Adhesion of Cells, Viruses and Nanoparticles

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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.

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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

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Contents

Part I Fundamentals

1 Background to Adhesion of Cells, Viruses and Nanoparticles	3
1.1 The Problem of Understanding Adhesion	4
1.2 van der Waals Forces Cause Adhesion	5
1.3 Adhesion Molecules: Learning from the Gecko	6
1.4 False Hypotheses	7
1.5 van der Waals Force	8
1.6 Difference Between van der Waals and Electrostatic Forces: Yeast Adhesion	9
1.7 Fall in Adhesion Under Water	11
1.8 The Short Range of van der Waals Force	12
1.9 Measurement of van der Waals Force on Polymer Spheres.....	13
1.10 Effect of Contaminant Molecules on the Surfaces	15
1.11 Effect of Roughness	16
1.12 Effect of Elasticity on Adhesion	17
References	19
 2 Phenomenology of Adhesion: From Macro- to Nano-Systems	 21
2.1 Showing the van der Waals Adhesion Force	22
2.2 The First Demonstration of Nanoparticle Adhesion.....	23
2.3 Arguments Against van der Waals Adhesion	25
2.4 Definition of van der Waals Adhesion	25
2.5 Definition of W , the Work of Adhesion in Peeling	27
2.6 Nature of Bonds in the Equilibrium Theory of Adhesion	28
2.7 Bradley's Adhesion Rule	29
2.8 The Significance of Bradley's Rule	32
2.9 Adhesion of Spheres; Hertz Theory	34
2.10 The JKR Contribution.....	35
2.11 The Nature of Adhesive Contact Between Polymer Spheres	37
2.12 Application to Nanoparticles, Viruses and Cells	38
2.13 Conclusions.....	42
References	42

3	Modelling Nanoparticle, Virus and Cell Adhesion	45
3.1	Two Parameter Model of Atomic Interaction	
	Force and Energy	46
3.2	Demands on the Model	48
3.3	Modelling Simple Nanoparticle Adhesion	50
3.4	Sodium Chloride Nanoparticle Results	52
3.5	Elastic and Plastic Adhesion.....	54
3.6	Influence of Surface Contamination	55
3.7	Effect of Surfactants	58
3.8	Proteins as Surfactants.....	61
3.9	Models of Polymer ‘Adhesion Molecule’	64
3.10	Membrane Models	65
3.11	Three Components: Surface, Water, Adhesion Molecule.....	66
3.12	Conclusions.....	68
	References.....	69

Part II Mechanisms

4	Macroscopic View of Adhesion for Nanoparticles, Viruses and Cells	75
4.1	Fundamental Definitions.....	75
4.2	Theory Using Work of Adhesion W	77
4.3	Different Geometries; Wedging, Peeling and Spheres	78
4.4	Effect of Elasticity; Scraping and Stretching.....	79
4.5	More Complex Geometries; Button Test, Tension and Probes	81
4.6	Measured Values of Adhesion Energy.....	83
4.7	Reducing W by Adding Surface Active Agents.....	84
4.8	Measurements of Cell Adhesion by Probe Methods	87
4.9	Crack Stopping by Geometry Change	89
4.10	Elastic Changes Affecting Adhesion: Shrinkage and Pre-stressing	92
4.11	Stringing and Crazing	94
4.12	Biofilm Adhesion.....	96
4.13	Conclusions.....	97
	References.....	98
5	Statistics of Adhesion at Nanoscale	101
5.1	The Flickering Black Spot; Large Contacts.....	101
5.2	The Flickering Black Spot; Small Contacts.....	103
5.3	The Dwell-Time Effect	104
5.4	Reaching Equilibrium	106
5.5	Adhesion with Water Present at Surfaces	108
5.6	Adhesive Drag	110
5.7	Adhesive Hysteresis.....	111

5.8	Peel Stopping by Viscoelastic Loss	114
5.9	Rolling Resistance as a Measure of Adhesion Hysteresis, Drag and Dwell-Time Effect.....	116
5.10	Aggregation Statistics of Nano-Particles	117
5.11	Conclusions.....	120
	References.....	120
6	Subdivision and Separation of Contact Spots	123
6.1	Increase in Adhesion Force for Subdivided Contact Spots	123
6.2	Force Versus Energy	125
6.3	Peeling Off the Gecko Foot	127
6.4	Measurement of Single Seta Adhesion Force.....	128
6.5	Possibility of Adhesive Dislocations	129
6.6	Subdividing Contact Spots Increases Adhesion	132
6.7	Gecko Tape	133
6.8	Micro-Patterning.....	136
6.9	Stiffness and Adhesion of Multiple Contacts	138
6.10	Conclusions.....	141
	References.....	142
7	Measurement Methods	145
7.1	Light Microscopy.....	146
7.2	Reflectance Interference Contrast Microscopy.....	147
7.3	Fluorescence Microscopy, Interference Contrast, Total Internal Reflection	148
7.4	Atomic Force Microscopy	149
7.5	Optical Tweezers.....	151
7.6	Micropipette Aspiration.....	152
7.7	Spinning Disc.....	152
7.8	Cell Adhesion by Flow Methods	153
7.9	Cell Counting Methods.....	157
7.10	Adhesion by Counting Doublets	158
7.11	Experimental Results	161
7.12	Conclusions.....	163
	References.....	164
 Part III Detailed Research		
8	Adhesion of Nanoparticles	169
8.1	Nanoparticles in Space	169
8.2	Nanoparticles in the Atmosphere.....	171
8.3	Characterisation of Atmospheric Nanoparticles and Their Health Effects	173
8.4	Nanoparticles in Water.....	176
8.5	Synthetic Nanoparticle Polymers; Latex Coalescence	178

8.6	Synthetic Inorganic Nanoparticles.....	180
8.7	Gas-Phase Nanoparticle Production	183
8.8	Liquid Phase Preparation of Nanoparticles	184
8.9	New Method for Nanoparticle Tracking.....	186
8.10	Adhesion from Doublet Numbers.....	188
8.11	Detection of Adhesion with FemtoNewton Resolution.....	190
8.12	Conclusions.....	191
	References.....	191
9	Adhesion of Viruses	195
9.1	Variety of Virus Particles	196
9.2	Observing the Adhesion of Viruses by TEM & X-Ray.....	197
9.3	TEM Investigations of Adhesion Mechanism	199
9.4	Atomic Force Microscope (AFM) Studies	200
9.5	Sensor Methods for Detecting Adhesion.....	204
9.6	Single Particle Fluorescence.....	206
9.7	Self Adhesion and Aggregation by Light Scattering.....	208
9.8	Virus Calibration Using Standard Polystyrene Latex	211
9.9	Self-Adhesion of Viruses	212
9.10	Drug Treatments Associated with Adhesion	213
9.11	Preventing Virus Detachment	216
9.12	Conclusions.....	218
	References.....	218
10	Adhesion of Cells.....	221
10.1	Cell Adhesion Is a Vital Phenomenon.....	221
10.2	The Emergence of Cell Culture as Investigative Tool	223
10.3	Factors in Cell Adhesion – More than Lock and Key.....	224
10.4	Substrate Elasticity and Cell Health	227
10.5	Model Systems for Cell Adhesion Measurements.....	228
10.6	Substrate Geometry Effects on Cell Health.....	231
10.7	Elasticity Drives Stem Cell Differentiation	233
10.8	Physical Models for Cell-Substrate Interactions	233
10.9	Conclusions.....	238
	References.....	239
11	Nanoparticles Adhering to Cells; Toxicity Effects.....	241
11.1	Pathways into the Body	241
11.2	Variety of Nanoparticles	243
11.3	Measures of Nanoparticle Toxicity.....	245
11.4	Nanoparticle Surface Interactions with Extracellular Molecules.....	246
11.5	Nanoparticles Approaching the Cell Surface.....	249
11.6	Nanoparticles Entering Cells	251

11.7	Toxicity Mechanics	253
11.8	Translocation of Nanoparticles Within Organisms	256
11.9	Nanoparticle Toxicity: Lessons from the Lung.....	257
11.10	Conclusions	260
	References	261
12	Cell, Virus and Nanoparticle Adhesion: Significance and Future.....	265
12.1	Key Questions of Adhesion	265
12.2	Adhesion Fundamentals	267
12.3	Adhesion at the Molecular Level	268
12.4	Subdivision of Contact Spots	270
12.5	Connexion Between Nanoparticles, Viruses and Cells	272
12.6	Future Problems and Trends	273
12.7	A Vision of the Future	274
	References	275
	Index	277