Chapter 3
Systems Approach to Understanding Oral Diseases

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ABSTRACT

This chapter reviews the principles of systems biology and their application through computational methods (bioinformatics, computational biomodeling, genomics, proteomics, oral human microbiome, molecular modeling, systems biology, protein structure prediction, structural genomics, computational biochemistry and computational biophysics methods and projects) that have been applied to oral diseases research. The emphasis of the chapter is on concepts from molecular biology, genetics, and traditional pathology to provide new insights into oral diseases, and the associated technologies to provide new diagnostic, therapeutic and prognostic information. Another goal of the manuscript will be to serve as a central reference to access of information about systems biology resources for research into oral diseases.

INTRODUCTION

Factors underlying biological and socio-biological states include a complex interplay of several biological, behavioral, economic, and social factors. A reductionist view usually assesses the interplay of factors using a "drill-down" approach by examining smaller parts of a system under the paradigm that these parts, when fit-together, will translate to a fully functional whole. However, often such aggregative method does not work properly. The systems dynamics approach, developed by JW Forester in the mid 1950s (Forrester, 1985) and has been since used in business, engineering, and transportation. Its use to address problems in biology and health is recent. Models developed in this way can be limited by the available information, experience and expertise at hand from a group of persons who are involved in the process and therefore is a function of the insight of the group developing these models as well as the available data.

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Table 1. Commonly used terms in context of systems biology (Adapted from Fisher & Henzinger, 2007)

Biomics	Systems analysis of the biome (climatically and geographically defined areas of ecologically similar climatic conditions such as communities of all types of life forms).
Fluxomics	Study that deals with the dynamic changes of molecules within a cell over time.
Genomics	Study of the genomes of organisms.
Glycomics	Study dealing with identification of the entirety of all carbohydrates in a cell or tissue.
Interactomics	Study dealing mostly with protein-protein interactions but is also applicable to study of interactions between all molecules within a cell.
Metabolomics	Study dealing with identification and measurement of all small-molecules metabolites within a cell or tissue.
Proteomics	Study dealing with complete identification of proteins and protein expression patterns of a cell or tissue.
Transcriptomics	Study dealing with whole cell or tissue gene expression measurements.
Closed system	A closed system is completely self-contained and is not modified by the environment.
Deterministic system	A deterministic system always has the same response to a particular stimulus under a set of conditions. Therefore, the output from such a system can always be predicted.
Distributed system	A distributed system consists of a collection of autonomous computers connected through a network of that enables them to coordinate their activities and to share the resources of the system so that users perceive the system as a single, integrated computing facility.
Nondeterministic system	A nondeterministic system has several different possible reactions to the same stimulus under the same set of conditions. Therefore, the output cannot be predicted from the input.
Non-reactive system	A non-reactive system carries on the same process irrespective of the changes in other processes.
Open system	An open system is interacts with the environment and is modified by these environmental interactions.
Reactive system	A reactive system consists of parallel processes, where each process may change in reaction to another process changing its state.

BIOLOGICAL SYSTEMS

Several types of biological systems can be described based on their inherent properties (Table 1). Biological systems are complex open systems for which four fundamental universal properties of complex biological systems have been recognized that are not are not apparent from study of the parts. These properties are: emergence, irreducibility, modularity and robustness.

- **Emergence:** This implies that the system has unique properties that occur due its existence as a system, and are not inherent in or integral to their parts and cannot be projected from the individual properties of the parts. Therefore, the system is more than the sum of its parts i.e. the system emerges as a more complex entity than a simple mix of its individual parts. For example, the life in a cell is an emergent property because it does not occur just by putting together DNA, RNA, proteins, carbohydrates and lipid along with other minerals in a soup. Emergence is a key to complex biological systems and is a result of interactions between the different composing parts in specific manners. It is seen at different levels of biological organization and a direct result of the complexity of this organization. Other examples of emerging properties include: the functional properties of proteins are not evident only in the linear chain of their constituting amino acids, but "emerge" from the secondary, tertiary and quaternary structure of the proteins – changing these complex structures also takes away the protein function.

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