviated manner and the bibliography has been used to provide some indication of historical perspective. The chief dangers of this approach are of course that the generalizations will be too sweeping and the promise of the more recent areas of advance will in time be shown to have been evanescent. Being aware of a danger helps, of course, but is no guarantee that it can always be avoided.

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Some of the electron micrographs have been produced in my laboratory and for them I have depended upon the expert technical assistance of Hazel Smith. For the background, often tedious, jobs that have to be done in compiling a text of this kind I am pleased to acknowledge the willing and often innovative help of Annie Pritchard. For much of the typing I am grateful to my secretary, Mrs Doreen Godsell.

To my departmental colleagues and students who over the years have both knowingly and unknowingly made their contributions, I wish to express my thanks.

Finally I thank my wife for her loving support and constant encouragement.

Colin R. Hopkins

LIST OF ILLUSTRATIONS

- Figure 1.** Resolution and magnification. From J. James (1976) *Light Microscope Techniques in Biology and Medicine*. The Hague: Nijhoff Medical. With kind permission of the author and the publisher.
- Figure 2.** The angular aperture of an objective lens.
- Figure 3.** Oil immersion.
- Figure 4.** The arrangement of lenses and two-stage magnifications in the light microscope.
- Figure 5.** Imaging and illumination systems in the light microscope. After L. H. Greenberg (1975) *Physics for Biology and Pre-med Students*. Philadelphia: W. B. Saunders.
- Figure 6.** The substage condenser system.
- Figure 7.** The electron gun.
- Figure 8.** The electromagnetic lens.
- Figure 9.** The path of electrons in an electron microscope. After A. W. Agar (1974) In *Practical Methods in Electron Microscopy. Volume 2: Principles and Practice of Electron Microscope Operation*. (Ed.) A. Glauert. Amsterdam: North Holland.
- Figure 10.** The Philips EM 400 research microscope. Courtesy of Philips Ltd., Eindhoven.
- Figure 11.** The electron microscope in use—using the binocular magnifier to view the fluorescent screen. Courtesy of Philips Ltd., Eindhoven.
- Figure 12.** The electron microscope in use—inserting the carrier rod via the air lock. Courtesy of Philips Ltd., Eindhoven.
- Figure 13.** A scanning electron micrograph to show the depth of focus that can be obtained. Courtesy of T. D. Allen, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester.
- Figure 14.** Some properties of light.
- Figure 15.** The paths of direct and diffracted rays in the light microscope.
- Figure 16.** The arrangement of the substage condenser annulus and the phase plate in a phase contrast microscope.
- Figure 17.** A comparison of conventional light and phase contrast microscopy.
- Figure 18.** The light microscope.
- Figure 19.** Cutting a ribbon of sections on a microtome.
- Figure 20.** LKB Ultramicrotome III. Courtesy of LKB Instruments Ltd., Selsdon, Surrey.
- Figure 21.** Cutting and mounting ultrathin sections.
- Figure 22.** A tissue section stained with uranium and lead salts.
- Figure 23.** A liver section stained with the PAS technique.
- Figure 24.** Acid phosphatase localized by the lead salt method.
- Figure 25.** Fluorescence immunocytochemistry—indirect method.
- Figure 26.** A comparison of conventional light microscopy with fluorescence microscopy. Courtesy of C. Vaillant, Department of Histology and Cell Biology, University of Liverpool.
- Figure 27.** The preparation of sections for autoradiography.
- Figure 28.** Autoradiography used to follow the incorporation and subsequent fate of radioactive proline in the tooth. From M. Weinstock and C. P. Leblond (1974) *Journal of Cell Biology*, **60**, 92–127. With kind permission of the authors and the editor.
- Figure 29.** Nerve cells in culture. From J. M. England (1969). *Journal of Cell Science*, **4**, 677–693. With kind permission of the author and the editor.
- Figure 30.** Cell fractionation by differential centrifugation.
- Figure 31.** The essentials of cell structure.
- Figure 32.** The trilaminar substructure of membranes—a section across a red blood cell, capillary wall and muscle cell. Courtesy of N. and M. Simionescu, Section for Cell Biology, Yale University, New Haven, Connecticut.
- Figure 33.** The trilaminar substructure of membranes—a section across the plasma membranes and organelles of two exocrine pancreas cells. From N. and M. Simionescu (1976) *Journal of Cell Biology*, **70**, 608–633. With kind permission of the authors and the editor.
- Figure 34.** The freeze-fracture technique.
- Figure 35.** A phospholipid molecule.
- Figure 36.** The lipid bilayer of a membrane.
- Figure 37.** The fluid mosaic model. After S. J. Singer and G. L. Nicolson (1972) *Science*, **175**, 720.
- Figure 38.** The form and distribution of glycophorin on the erythrocyte plasma membrane. After V. T. Marchesi (1975) *The Structure and Orientation*

- of a Membrane Protein. In *Cell Membranes, Biochemistry, Cell Biology and Pathology*. New York: Hospital Practice Publishing Company.
- Figure 39.** Freeze-fractured plasma membranes to show the distribution of intramembranous particles. From L. Orci and A. Perrelet (1975) *Freeze-Etch Histology*. Berlin: Springer Verlag. With kind permission of the authors and the publisher.
- Figure 40.** The fusion of cultured mouse and human cells using Sendai virus. From the work of Frye and Edidin (1970).
- Figure 41.** Patching and capping induced by a lectin.
- Figure 42.** The relative dimensions of the plasma membrane and its associated cytoskeletal elements. After F. Loor, Basel Institute for Immunology, Switzerland.
- Figure 43.** The distribution of hormone receptor sites on a pituitary cell. From C. R. Hopkins and H. Gregory (1977) *Journal of Cell Biology*, **75**, 528–540. With kind permission of the authors and the editor.
- Figure 44.** Scanning EMs of normal and transformed cells in culture. From J. G. Collard and J. H. M. Temnink (1976) *Journal of Cell Biology*, **68**, 101–112. With kind permission of the authors and the editor.
- Figure 45.** The distribution of monovalent ions across the plasma membrane.
- Figure 46.** The distribution of monovalent ions across the plasma membrane—in the erythrocyte, frog muscle and squid axon.
- Figure 47.** An action potential and the changes in Na^+ and K^+ permeability.
- Figure 48.** The generation of a local circuit.
- Figure 49.** The propagation of an impulse in a myelinated nerve fibre.
- Figure 50.** The axon of a myelinated nerve fibre in cross section. Courtesy of C. Peracchia, Department of Physiology, University of Rochester, New York.
- Figure 51.** Apical brush border of a mucosal epithelial cell at low magnification.
- Figure 52.** Apical brush border of a mucosal epithelial cell at high magnification. Courtesy of C. Peracchia, Department of Physiology, University of Rochester, New York.
- Figure 53.** The infolded plasma membranes of epithelial cells in the distal convoluted tubule of the kidney. From R. E. Bulger (1973) *The Urinary System*. In *Histology* (Ed.) R. O. Greep and L. Weiss. Third edition. New York: McGraw-Hill. With kind permission of the author and the publisher.
- Figure 54.** Phagocytosis by a polymorphonuclear leucocyte. From D. F. Bainton (1973) *Journal of Cell Biology*, **58**, 249–264. With kind permission of the author and the editor.
- Figure 55.** Absorptive and fluid endocytosis.
- Figure 56.** The exocytosis of secretory product.
- Figure 57.** The different routes that can be taken by macromolecules across the capillary wall.
- Figure 58.** Evidence of cytolysis in an unfenestrated capillary. Courtesy of N. and M. Simionescu, Section for Cell Biology, Yale University, New Haven, Connecticut.
- Figure 59.** The transport of a tracer (microperoxidase) across the capillary wall by cytolysis. From N. Simionescu, M. Simionescu and G. E. Palade (1975) *Journal of Cell Biology*, **64**, 586–607. With kind permission of the authors and the editor.
- Figure 60.** The distribution of fenestrae in a capillary wall—shown by freeze-fracture. Courtesy of C. Peracchia, Department of Physiology, University of Rochester, New York.
- Figure 61.** Secretory granules at the apical borders of two cells in the exocrine pancreas. From D. S. Friend and N. B. Gilula (1972) *Journal of Cell Biology*, **53**, 758–776. With kind permission of the authors and the editor.
- Figure 62.** A tight junction in mucosal epithelium from the duodenum. From D. S. Friend and N. B. Gilula (1972) *Journal of Cell Biology*, **53**, 758–776. With kind permission of the authors and the editor.
- Figure 63.** Desmosomes in the skin epidermis.
- Figure 64.** A reconstruction of the gap junction. After D. Goodenough, Department of Anatomy, Harvard Medical School, Boston.
- Figure 65.** A gap junction from the liver. From N. B. Gilula (1974) In *Cell Communication* (Ed.) R. P. Cox. Chichester: John Wiley and Sons. With kind permission of the author and the publisher.
- Figure 66.** Gap junctions between ovarian granulosa cells. From D. F. Albertini and E. Anderson (1974) *Journal of Cell Biology*, **63**, 234–250. With kind permission of the authors and the editor.
- Figure 67.** Communication between cells in culture. Courtesy of J. D. Pitts, Department of Biochemistry, University of Glasgow.
- Figure 68.** A reconstruction of the kinds of junctional complex between cells in a lining or glandular epithelium.
- Figure 69.** The interphase nucleus of a liver parenchyma cell.
- Figure 70.** The replication of DNA. After C. A. Villee, Harvard University Medical School.
- Figure 71.** Transcription and translation in *E. coli*. From B. A. Hamkalo (1972) *International Review of Cytology*, **33**, 7. With kind permission of the author and Academic Press, New York.
- Figure 72.** A model of DNA and its histones arranged within nucleosome subunits.
- Figure 73.** Electron micrograph of a whole mounted human chromosome 12. From E. D. P. De Robertis, F. A. Saez and E. M. F. De Robertis (1975) *Cell Biology*. Sixth edition. Philadelphia: W. B. Saunders. With kind permission of E. J. Du Praw, the authors and the publishers.
- Figure 74.** The influence of serum on cells growing in culture.
- Figure 75.** Some of the events during the cell cycle.
- Figure 76.** The changes in the surface contour of cultivated cells during division. From S. Knutton, M. C. B. Sumner and C. A. Pasternak (1975)

- Journal of Cell Biology*, **66**, 568–576. With kind permission of the authors and the editor.
- Figure 77.** The effect of epidermal growth factor on epidermal cell division.
- Figure 78.** The cell cycle and its relationship to differentiation. After M. J. Berridge, Department of Zoology, Cambridge.
- Figure 79.** Gene regulation in bacteria—the lac operon.
- Figure 80.** The effect of a steroid hormone upon its target cell.
- Figure 81.** An erythroblast at an early stage in its development.
- Figure 82.** An erythroblast at a later stage in its development.
- Figure 83.** A lymphocyte.
- Figure 84.** Pre-mRNA in a rat liver cell. Courtesy of G. Moyne, Institut de Recherches Scientifiques sur le Cancer, Villejuif, France.
- Figure 85.** The events leading to the reactivation of an avian erythrocyte nucleus in a heterokaryon.
- Figure 86.** Heterokaryons in which a cultivated human cell contains a hen erythrocyte nucleus. From H. Harris (1967) *Journal of Cell Science*, **2**, 23–32. With kind permission of the author and the editor.
- Figure 87.** A nucleolus in a nucleus of a nerve cell.
- Figure 88.** The nucleolar region in a liver parenchyma cell nucleus. Courtesy of G. Moyne, Institut de Recherches Scientifiques sur le Cancer, Villejuif, France.
- Figure 89.** The locations where post-transcriptional processing of RNA takes place.
- Figure 90.** Nuclear pores on the nuclear envelope of a kidney cell. From L. Orci and A. Perrelet (1975) *Freeze-Etch Histology*. Berlin: Springer Verlag. With kind permission of the authors and the publisher.
- Figure 91.** The periphery of the nucleus of pancreatic acinar cell.
- Figure 92.** Translation in prokaryotes.
- Figure 93.** Transfer RNA.
- Figure 94.** Rough endoplasmic reticulum cisternae in a pancreatic acinar cell.
- Figure 95.** Polyribosomes on the surface of a rough endoplasmic reticulum cisterna. Courtesy of M. Steer, Department of Botany, Queen's University, Belfast.
- Figure 96.** Translation on an attached polyribosome. The signal hypothesis. After G. Blobel, Rockefeller University, New York.
- Figure 97.** A plasma cell.
- Figure 98.** The cytoplasmic contents of a tissue culture cell revealed by a high-voltage EM. From I. K. Buckley (1975) *Tissue and Cell*, **7**, 325–341. With kind permission of the author and the editor.
- Figure 99.** Rough endoplasmic reticulum and secretory granules within an acinar cell in the exocrine pancreas. From K. R. Porter and M. Bonneville (1973) *Fine Structure of Cells and Tissues*. Pennsylvania: Lea and Febiger. With kind permission of the authors and the publisher.
- Figure 100.** The distribution of myeloperoxidase within a developing eosinophil leucocyte. From D. F. Bainton (1970) *Journal of Cell Biology*, **45**, 54. With kind permission of the author and the editor.
- Figure 101.** The pathway of newly synthesized plasma membrane constituents according to the 'membrane flow' model.
- Figure 102.** The cytoplasm of a columnar epithelial cell in the small intestine.
- Figure 103.** The cytoplasmic organization of a liver parenchyma cell.
- Figure 104.** A diagram of the sarcoplasmic reticulum in a striated muscle fibre.
- Figure 105.** A cross section of a striated muscle fibre to show the distribution of the sarcoplasmic reticulum. Courtesy of C. Peracchia, Department of Physiology, University of Rochester, New York.
- Figure 106.** The cytoplasmic organization of the perinuclear region of a megakaryocyte.
- Figure 107.** Fragmentation of a megakaryocyte by fusion of smooth-surfaced cisternal membranes with plasma membrane.
- Figure 108.** The classical Golgi silver impregnation technique.
- Figure 109.** The organization of the cytoplasmic organelles in the cell body of a neurone. Courtesy of S. L. Palay, Department of Anatomy, Harvard Medical School, Boston.
- Figure 110.** A reconstruction of a stack of flattened Golgi cisternae.
- Figure 111.** The Golgi area in a pituitary secretory cell.
- Figure 112.** Some of the routes into and out of the Golgi area.
- Figure 113.** The location of a radioactive precursor in the Golgi area—30 minutes post pulse. From C. R. Hopkins (1972) *Journal of Cell Biology*, **53**, 642–653. With kind permission of the editor.
- Figure 114.** The location of a radioactive precursor in the Golgi area—50 minutes post pulse. From C. R. Hopkins (1972) *Journal of Cell Biology*, **53**, 642–653. With kind permission of the editor.
- Figure 115.** The Golgi complex of a goblet cell in the small intestine.
- Figure 116.** The severed proinsulin molecule. After D. F. Steiner, University of Chicago.
- Figure 117.** The edge of a Golgi area in a pituitary secretory cell, stained for acid phosphatase. From C. R. Hopkins (1968) *Journal of Cell Science*, **3**, 357–364. With kind permission of the editor.
- Figure 118.** A macrophage from the lung of a smoker. From A. R. Brody and J. E. Craighead (1975) *Laboratory Investigation*, **32**, 125–132. With kind permission of the authors and the editor.
- Figure 119.** The fractionation of lysosomes. From H. Glaumann, H. Jansson, B. Arborgh and J. L. E. Ericsson (1975) *Journal of Cell Biology*, **67**, 887–891. With kind permission.
- Figure 120.** The Golgi area in an epithelial cell lining the respiratory tract.
- Figure 121.** Acid phosphatase in lysosomes. From C. R. Hopkins (1970) *Tissue and Cell*, **2**, 71–81. With kind permission.
- Figure 122.** The intracellular pathways followed by lysosomal elements.
- Figure 123.** The steps in autophagy. Courtesy of M.

- Locke, Cell Science Laboratories, Department of Zoology, University of Western Ontario, Canada.
- Figure 124.** The 'specific' granules of an eosinophil leucocyte.
- Figure 125.** A portion of a thyroid follicle wall.
- Figure 126.** The participation of lysosomes in the processing of thyroglobulin and the release of the thyroid hormones.
- Figure 127.** Peroxisomes in the cytoplasm of a liver parenchyma cell. From H. D. Fahimi (1969) *Journal of Cell Biology*, **43**, 275–288. With kind permission of the author and the editor.
- Figure 128.** Secretory granules in the cytoplasm of a cell from the pituitary gland—in the storage phase.
- Figure 129.** Secretory granules in the cytoplasm of an 'active' secretory cell in the pituitary gland.
- Figure 130.** Zymogen granules in an acinar cell of the exocrine pancreas. From R. P. Bolender (1974) *Journal of Cell Biology*, **61**, 269–287. With kind permission of the author and the editor.
- Figure 131.** A diagram of the arrangement of the cisternal organelles and the secretory granules in a polarized secretory cell.
- Figure 132.** The secretory pathway of peroxidase secretory product in a lachrymal gland cell. From V. Herzog and F. Miller (1972) *Journal of Cell Biology*, **53**, 662–680. With kind permission of the authors and the editor.
- Figure 133.** A neuromuscular end-plate.
- Figure 134.** Mitochondria within fibroblasts in tissue culture.
- Figure 135.** A mitochondrion in an acinar cell in the exocrine pancreas. Courtesy of K. R. Porter, Department of Molecular, Cellular and Developmental Biology, University of Colorado, Boulder, Colorado.
- Figure 136.** The form of mitochondria in two adjacent cardiac muscle fibres. Courtesy of C. Peracchia, Department of Physiology, University of Rochester, New York.
- Figure 137.** The loss of free energy as electron pairs are transferred along the electron transport chain. Modified from A. L. Lehninger (1975) *Biochemistry*. Second edition. New York: Worth Company.
- Figure 138.** The internal organization of the mitochondrion and its relationship to oxidative phosphorylation.
- Figure 139.** The typical features of a steroid-secreting cell. From D. S. Friend and G. Brassil (1970) *Journal of Cell Biology*, **46**, 256–266. With kind permission of the authors and the editor.
- Figure 140.** A view of the cytoplasmic organization shown in Figure 139, at higher magnification. From D. S. Friend and G. Brassil (1970) *Journal of Cell Biology*, **46**, 256–266. With kind permission of the authors and the editor.
- Figure 141.** A relaxed striated muscle fibre.
- Figure 142.** A relaxed striated muscle fibre showing Z-lines and I- and A-bands.
- Figure 143.** The force-generating components of the contractile unit in striated muscle.
- Figure 144.** The disposition of the thick and thin filaments in striated muscle, seen in cross section. Courtesy of H. E. Huxley, MRC Laboratory of Molecular Biology, Cambridge.
- Figure 145.** Contracted myofibrils from striated muscle, seen in longitudinal section. Courtesy of H. E. Huxley, MRC Laboratory of Molecular Biology, Cambridge.
- Figure 146.** The arrangement of the myosin and actin molecules in thick and thin filaments.
- Figure 147.** Myosin molecules. Courtesy of A. Elliot and G. Offer, Department of Biophysics, University of London, King's College.
- Figure 148.** Isolated filaments of F-actin. From R. V. Rice (1965) *Journal of Molecular Biology*, **12**, 302. With kind permission of the author and the editor.
- Figure 149.** The arrangement of the tropomyosin and troponin complex components along the F-actin helix. After S. V. Perry, Department of Biochemistry, University of Birmingham.
- Figure 150.** A model of the movement of the tropomyosin filament which allows the myosin head to bind to the actin subunit. After J. M. Squires (1975) *Annual Review of Biophysics and Bioengineering*, **4**, 137–163.
- Figure 151.** The cytoplasmic organization of the epithelial mucosal cells and smooth muscle cells of the intestinal wall. From C. Peracchia (1972) *Journal of Cell Biology*, **53**, 234–238. With kind permission of the author and the editor.
- Figure 152.** Smooth muscle fibres in cross section (low magnification). From A. P. Somlyo, C. E. Devine, A. V. Somlyo and R. V. Rice (1973) *Philosophical Transactions of the Royal Society B*, **265**, 223. With kind permission.
- Figure 153.** A smooth muscle cell in cross section (high magnification), to show the distribution of the myofilaments. From A. P. Somlyo, C. E. Devine, A. V. Somlyo and R. V. Rice (1973) *Philosophical Transactions of the Royal Society B*, **265**, 223. With kind permission.
- Figure 154.** A reconstruction of the possible relationships between the filamentous components of the smooth muscle cell.
- Figure 155.** The distribution of the filaments containing actin within fibroblast cells in culture. From E. Lazarides (1975) *Journal of Cell Biology*, **65**, 549–561. With kind permission of the authors and the editor.
- Figure 156.** The arrangement of stress fibres in cultured cells. After N. K. Wessels, Department of Biological Sciences, Stanford University, California.
- Figure 157.** The form and distribution of microfilaments in the microvillous border of a cell lining the small intestine. From M. S. Mooseker and L. G. Tilney (1975) *Journal of Cell Biology*, **67**, 724–743. With kind permission of the authors and the editor.
- Figure 158.** Alpha actinin and actin elements within the microvillus of a cell lining the small intestine. From M. S. Mooseker and L. G. Tilney (1975) *Journal of Cell Biology*, **67**, 724–743. With kind permission of the authors and the editor.

- Figure 159.** A diagram summarizing the filamentous arrangement in the brush border of the epithelium lining the intestine. Based on accounts by Mooseker and Tilney, and Roedwald, Newman and Karnovsky.
- Figure 160.** The distribution of microfilaments in periphery of a cultured fibroblast.
- Figure 161.** Monocytes moving over a flat, 'non-biological' surface. Courtesy of T. Allen, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester.
- Figure 162.** Locomotion in actively mobile cells. (a) Courtesy of M. Abercrombie, Strangeways Laboratory, Cambridge. (b) From J. D. Watson (1975) *Molecular Biology of the Gene*, Third edition. Menlo Park, California: W. A. Benjamin. With kind permission of R. Pollack, the author and the publisher.
- Figure 163.** The arrangement of tubulin subunits in a microtubule.
- Figure 164.** Cilia on the apical surface of ependymal cells lining a ventricle in the brain. From P. W. Coates (1976) *Cell and Tissue Research*, **162**, 256–263. With kind permission of the author and the editor.
- Figure 165.** The interrelationships of the axoneme components.
- Figure 166.** A three-dimensional view of the axoneme.
- Figure 167.** Details of a centriole in cross section. From E. de Harven (1968) In *The Nucleus* (Ed.) A. J. Dalton and F. Hageneau. New York: Academic Press. With kind permission of the author and the publisher.
- Figure 168.** The apical boundary of ciliated cells lining the oviduct. From N. Bjorkman (1962) *Zeitschrift für Zellforschung und Mikroskopische Anatomie*, **58**, 387–404. With kind permission of the author and the editor.
- Figure 169.** Centrioles within the Golgi area in a mast cell. From D. Lagunoff and Y. Chi (1976) *Journal of Cell Biology*, **71**, 182–195. With kind permission of the authors and the editor.
- Figure 170.** Centrioles in the cytocentrum of a non-dividing mast cell. From D. Lagunoff and Y. Chi (1976) *Journal of Cell Biology*, **71**, 182–195. With kind permission of the authors and the editor.
- Figure 171.** Mitosis in outline.
- Figure 172.** Early prophase. From B. R. Brinkley and E. Stubblefield (1970) In *Advances in Cell Biology*, volume 1. (Ed.) D. M. Prescott. New York: Appleton-Century-Crofts. With kind permission of the authors and the publisher.
- Figure 173.** The onset of metaphase. From B. R. Brinkley and J. Cartwright (1971) *Journal of Cell Biology*, **50**, 416–431. With kind permission of the authors and the editor.
- Figure 174.** Microtubules inserting into the kinetochores of two chromatids. Courtesy of J. R. McIntosh, Department of Molecular, Cellular and Developmental Biology, University of Colorado, Boulder, Colorado.
- Figure 175.** The kinetochore.
- Figure 176.** Metaphase. From B. R. Brinkley and P. N. Rao (1973) *Journal of Cell Biology*, **58**, 96–106. With kind permission of the authors and the editor.
- Figure 177.** Anaphase. From B. R. Brinkley and P. N. Rao (1973) *Journal of Cell Biology*, **58**, 96–106. With kind permission of the authors and the editor.
- Figure 178.** Division phase. From B. R. Brinkley and J. P. Chang (1975) In *Methods in Cancer Research*, volume XI, pages 247–291. (Ed.) H. Busch. With kind permission of the authors and Academic Press.
- Figure 179.** The distribution of microtubules in a cell in culture demonstrated immunocytochemically. Courtesy of K. Weber, Department of Biochemistry, Max-Planck Institut für Giophysikalische Chemie, Goettingen.

CONTENTS

PART 1	TECHNIQUES IN THE STUDY OF CELL STRUCTURE	1
1	The Microscope	3
	<i>Magnification and resolution</i>	3
	<i>The basic plan of the light microscope</i>	6
	<i>The basic plan of the electron microscope</i>	10
	<i>Scanning electron microscopes</i>	15
	<i>Phase and interference contrast microscopes</i>	15
	<i>Appendix to the microscopy section</i>	22
2	Preparation of the Specimen for Microscopy—Routine Methods	25
	<i>The preservation of cellular components—fixation</i>	25
	<i>Embedding and tissue sectioning</i>	27
	<i>Preparing sections for light microscopy</i>	31
	<i>Preparing sections for electron microscopy</i>	33
3	Preparation of the Specimen for Microscopy—Applied Techniques	35
	<i>Histochemistry</i>	35
	<i>Immunocytochemistry</i>	41
	<i>Autoradiography</i>	44
	<i>Cell and tissue culture</i>	47
	<i>Cell fractionation</i>	52
PART 2	THE NATURE, FORM, AND FUNCTION OF CELL COMPONENTS	55
4	The Plasma Membrane	57
	<i>Introduction</i>	57
	<i>Plasma membrane structure</i>	58
	<i>Plasma membrane function</i>	70
	<i>The role of the cell surface in receiving extracellular signals</i>	70
	<i>The plasma membrane and malignancy</i>	72
	<i>The plasma membrane and transport</i>	74
	<i>The plasma membrane and cell attachment</i>	94

5	The Nucleus	105
	<i>General features</i>	105
	<i>Functions of the nucleus</i>	105
	<i>The prokaryotic system</i>	105
	<i>The eukaryotic system</i>	109
	<i>The regulation of nuclear activity</i>	111
	<i>The fine structure and function of the nucleolus</i>	130
	<i>The nuclear envelope</i>	133
	<i>Protein synthesis – cytoplasmic events</i>	135
6	Intracellular Compartments	143
	<i>The rough endoplasmic reticulum</i>	143
	<i>The agranular or smooth-surfaced endoplasmic reticulum</i>	151
	<i>The vacuolar system</i>	161
	<i>The Golgi complex</i>	161
	<i>Lysosomes</i>	173
	<i>Peroxisomes</i>	187
	<i>Secretory granules</i>	187
	<i>The mitochondrion</i>	195
7	The Cytoplasmic Matrix	207
	<i>Formed storage products – glycogen and lipid</i>	207
	<i>Structural components of the cytoplasmic matrix</i>	208
	<i>Microfilaments and muscle contraction</i>	208
	<i>Microfilaments and muscle proteins in non-muscle cells</i>	221
	<i>Microtubules</i>	233
	Glossary	251
	Bibliography	256
	Index	261

Techniques in the study of cell structure

Much of our current understanding of cellular structure and function is very closely bound up with a proper appreciation of the strengths and weaknesses of the available technical methods employed in their study. It will, therefore, be instructive for us to preface our discussion of the cell with an account of the most widely used microscopes and their associated preparative and applied techniques.

THE MICROSCOPE

MAGNIFICATION AND RESOLUTION

In their most basic essentials all microscopes aim: (a) to magnify the object, and (b) to display the object in greater detail. These aims are interdependent and it is important to realize that to increase magnification without a commensurate improvement in the degree of discernible detail is of little advantage.

Magnification

The magnification of any optical system is dependent upon the focal length of the lenses in the system and their mutual arrangement. It is usually expressed as the ratio of the length of the final image to that of the object, and for the ordinary class microscope it is usually between $\times 25$ and $\times 1500$.

Resolution

The resolving power of a lens indicates the fineness of detail that it allows to be seen. Thus, if one examines two small objects with a microscope lens, provided the objects are well separated, they will be resolved as separate entities. If, however, they are then gradually moved closer together, a situation will eventually arise in which the two objects, though still separate, can no longer be seen to be distinct from each other. In this situation, only by improving the resolution (i.e. by using a lens with better resolving power) will it again be possible to render the two objects as separate entities (see Figure 1).

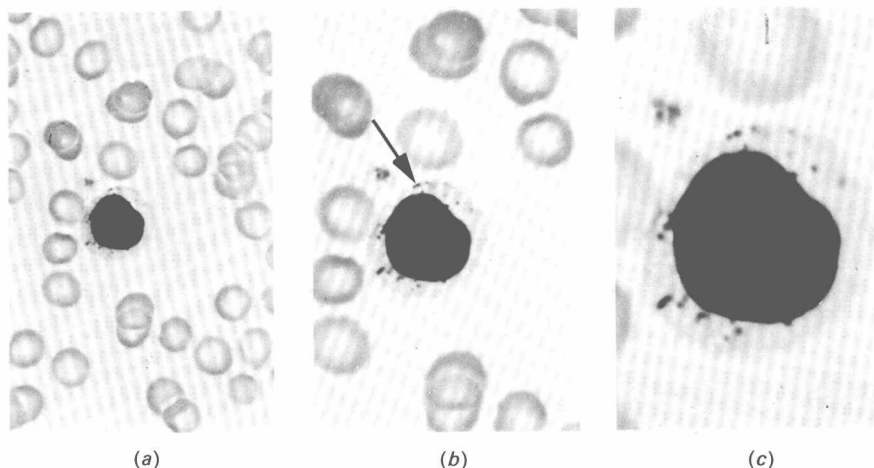


Figure 1. Resolution and magnification. A leucocyte in a blood smear photographed at increasing magnifications with the same objective lens ($\times 100$; $NA=1.32$). Thus, although in Figures (a) to (c) the final magnification is increased, the resolving power remains the same.

In (b), at a magnification of $\times 1150$, two granules (arrowed) within the leucocyte are resolved and seen as separate entities, while in (a), at a lower magnification of $\times 650$, although the lens resolves the granules, they are not seen to be separate. In (c), where the magnification is increased to $\times 2250$, the granules are larger than in (b) but there is no more detail to be seen.

Increasing the magnification over (b) without increasing the resolution is thus of no advantage (i.e. it produces 'empty magnification').

Courtesy of J. James, Histologisch Laboratorium Amsterdam, University of Amsterdam.

Factors that determine resolution

1. Numerical aperture

When light rays pass through a specimen containing fine detail they interfere with each other and they are variously diffracted; increasingly fine detail increases their angles of diffraction. Since the resolving power of a lens depends upon its ability to collect these diffracted rays, the wider the angle of rays collected the better is the resolution.

The capacity of a lens to collect rays emerging from an object is defined by its *numerical aperture* (NA), and this depends upon both its *angular aperture* (u in Figure 2) and the *refractive index* (n) of the medium through which the rays pass.

The relationship is expressed as:

$$NA = n \cdot \sin u$$

In any given lens, the NA (and thus the resolution) is at its best when the cone of rays emerging from the object just fills the angular aperture. When setting up a microscope this optimum requirement is only obtained by careful focusing of the illumination system (see section below relating to the substage condenser).

In the conventional light microscope the medium between the low-power (less than $\times 40$) objective lenses and the specimen is air (i.e.

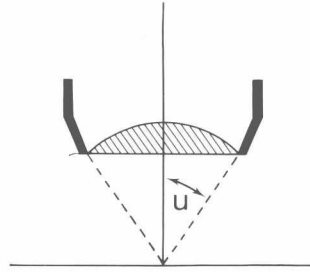


Figure 2. The angular aperture of an objective lens.

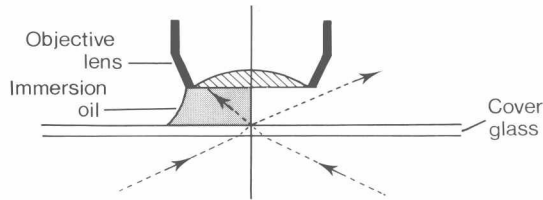


Figure 3. Oil immersion. Light rays emerging from the coverglass into air (i.e. from a dense to a less dense medium) will be bent by refraction towards the glass. Immersion oils (such as cedar wood oil) have the same refractive index as glass and thus refraction is much reduced.

the refractive index, $n = 1$). However, for lenses of higher power, where maximum resolution is required, the refractive index may be increased by filling this space with a special 'immersion' oil. The refractive index of the immersion oils used with glass-covered microscope slides is optimally about 1.55. As indicated in the equation above and as shown in Figure 3, this arrangement increases the NA and results in fewer light rays being lost due to refraction. Resolution is thus improved.

2. Wavelength

Resolution also depends upon the wavelength of the transmitted wave form; the smaller the wavelength the better is the resolution. It is primarily for this reason that the electromagnetic lenses of the electron microscope, which depend upon the extremely short wavelength of the electron (0.005 nm at a 60 kV accelerating voltage), can resolve details that are orders of magnitude smaller than those resolved by the light microscope (see below).

The resolution limit (r)

The resolution limit of a lens (which is the converse of its resolving power) can be defined as the minimum separation between two points