Chapter 26
Nanotechnology-Based Studies in Systems Biology

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ABSTRACT

In recent years, nanotechnology-based studies have been employed in the area of systems biology. The current chapter aims to give a concise view of this emergent field of research, namely nano systems biology. A large number of such studies are based on understanding surface reactivities of a biological system. Another stream of studies is focused on imaging approaches using nano systems biology. In this chapter, the authors also illustrate state-of-the-art work using these approaches in nanomedicine.

INTRODUCTION

Nanotechnology has its roots in engineering design where it is important to generate useful design without much focus on the precision, where as systems biology is an area with the main focus on prediction of precise cellular response(s) to the specific stimuli. The term "systems biology" was first used in the 1960s, when theoretical biologists began creating computer-run mathematical models of biological systems (Spivey, 2004). Systems biology captures global sets of biological information from as many hierarchical levels of information as possible (DNA, RNA, protein, protein interactions, protein and gene regulatory networks, cells, organs, individuals, populations, ecologies) and integrates them. This is the start point for the formulation of detailed graphical or mathematical models of biological systems, which are then refined by hypothesis driven, iterative systems perturbations and data integration. The key is that phenotypic features of the system must be tied directly to the behavior of the protein and gene regulatory networks. Ultimately, these models will explain the systems of emergent properties of the biological system of interest. Once the model is sufficiently accurate and detailed, it will allow biologists to accomplish two tasks never before possible: 1) predict the behavior of the system given any perturbation, and 2) redesign or perturb (e.g., with drugs) the gene regulatory networks to create completely new emergent

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systems properties. This latter possibility lies at the heart of preventative medicine. Thus, systems biology is hypothesis driven, global, quantitative, iterative, integrative, and dynamic in nature (Hood et al., 2004).

NANOTECHNOLOGY BASED STUDIES IN SYSTEMS BIOLOGY

Nanotechnology is the science and engineering of manipulating matter on unprecedentedly small scales (a nanometer is a billionth of a meter) to create devices with novel chemical, physical and biological properties. Entirely new scientific questions may be inspired and addressed by the reagents and devices at the nano scale. The central components of systems biology are genetically programmed networks within cells and networks of cells. These components establish the organization and function of individual cells and tissues in response to environmental signals such as cell-to-cell communication within organ systems and whole organisms. In this context, disease is considered as a genetic or environmental reprogramming of cells to gain or lose specific functions that are characteristics of disease (Hood et al., 2004). A renowned work in this area is the renowned discovery of DNA coating nanoparticles (Spherical Nucleic Acid (SNA) constructs) by Mirkin et al (Mirkin, 2012). The attempt was to miniaturize the chemical systems and to design programmable nano particles. These gold nanoparticles became equivalent of a litmus-like test for DNA. Importantly, SNA can enter the cells; knock down genes without setting of cellular immune response (Nanoflares). Table 1 enlists state of the art system biology studies that employ nanotechnology methods.

Nano Scale Systems for Studying Surface Reactivities

Studying and controlling reactions at surfaces is of great fundamental and applied interest in biology, electronics and catalysis. Because reaction kinetics is different at surfaces compared with solution, frequently, solution-characterization techniques cannot be used. The solution gradients prepared by electrochemical means can be used for controlling

Table 1. Nanotechnology based studies in Systems biology

S.No.	Topic	References
1	Systems biology and nanomedicine in predictive, preventative, and personalized approach to medicine.	(Hood et al., 2004; Weston and Hood, 2004)
2	Cellular signaling dynamics analysis in development of micro fluidics, micro- and nanodevices, models.	(Wikswo et al., 2006)
3	Single molecule imaging and mathematical modeling used for making dynamic and kinetic models explaining unitary biological reactions in cells.	(Du et al., 2006; Sako, 2006; Sako et al., 2012)
4	Systems biology analysis revealed that unfolded protein-associated endoplasmic reticulum (ER) stress response as the predominant event.	(Tsai et al., 2011)
5	Super paramagnetic iron oxide nanoparticles used for protein separation and therapeutic delivery of DNA and drugs (interactions identified using STRING database).	(Salaklang et al., 2008)
6	Computational methods for reverse-engineering complex gene regulatory networks to find suspect genes those seem to mediate cancer development.	(Brock et al., 2014)
7	System of interacting molecular networks and targeting disruptions in the system with nanoscale technologies.	(Heath et al., 2009)
8	Systems biology principles and nanoscale technologies are used for understanding synthetic systems with cell-like complexity.	(Doktycz and Simpson, 2007)