University of Birmingham

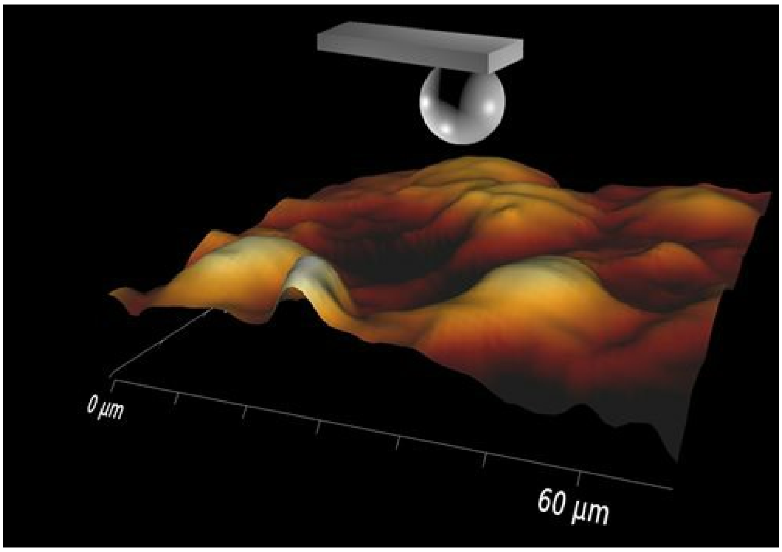
The ABC of indentation

Posted on Wednesday 13th November 2013

Accurately probing cells and tissues

About the authors

Drs James Andrews, James Bowen, and David Cheneler (ABC) are leading research fellows within the College of Engineering and Physical Sciences, having between them many publications in journals of high international standing. Their recent efforts represent a significant and profound advancement in the characterisation of materials and description of their mechanical behaviour. The award winning contribution may be found here and is free to download. Their work was enabled by the broad range of perspectives they possess from the degrees they hold, which include the subjects chemistry, chemical engineering, mechanical engineering, physics and mathematics. This collaboration is one of a number of multi-disciplinary projects they have worked on together.



A brief history of indentation

Hardness is the property of a material to resist pressure. In 1900, Swedish engineer Johan August Brinell developed the first widely used and standardised hardness test in engineering and metallurgy. Brinell’s test involves applying a compressive load to material using a sphere and observing the deformation of the material; this is an indentation measurement. The sphere is much harder than the indented material, and hence the deformation of the sphere is negligible compared to the deformation of the material. This is effectively the approach taken to understand materials right through to the current day, although more exotic indenter shapes such as pyramids and cones are used in addition to spheres.

Indentation is a versatile method of acquiring data regarding material deformation, but converting the data into material properties requires careful consideration. In order to measure a compressive load, the instrument requires a flexible element, the stiffness of which can vary greatly depending on the load. For the lowest load, consider the weight of a single bacterium; for the highest load, consider the weight of a four-wheel-drive family car. Hence, the stiffness of the measuring element correspondingly varies greatly also. The stiffness of the measuring element is described by a spring constant, a parameter which describes the force required to deform the spring by a given distance. There exist a range of scientific instruments to measure deformation; each instrument serves a restricted range of loads and length scales. Each instrument consists of common components assembled in the same way. It is not possible to pick up a single cell with a device designed to lift a car, similarly a device designed to pick up a cell will not lift a car, and there are similar restrictions when indenting.

Indentation and the problems resolved

Indentation is the most common method for determining material properties, however the underlying theory has developed little in the past 40 years. Over the past 20 years indentation has been used to determine the material properties for materials which have not been considered theoretically. The following issues are a direct result of this:

1. Poor material characterisation, leading to poor selection of alternative materials, i.e. materials used in hip replacement technologies.
2. Inability to accurately predict material behaviour during nanoscale fabrication, i.e. nanolithography to develop nanocircuitry.
3. Indentation using optical tweezers within a cell cannot be interpreted despite the advancement this offers to mechanotransduction, the field relating mechanical sensing to chemical signals which a cell can interpret.

The benefits to humanity by resolving these issues are profound and far-reaching, from rapid development of biomedical devices to nanoscale structures increasing the capability of circuitry beyond our current limits. Further, the field of mechanotransduction has only the crudest tools available to elucidate the behaviour of cells. The remaining discussion details how the issues have been resolved for these complex materials.

Complex materials

A mathematical model was developed and solved by ABC to determine the best possible guidance regarding how stiff the measuring element should be, or rules for how quickly or how deep the measurement should be performed. Further, if comparisons are to be made for a range of different length, time or stiffness scales, this is now possible. Previously the selection of stiff springs masked the time-dependent nature of the materials, giving them the appearance of a more elastic material. As an example of where this effect was detrimental, poor choices of material selection for hip replacements were made because of this, trial and error resolved these issues. Biomedical implants and devices need no longer suffer from a poor choice of material selection.

Nanoindentation is the application of a nanoscale deformation, typically much less than one micrometre, and measurement of the compressive load required. Previously, the biggest problem with nanoindentation is that the stiffness of the spring pushing the indenter into the material is comparable to the effective stiffness of the material; hence the mutual compliance of these two elements cannot be neglected. Until the work of ABC there was no way to include this in the determination of time-dependent material parameters. No-one wants a replacement hip that is uncomfortable, fails to perform, or yields prematurely, yet this is exactly what resulted from the previous approaches to material determination. To counter this, hip replacement went through a rapid evolution to find suitable materials; in the future this will be far simpler as the material parameters can now be determined.

Since the advent of nanolithography, the art of fabricating nanoscale structures for nanocircuitry, there has been an increasing interest in indenting soft materials to make such structures cheaply and effectively. Thanks to the efforts of ABC this cannot only be modelled but also controlled enabling structures and nanocircuitry which were previously difficult to create.

The mathematical model also describes the indentation using optical tweezers within a cell and determines useful information about the structure, function, dynamic properties and diseased state of a cell which were previously unachievable all thanks to the work of ABC. Further, by combining this information with the novel methodology of Rawson et al., which can be found here, a powerful and robust tool for investigating mechanotransduction is created.

Acknowledgement
This work was supported by the European Union under the FP7 programme (NANOBIOTOUCH Project: FP7-NMP-228844).