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The Coming Age of Future Medicine: Next Frontier

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Introduction

The era of modern medicine is driven by recent advances in bioanalytical and bioinformatics technologies and the novel insights into human biology that are emerging through the application of these technologies. Physics and its discoveries have been at the forefront of medical diagnosis and treatment since the discovery of X-rays in 1895 [1]. Since then, biological researches have been renovating from a descriptive or phenomenological to a quantitative and predictive discipline by employing the physics covering possible degrees of freedom leading to changes in the way biological systems are understood [2]. Rutherford's elucidation of atomic structure had amalgamated physics, chemistry and biology to better understands nature. Innovations and theoretical progression in these fields leads to developments of advanced molecular medicine. These days, medicine is greatly affected by new innovations like systems medicine, data-driven science and medicine, nanotechnology and medicine, as well as measurement and the medical front line and eventually, enabled the development of strategies for personalized health care in the future [3]. This observation highlights the cornerstones of new biology that incarnate the principles of multidimensional fields. These are likely to contribute to and are attributes of next-generation medicine and indicate some of the interdisciplinary and multidisciplinary advances that will affect future medicine [4].

Systems biology advances the interaction of all of the individual components of a biological system interacting in time and space to determine the functioning of the system. It permits integration of big-data from molecular biology and genomic research with an understanding of physiology, to model the complex function of cells, organs and whole organisms, bringing with it the potential to improve our knowledge of health and disease. To eradicate complex human diseases, physicists seek to comprehend the function of complex biological systems with vigorous *ab-initio* attempts to deduce structural biochemical networks at different level of molecular, cellular and physiological dynamics [5].

Bioinformatics' approach particularly target-based drug discovery sets systems biology apart from those of more classic and reductionist bimolecular biology approaches. Science is about the marshalling of information, and machine-learning methods are just a part of the world of information science. Traditional strategies for the design of experiments cannot be adequately used to deal with these situations, that is why heuristic methods of machine learning seems preferable. In machine learning and optimization, we hypothesize enormous multi-dimensional search space of possible experiments out of which we choose the one that potentially gives us the best chance of success in mainstream medicine [6].

Technology Development for Omics Medicine

Modern medical technology is all about the identification and treatment of diseases with any of the several techniques with emphasis on improved sensitivity, low cost, and ease in use of the equipment for reasonably high throughput [7]. These measurement modalities for molecular identification coupled with low-cost-assay chip production, leads to personalized health care based on some of the definitions for systems or omics [8]. The human genome project ushered with omics revolution leads to complete inventories of other biomolecules related to particular classifications. For example, the availability of whole-genome sequences with scientific literature in a digital format allows the reconstruction of the metabolic networks that exist in cells [8]. Similarly, molecular pattern analysis of proteins offers a way to identify diseases that might be *hitherto* ill-defined at the genomic level [9]. Representations of these networks and molecular pattern analysis will be an important resource for systems biology and future medicine for which the availability of different methods of data analysis is increasing.

Data-Driven Medicine

With the spread of electronic health records for patient molecular data, powerful data repositories with tremendous potential for biomedical research, clinical care and personalized medicine are being fabricated [8]. This change is driven partly by a desire to improve the current state of medicine using new technologies, partly by supply-and-demand economics, and partly by the utility of wireless devices. These hold vast potential for revolutionizing medical science including population health, and genomic medicine. The genomic medicine includes the mapping and sequencing of genes to discover and create individualized treatments for genetically driven diseases like cancer and diabetes. It necessitates methods of data or information handling intelligibly with innovative insight gained through biological research to aid physicians if any kind of systems-biology-based health-care service is to be established as clinical decision support systems [10]. The development of omics, including advanced methods for metabolomics and emergence of biobanks can offer the medical practitioner a portrait of a patient's health at any particular time to provide personalized medicine by monitoring metabolites routinely and to discover genetic markers to ailments to overt disease early [3]. However, wired technology can be cumbersome for patient monitoring and can restrict the behaviour of the monitored patients, introducing bias or artefacts. However, wireless technologies, while mitigating some of these issues, have introduced new problems such as *data dropout* and *information overload* for the clinical team.

For example, the impact of multidisciplinary approach to impinge on disease symptoms is being recognized for neurodegenerative diseases, cancer, diabetes etc. The high attrition rates of drug candidates in clinical trials could partly result from underestimation of the complexity of the pathophysiology in these diseases [11]. For example,

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type 1 diabetes (T1D) is a chronic degenerative disease caused by less known genetic or environmental or both factors and is characterized by gross dysregulation of glycaemia, owing to autoimmune destruction of β-cell function, and by long-term complications associated with hyperglycaemia. The hyperglycaemia provokes several complications like retinal damage that can lead to blindness, renal insufficiency, destruction of nerve fibres or what is called diabetic foot where ulcers form, leading eventually to the need to amputate. About 0.3% of the population particularly children and young adults are suffering and its incidence is increasing by 3% to 4% a year [3].

Currently two approaches to improve the long-term complications of type 1 diabetes are used to try to replace insulin physiologically, with the goal of achieving near-normal glycaemia and henceforth to reduce the progression of microvascular and cardiovascular disease among diabetic patients. The *biologic* approaches replace missing β-cell function by transplanting whole organ pancreas or isolated islets. It has limitations as it need for immunosuppression and has limited survival of transplanted tissue, particularly isolated islets and hence necessitates adding exogenous insulin therapy within 2 to 4 years of transplantation. Given the inconstancy and hectic pace of modern life, compounded by the guesswork of insulin dosing and the inconsistent absorption, duration and peak effects of insulin with current methods of insulin therapy, a promising *mechanical* approach uses an artificial or bionic pancreas that emulate physiologic insulin levels. These devices replace decision-making by patients with a computer algorithm that receives frequent data from a continuous glucose monitor, calculates insulin dosing and automatically administers the insulin. It has the advantage of using data from continuous glucose monitors to adjust insulin dosing to the patient's changing needs, even during the vulnerable period of sleep. Treatment with the artificial pancreas increased the amount of time patients spent in the target range of blood glucose levels and decreased hypoglycemia.

If these approaches are equipped with virtual screening technologies *viz.,* structure-based methods, ligand-based approaches, QSAR or docking simulation, large-scale correlation analysis for chemical structures and gene expression from PubChem and Library of Integrated Network-based Cellular Signatures (LINCS) etc., the connection among small molecules, genes and diseases could guide to develop future quantitative polypharmacology model for human drug targets efforts. The use of structure based methods (The RCSB Protein Data Bank; http://www.rcsb.org) to search second- and off-targets will improve the understanding of diseases and drugs. A retrospective cohort study of population-based electronic healthcare records could provide early drug safety profiles [12].

Synergism Driven Drug Combinations

Useful tools for predicting drug combinations with a synergistic effect can increase the success rates of drug action. The identification of effective, synergistic drug combinations could lead to an increased understanding of complicated disease pathophysiology and to the design of better treatments for the disease [13]. This method used a phenotypic cell viability assay to generate dose–response curves for each drug first. Then, a differential evolution algorithm was used to predict new combinations from applied drug combinations. DrugBank provides a drug–target network that reveals the potential target, off-target, DDIs and side effects of FDA-approved drugs [14]. PharmGKB offers ample information on pharmacogenetics interactions while SIDER, FDA Adverse Event Reporting System (FAERS) and DailyMed databases are the side effect resource. In addition, several systems have been developed to explore existing DDIs swiftly from published results [15].

Nanotechnology and Nanomedicine

Nanotechnology is being seen as humanity's attempt to build and control macromolecular structures as a facsimile of what living cells do much more elegantly with much greater effectivity. This specialty seems likely to offers real promise for progressing our understanding of many medical applications like genome sequencing and use in microarray chips. Some advanced automatons of nanoparticle-based technologies include smart vaccines and computational gene for early prevention of disease. The structural automaton consists of a normal gene as a template to encode the input and elicit transitions to functional automaton. The functional automaton is designed to have any number of different properties- e.g., the possibility of repairing damaged DNA (genes) [16]. These possibilities are speculative but in due course achievable.

The T1D project is an example of this in operation where researchers at *Germans Trias Research Institute* in collaboration with *Catalan Institute for Nanoscience and Nanotechnology*, Barcelona have formulated an autoantigen loaded phosphatidylserine liposome nanoparticles. Liposomes created here ranges from half to one micron droplets of fat and water and were specifically generated to imitate beta cells of the pancreas that are in the process of apoptosis. When these particles are introduced into the body they arrest the destruction of the beta cells and allow it to recuperate immunological tolerance by arresting autoimmunity in T1D. This technique could be a much better candidate for a human vaccine. The next steps are to confirm the efficacy *in vivo* with cells from patients and to carry out clinical trials to prevent the disease and for preventive vaccination and to cure the disease by combining the vaccine with regenerative therapies as well as to optimize the product for personalization (Figure 1).

On the whole, we actually need a formal mathematical model of the organism to understand the function of an organism in health and disease e.g., the digital human being modelled with the knowledge of generalized anatomy and physiology. This model is then used for the occurrence and severity of complex diseases and biomarker profiling to identify whether an individual has a disease, stratify individuals for treatment with different drugs, assessment of the efficacy of the drug regimen, or assessment for other medical procedures. The effects of different treatments can be tested *in silico* and the model can be adjusted so that it is aligned with our knowledge of the changes in variables in a particular system; these procedures are done iteratively. Thus, the medicine of the future, then, will be based much more on information science than is the case, will focus on health and not disease (eg, traditional Ayurvedic medicine), and will be predictive, preventive, and personalised.

Last Words

Today, technological innovations in the form of automation owing to demands from omics research have led increasingly too cheap, sensitive and high-throughput applications and eventually have use in point-of-care medicine. Personalized medicine will increase the effective deployment of health care, facilitate the discovery and clinical testing of new products, and help determine a person's predisposition to a particular disease or condition. Data-driven medicine will become a priority in the future as the health systems are transformed by technology. Additionally, a record of an individual's genome sequence and internet-based methods will enable access to all knowledge

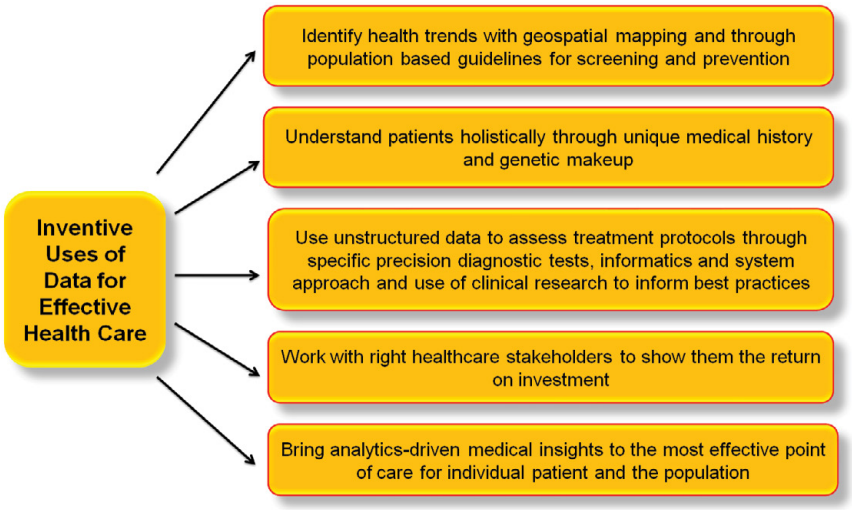

Figure 1: Inventive uses of data for most effective health care **(**The complexity of data supporting most effective health care will require health systems to provide diagnostics, informatics, and decision support to health care providers. The most effective health care for a patient population reflects a combination of generalized screening and prevention measures in combination with the application of individualized diagnostic tests and treatments that are based on a patient's unique genetic predisposition and history).

pertaining to human beings, thereby allowing a unique and accurate assessment of the patient. The output of systems approaches could be useful for understanding living systems but effective implementation of the science into practical medicine will require articulate biophysicists and biochemist as well as a receptive community of systems-savvy physicians.

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