Cell adhesion century: culture breakthrough

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This theme issue, based on a Royal Society Discussion Meeting held in April 2014, is a celebration, a reflection and a prediction.

To start, we celebrate the memory of Ross Granville Harrison FRS who first showed a century ago that chicken embryo nerve cells could be grown outside the animal [1]. This was the invention needed to begin the animal cell culture industry. Adhesion to a substrate was shown to be essential to survival and proliferation of the cells outside the organ. Harrison showed that there were several requirements for success, as he wrote in his paper

‘three principal factors, the tissue . . . the fluid . . . the solid support’.

Then we discuss the progress of cell adhesion studies in natural phenomena, ranging from geckos climbing walls using the nano-hairs on their feet, to ants sticking in water, bacteria adhering to the gut, virus and nanoparticles penetrating cells, cancer cell metastasis and organs growing industrially on special substrate materials [2].

Finally, our objective is to look ahead to the next century. What advances and innovations can we expect to arise through fresh insights in theoretical argument about the very small forces involved in cell adhesion, in the creation of new adhesion molecules at their surfaces, in genetic modification of the interface processes, and in the rapidly advancing computer modelling and measurement of cells in contact? Our main aim is to achieve the understanding necessary to progress. But understanding is an enigma only glimpsed in the eureka moment.

In his book ‘Opticks’, Isaac Newton [3] discussed forces of adhesion and stated ‘we must learn from the Phaenomena of Nature what Bodies attract one another and what are the Laws and Properties of the Attraction’. Newton worked for 30 years on the adhesion of fine particles, studied a range of nanoparticle materials ranging from antimony oxide to arsenic trioxide, and did fall sick, possibly as a result of these noxious solid particles making adhesive contact with the cells of his body [2]. The purpose of this volume is to follow Newton in exploring the attractions observed between many different types of cells and several varieties of substrates in order to arrive at a proper theory of the forces involved. One of the most interesting situations is when a nanoparticle of solid material attaches to a cell, as illustrated schematically in figure 1, and causes damage. This is particularly relevant to the nanoparticle pollution from car exhausts, an emissions problem recently seen increasing within large cities such as London, Paris and Beijing.

In figure 1, a nanoparticle is shown dispersed in a liquid, which also contains surface active molecules (‘adhesion molecules’). The particle diffuses towards the cell surface, makes contact and then wanders around the local area. It may find a point of entry or it may dislodge and continue its Brownian exploration of the fluid [4]. This process is similar to that involved in a virus infecting lung cells. A paper in this volume shows that the presence of nanoparticles can influence the progress of influenza virus infection [5].

To start this volume, we describe van der Waals force which is the source of adhesion in geckos that run up walls and under ceilings without any adhesive [6]. Next, by considering adhesion of ants feet under water [7], it becomes clear that the presence of a liquid has a large influence on van der Waals adhesion, decreasing the adhesion force by an order of magnitude. However, there is also the confusing effect that liquids may hugely increase the contact area, which may give an apparent rise in the attractive force. Also there is the

Subject Areas:
biophysics

Keywords:
cell adhesion, adhesion molecules,
Ross Granville Harrison, particle adhering to cell

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problem that many researchers are seeking lock and key mecha-
nical mechanisms which operate at the micrometre scale, not the nanometre scale. Here, we focus mainly on the
nanometre molecular interactions which are electromagnetic,
not mechanical [8].

Added surfactant molecules, often called adhesion mol-
ecules, further reduce the adhesion force to low levels,
perhaps approaching Brownian levels, where adhesion is
comparable to thermal fluctuations associated with \( kT \). The
theory of such intermolecular adhesion forces, and the con-
nection with elasticity and surface patterning with surface
chemical modification have been considered [9].

As cells become smaller, as with bacteria [10], the
adhesion forces depend greatly on the extracellular polymers
forming a molecular architecture promoting agglomeration
and possible fusion with cells. Conversely, parasites such as
viruses [11] need to remain disaggregated with very low
adhesion if they are to approach the cell membrane through
Brownian movement. How does a virus, a malarial parasite,
a sperm cell or indeed a simple polymer nanoparticle like
polystyrene, approach, then adhere and subsequently gain
entry through the cell membrane? That question ‘What
switches on the stronger penetration adhesion?’ remains to
be answered. A paper here on the ‘conception molecule’
which is necessary for a sperm cell to fertilize an ovum illu-
minates the complexity of such processes [12]. A similar
question arises when considering the metastasis of cancer
cells from a tumour to new locations in other organs.
Although it is known that cadherin adhesion molecules
have an influence, the mechanism is still unclear and requires
elucidation [13,14].

The main present application of our understanding of cell
adhesion is in cell culture and organ growth in the laboratory.
By producing templates of suitable materials, with correct
surface molecules, organs can be grown to allow skin trans-
plants, dental transplants and the possibility of organ
production in factories. One outcome of this collection of
papers will be an understanding of the modern engineering
applications of cell adhesion and its control, even in mun-
dane inflammations like gingivitis which are related to the
adhesive plaque on the tooth surface [15–17].

Finally, it is our objective to make predictions about the
next century of cell adhesion advance. The suggestion is that
better models of cell interactions at surfaces will be produced,
more refined measurements of the adhesion mechanisms at
the nano-level will be obtained, new molecules will be found
in order to control the interface structure, and novel nano-
mechanisms, such as those involved in nanotoxicity [18] may
be discovered.

My thanks are due to the Royal Society, the several organ-
izers of this meeting, to all the speakers and poster presenters
who travelled far to be present, and to the audience for
wide-range discussion contributions.

**Guest editor biographies**

**Professor Kevin Kendall** received his PhD from Cambridge and has worked for 20 years in industrial
research at ICI, and also 20 years in universities at Monash, Akron, Keele and now Birmingham. He
started his research career studying friction and adhesion and became interested in the energy balance
method for calculating adhesion forces. He has applied this method to many different areas including
adhesive joints, composites, slurries, nanoparticles, cells and viruses. He has also been involved in the
fossil energy crisis and applies fuel cells to avoid carbon emissions, especially operating a fleet of
hydrogen fuel cell vehicles with a filling station on the Birmingham University campus as shown
in the picture. He is now back in industry, CEO of Adelan Ltd, an SME developing several EU
projects. He has written more than 300 publications and patents and was elected FRS in 1993.

**Professor Stephen Busby** received his doctorate from Oxford University and then moved to the
Pasteur Institute in Paris, where he became interested in bacteria and how they organize and regul-
rate their genes. Since moving back to the UK in 1983, Steve and his colleagues have contributed to
our understanding of transcription initiation and gene activation in bacteria, as well as developing
new methodologies to study global regulation. He has produced over 200 original research articles
and a score of seminal reviews. Steve was elected FRS in 2005 and is currently Professor of Biochem-
istry at the University of Birmingham and Head of the School of Biosciences.
References