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Review Article

Probing mechanical principles of cell–nanomaterial interactions

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ABSTRACT

With the rapid development of nanotechnology, various types of nanoparticles, nanowires, nanofibers, nanotubes, and atomically thin plates and sheets have emerged as candidates for an ever increasing list of potential applications for next generation electronics, microchips, composites, barrier coatings, biosensors, drug delivery, and energy harvesting and conversion systems. There is now an urgent societal need to understand both beneficial and hazardous effects of nanotechnology which is projected to produce and release thousands of tons of nanomaterials into the environment in the coming decades. This paper aims to present an overview of some recent studies conducted at Brown University on the mechanics of cell–nanomaterial interactions, including the modeling of nanoparticles entering cells by receptor-mediated endocytosis and coarse-grained molecular dynamics simulations of nanoparticles interacting with cell membranes. The discussions will be organized around the following questions: Why and how does cellular uptake of nanoparticles depend on particle size, shape, elasticity and surface structure? In particular, we will discuss the effect of nanoparticle size on receptor-mediated endocytosis, the effect of elastic stiffness on cell-particle interactions, how high aspect ratio nanomaterials such as carbon nanotubes and graphenes enter cells and how different geometrical patterns of ligands on a nanoparticle can be designed to control the rate of particle uptake.

Contents

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1. Introduction

This paper is dedicated to the memory of Prof. Rodney Hill (11 June 1921–2 February 2011) who was the founding editor of the Journal of the Mechanics and Physics of Solids and is widely regarded as among the foremost contributors to the foundations of solid mechanics over the second half of the 20th century. His early work was central to founding the mathematical theory of plasticity. During World War II, the 22 year old Hill joined a team established under Nevill Mott at Fort Halstead, near Sevenoaks, Kent, to carry out theoretical research on military armaments. One of his initial assignments was to examine the penetration of steel armor by high-velocity shells with tungsten-carbide cores, an investigation which aroused his lifelong interest in the mechanics of plastic deformation[1]. Time fast forward to 2013, World War II is long gone, and the interests of solid mechanicians have grown much beyond the traditional topics of the field such as elasticity and plasticity. Somewhat analogous to Hill's problem of a plastically deforming steel armor pierced by a shell (Fig. 1a), a current problem of immediate concern to the society is that nanomaterials, which include various types of nanoparticles, nanowires, nanofibers, nanotubes and atomically thin plates and sheets, could penetrate the membrane of human and animal cells, as shown in Fig. 1b. This lecture aims to demonstrate that such problems in biology could present challenges to solid mechanicians in the 21st century, as plastic deformation of solids did in much of the 20th century and even today. In the following, we summarize a number of recent studies (Gao et al., 2005; Shi et al., 2008a, 2008b, 2011; Yi et al., 2011; Li et al., 2012, 2013) conducted at Brown University on the mechanics of cell–nanomaterial interactions, including the modeling of nanoparticles entering cells by receptor-mediated endocytosis and coarse-grained molecular dynamics simulations of nanoparticles interacting with cell membranes.

The objective of this research is to develop a systematic, multiscale theoretical framework for modeling uptake and release of nanoparticles in human and animal cells. It is well known that cells can internalize extracellular materials via endocytosis, a term used to describe a number of cellular uptake mechanisms including phagocytosis, pinocytosis, clathrin-dependent receptor-mediated endocytosis, and clathrin-independent endocytosis (Mukherjee et al., 1997; Alberts et al., 2002). Research on endocytic pathways is of significance not only to the understanding of hazardous effects of viruses and nanomaterials in general but also to the medical applications such as gene/drug delivery and medical imaging (Peppas and Langer, 1994; Saltzman, 2001). A major part of our study has been focused on the influence of particle properties on receptor-mediated endocytosis which is one of the most important vesicular traffic mechanisms in cellular transport. During the last few years, it has been found that particle properties such as size, shape, elastic modulus, surface microstructure and porosity can substantially influence phagocytosis (Champion et al., 2007), circulation (Geng et al., 2007) and targeting (Tao and Desai, 2005). Mechanical properties strongly influence the functioning of the immune system; for example, macrophages are unable to phagocytose very soft targets (Tao and Desai, 2005). The reader is referred to Albanese et al. (2012) for a review of recent experimental studies on the subject. Mechanics of cell–nanomaterial interactions aims to provide a fundamental understanding of these phenomena via systematic and multiscale studies on the mechanisms of uptake and release of nanoparticles in cells, focusing on the effects of particle size, shape, mechanical properties and surface structure of particles and other environmental factors on particle uptake and release processes.

1.1. Size effect

It is known that the physical process of endocytosis is size dependent (Peppas and Langer, 1994). The smallest particles near atomic dimension can enter cells through direct transmembrane diffusion or via protein channels. Larger particles can enter cells via a membrane wrapping mechanism with or without clathrin or caveolin coats. Still larger particles can be ingested via phagocytosis, a process driven by the actin myosin cortex in phagocytosis competent cells such as macrophages or amoeba. Particles on the order of several tens of nanometers are known to be most efficiently taken up via receptor

[1] "Obituaries: Professor Rodney Hill". The Telegraph. 8 March, 2011. (http://www.telegraph.co.uk/news/obituaries/science-obituaries/8369373/Professor-Rodney-Hill.html)