

Preface

It is now 100 years since adhesion of cells was shown to be vital for their growth and reproduction. Ross Granville Harrison, Fig. 1, invented the technique for culturing cells, a technique which is now of massive importance for studying genetics, cancer, tissue engineering and disease processes.

Harrison was a 37 year old lecturer at Johns Hopkins in the USA, observing the growth of nerve fibres in embryos, when he found that he could insert solid blood clot material into the animal and the cells would continue to propagate along the



Fig. 1 Ross Granville Harrison 1870–1959¹ (with permission of Royal Society)

foreign material. Subsequently in 1907 he found that the nerve cells would also grow on the blood clot in a dish outside the embryo. In his 1914 paper,² he then showed that the shape of the cells depended on the solid substrate by testing the cells on clotted plasma, spider web fibres and glass cover slips. This was the first indication that adhesion was essential for shape and differentiation of cells.

It is interesting that 100 years have also elapsed since the discovery that viruses can cause animal disease. Ellerman and Bang³ in 1908 showed that leukaemia could be transmitted to chickens by injecting cell free material. A few years later, Rous⁴ in 1910 and 1911 showed that solid tumours could be transferred from chicken to chicken to spread the disease and also isolated the infective agent in a cell free filtrate. It later became clear that the virus particles, which at that time could not be imaged by microscopy, were adhering to the cells to cause infection. Rous received the Nobel Prize for this work in 1966, more than 50 years after his observations. There was no model at that time to describe the mechanism by which the virus particle attached to and entered the cell.

The idea that fine particles in smoke caused damage to humans goes back much further: it is said that the city of London imposed smoke control in the thirteenth century because coal fires were 'prejudicial to health'.⁵ However, the understanding of the mechanisms of toxicity has only recently emerged. The particles in smoke, which are approximately the same size as cells or viruses, somehow adhere to the lung surfaces and cause organ failure, even heart disease. How does this adhesion process occur? Similarly, it was observed⁵ in the nineteenth century that chimney sweeps suffered disease from the soot which contacted them; 'I have known 8 or 9 sweeps lose their lives by the soot cancer. The parts which it seizes are entirely eaten off'. We examine some of the processes which contribute to nanoparticle toxicity in Chapter 11.

Ever since Robert Hooke⁶ viewed a slice of cork using his early microscope (Fig. 2), showing for the first time 'Cells distinct from one another', but clearly adhering very strongly to form the strong lightweight porous wood material, we have been fascinated by the adhesion forces which hold large multicellular organisms together. The purpose of this book is to address the description, definition and understanding of these adhesion forces in relation to three systems.

- Inanimate fine particles
- Virus particles
- Cells

In recent times, the theoretical idea which has dominated the field is that of the adhesion molecule, a complex protein like fibronectin for example, as described by Hynes.⁷ Such molecules have been thought to control the adhesion of cells. Indeed, an enormous amount of work has been done by thousands of scientists to define various adhesion molecules, whose range, variety, complexity and nomenclature have expanded substantially over the past decades.^{8–19} Unfortunately, the 'lock and key' model on which this science has been based, also around a century old,²⁰ is unacceptable. While there is no doubt that a coating of fibronectin on a surface definitely helps cell adhesion, we aim to show in this book that the adhesion

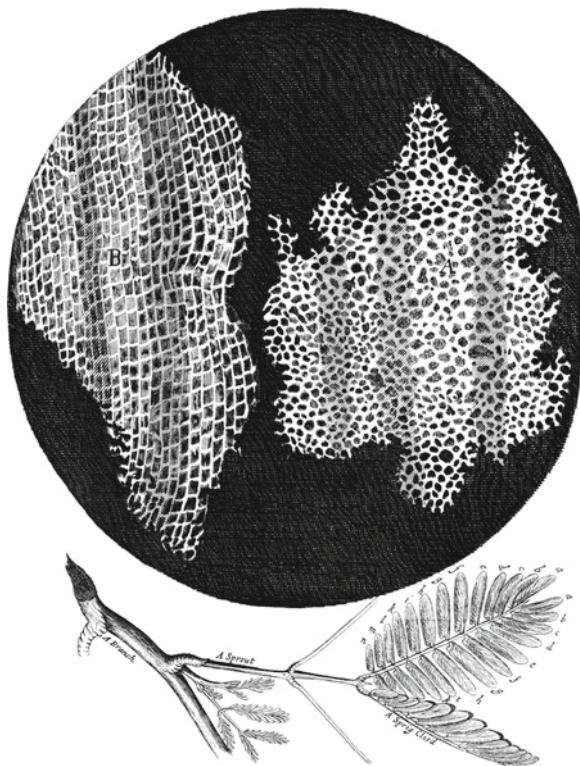


Fig. 2 Illustration from Robert Hooke's book which first showed cells and the adherence between them⁶ (with permission of Royal Society)

molecule is only one factor in the equation. Van der Waals forces are the key cause of the adhesion. Substrate elasticity and geometry are also important. In addition we aim to show that there are complex mechanisms such as Brownian motion and surfactant molecules in solution which display major effects.

Originally, the theoretical ideas used in this book were defined^{21,22} in 1970–1971. By considering the contact of elastic bodies, it became evident that three parameters generally entered the equation for adhesive force F , as indicated below.

$$F = K [WE d^3 / (1 - \nu^2)]^{1/2} \quad (1)$$

where K was a constant, W the work of adhesion in Jm^{-2} , E the elastic modulus in Pa, ν the Poisson's ratio and d the dimension in metres. From this model, it is clear that the adhesion molecules have an effect on W , but elasticity E, ν is equally influential and the geometry d is much more important. The most surprising thing about this new theory was that adhesion force was strongest when the surfaces were absolutely smooth and clean, with no adhesion molecules present. In other words the effect of adhesion molecules was to reduce the adhesion force, not to cause the adhesion force as intimated in references.^{7–19} The purpose of this book is to show

that this new theory gives a much more satisfactory account of the results than the simplistic adhesion molecule lock and key models which have dominated during the last century. Part I deals with the fundamentals, the phenomenology and the theory, Part II goes on to describe the mechanisms and measurements at both macroscopic and nanoscopic levels, then Part III looks at detailed research in adhesion of nanoparticles, viruses and cells.

In this endeavour, we have been assisted by many colleagues.

In particular KK and MK express thanks to Patricia Kendall for constant support over 40 years.

KK thanks the late David Tabor who set him on the path to studying this field and to Ken Johnson, Alan Roberts and Alan Gent who have been partners since 1966.

MK wishes to thank Morton Lippmann, Bob Maynard, Teresa Tetley and Howard Clark for timely advice, to Uludag University for solid support, and KK for making it all fun.

FR wishes to thank his mentors Erich Sackmann, Motomu Tanaka and Dennis E Discher for continuous support and inspiration and Andre EX Brown and Peter Zwiauer for critical reading and fruitful discussions.

If you have any comments on the ideas expressed here, please email us on k.kendall@bham.ac.uk, m.kendall@ex.ac.uk and rehfeldt@physik3.gwdg.de

February 2010

Kevin Kendall, Michaela Kendall and Florian Rehfeldt

References

1. Abercrombie, M, Biographical Memoirs of fellows of the Royal Society, 7 (1961) 110–126.
2. Harrison, R.G., The reaction of embryonic cells to solid structures, *J Expt Zool* 17 (1914) 521–44.
3. Ellerman, C. and O. Bang. *Centralbl. Bakteriöl.* 46 (1908) 595–609.
4. Rous, P. J. *Exp. Med.* 12 (1910) 696–705; Rous, P. J. *Exp. Med.* 13 (1911) 397–411
5. www.ace.mmu.ac.uk; British Parliamentary Papers, Session No.13, 1863: Report from the Committee of the House of Commons.
6. Hooke, R., *Micrographia*, Royal Society London 1665, available on www.gutenberg.net.
7. Hynes, R.O., *Fibronectins*, Springer Verlag, New York 1990.
8. Springer, T.A., Adhesion receptors of the immune system, *Nature* 346 (1990) 425–34.
9. Hortsch, M., Nott, P., *New Cell Adhesion research*, Nova Science 2009.
10. Umemori, H., *The sticky synapse: Cell adhesion molecules*, Springer Berlin 2009.
11. Garrod, D. R., *Structure and function in cell adhesion*, Portland Press 2008.
12. Cress, A.E., Nagle, R.B., (eds.), *Cell adhesion and cytoskeletal molecules in metastasis*, Springer, Dordrecht 2006.
13. Beckerle, M.C., (ed.), *Cell Adhesion*, Oxford University Press 2002.
14. Ley, K., (ed.), *Adhesion molecules: function and inhibition*, Birkhauser, Basel 2007.
15. Reutter, W., Schuppan, D., Tauber, R., Zeitz, M., *Falk symposium, Cell adhesion molecules in health and disease*, Kluwer 2003.
16. Coutts, A.S., *Adhesion protein protocols*, Humana Press London 2nd Ed 2007.
17. Behrens, J., Nelson, W.J., *Cell adhesion*, Springer Berlin 2004.

18. Collins, T., Leukocyte recruitment, endothelial cell adhesion molecules..., Kluwer Dordrecht 2001.
19. Barker, J., McGrath, J., (eds.), Cell adhesion and migration..., Harwood Academic Amsterdam 2001.
20. Kaufmann, S.H.E., Elie Metchnikoff and Paul Ehrlich's impact on infection biology, *Microbes and Infection* 10 (2008) 1417–9.
21. Kendall, K., The adhesion and surface energy of elastic solids, *J PhysD: Appl Phys* 4 (1971) 1186–95.
22. Kendall, K., Molecular adhesion and its applications; the sticky universe, Kluwer, New York 2001, chapter 12.

Adhesion of Cells, Viruses and Nanoparticles

Kendall, K.; Kendall, M.; Rehfeldt, F.

2011, XV, 282 p., Hardcover

ISBN: 978-90-481-2584-5