The Promise and Challenge of Digital Biology

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Introduction

The era of Digital Biology began in 2010 with the “rebooting” of a bacterial cell using a synthetic DNA genome created from a digital template stored on a computer [1]. With this event, the creation of Mycoplasma laboratorium (nicknamed “Synthica”), came the first complete proof that DNA was the true software of life. Cells could be simulated digitally and the simulations could be tested against reality by reprogramming cytoplasm with synthetic genomes generated from the digital DNA sequences driving those simulations. This in turn has created the expectation and promise that a deeper understanding of cellular function and thus life itself could be achieved on an infinite iterative loop of computer modeling and chemical synthesis (Figure 1) [2].

Key components of the digital biology loop are 1) a detailed digital mapping of living systems and their biomolecular parts and the interactions of such parts-biodigitization, 2) accessible databases containing/managing this biodata, 3) computer simulation algorithms of cells driven by digital DNA sequences encoding the biomolecular parts and interactions-biosimulation, 4) laboratory technologies to deeply analyze the resulting synthetic cells-biolab-and finally and centrally 5) the digital biological converter (digital bioconverter for short). In these early days of digital biology, each of these components presents exciting bioengineering, bioscience and biomedical challenges.

Biodigitization and Biodata

Every aspect of Earth’s biosphere is currently being digitized, from the molecular to the planetary levels and the data entered into an ever-growing collection of biologically oriented Internet databases-a mirror backup image of terrestrial life is literally being created (Figure 2A) [3]. The digital acquisition of DNA sequences of phage, viruses, bacteria and human cells, the 3D structures of biomolecules as well as the detailed cellular structures and tissue and organ architecture has been underway in earnest for more than two decades now. With the advent of molecular imaging, electronic medical records, and “Big Data” [4,5], every aspect of individual organisms, populations, and ecosystems are now also being fed into the Internet based DataStream. Online biological databases are also on track for doubling every 5 years [3,6] (Figure 2B). The sheer volume of such data now threatens to overtake current data storage and search technology, and may require the development of novel technologies, including nucleic acid based data storage [7] and quantum computing [8].

Biosimulation and Biolab

While a number of simulations of cells have been developed over the last two decades [9–11], so far only one specifically driven by a digitized DNA genome from a real cell [12], Mycoplasma genitalium, has been published. The advent of synthetic biology tools such as Tinkercell [12–14] and database driven animation [15] provide strong starts for the tools that will be needed. Detailed electronic images of biomolecules useful in simulations are already readily available from such sources as PubChem and Biosystems [6]. On the other side of the issue, biolab tools for analyzing and manipulating synthetically produced living cells are arising with breathtaking speed. Molecular imaging of structures within living cells is now possible [16–19], and even the direct physical manipulation of cellular components using optical tweezers is a routine technique [20]. Additive manufacturing tools now make the construction of artificial biofilms and organs for research a reality [21–28] (Figure 3).

Digital Bioconverter

The key “gadget” in digital biology, the digital bioconverter (Figure 4), currently exists as a prototype [2] and will likely eventually evolve...

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Figure 2: A: Biological data is being acquired at every level of Earth’s biosphere and B. the digitized biodata is being incorporated into Web accessible databases at a doubling rate of once every 5 years (from [8]).
into a miniaturized commercially produced laboratory instrument. Such a system would allow the convenient production of cells, viruses and biological molecules directly from digitized gene encoding DNA sequences, and eventually could be as central to basic bioscience research as automated DNA sequencers are today. Significant challenges must be met before this is realized, however. While synthesis of large genomes is now possible, it remains complex and expensive. An alternative to cell free systems-DNA tagged RNA system. Methods Mol Biol 714: 221-235.


mammalian organ systems and their integration into models of whole animals and humans. Lab Chip 13: 1201-1212.


