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A Vision for Biological and Chemical Information Technologies

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A Vision for Biological and Chemical Information Technologies[1]

Steen Rasmussen, Martyn Amos, John McCaskill and Peter Dittrich

1. Introduction

We present a vision for the emerging field of biological and chemical information technologies (bio/chem IT). We describe its background challenges and motivating factors, attempt to delineate its scope, introduce different approaches to its realisation, imagine possible impacts and illustrate it using five case studies of projects that fit within its remit. We conclude with a discussion of one possible "grand challenge" for bio/chem IT, which captures all of the various projects discussed in an over-arching context.

2. Challenges and Motivation

The capabilities of biological and chemical-based systems are being harnessed for the purposes of radically new forms of *computation* and nano- and micro scale *production*. Natural systems are inherently self-organizing, self- repairing, resilient, distributed and adaptive, and they can be interfaced with traditional, silicon-based substrates to offer the possibility of *truly hybrid* systems with properties from both substrates. The growth (and integration) of emerging research areas such as systems- and synthetic biology, artificial cells, chemical information processing, micro-electro-mechanical systems (MEMS), nanotechnology and artificial intelligence means that biological and chemical information technologies provide one of the most vibrant and important emerging research domains in recent years. Bio/chem IT is an *enabling technology*, with wide ranging application areas for current information and communication technologies (ICT) and beyond. The long term potential for creating more life-like and intelligent computational, information processing and production processes will open up applications in most sectors of our society. Possible mid-term application areas for technologies emerging from this work include engineered intelligent diagnostics and drug delivery systems, artificial tissues, nanotechnology for energy and environmental applications, adaptive bioelectronics and molecular synthesis.

Traditional information technology (IT) relies on human-engineered solutions implemented on a silicon-based substrate. Although powerful in terms of raw processing capabilities, modern computers lack the adaptability, resilience and flexibility of natural systems. Even the simplest organisms are capable of reconfiguring their internal architectures in response to combinations of external signals and internal programming; a process that is inherently *bio-chemical* in nature. Furthermore, bio-chemical systems continuously produce their own material building blocks. The field of biological and chemical IT (bio/chem IT) seeks to harness the capabilities of natural and chemical systems. Rather than simply *deriving* inspiration from living systems, bio/chem IT researchers seek to *directly use or construct* these systems for the purposes of engineering, computation and production.

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[1] Excerpts of this paper were taken from *Procedia Computer Science* **7**, 2011, 56-60, doi: 10.1016/j.procs.2011.12.019.

3. Scope

Several of the authors contributed to a FET Consultation Workshop in 2008, on the subject of "Designing alternative bio-inspired ICTs", and we quote from their report[2], in which they describe the emergence of bio/chem IT as a significant and sustainable field:

"[Bio/chem IT] expands radically on existing proactive challenges such as Nano-scale ICT devices and systems, Pervasive adaptation, Bio-ICT convergence and Embodied Intelligence. It is also associated with the complex systems proactive initiative in FP6, yet has achieved breakthroughs that make it a technology research and development area with concrete test systems and design goals. The focus can now be on gaining generic programmable control of evolvable chemical synthetic processes across scales. Areas such as organic computing and self-organizing systems, as well as areas such as molecular computing have already been identified and challenges formulated, for example in the FET Complex Systems and Bio-ICT convergence pro-active initiatives. The particular focus on self- assembly and evolvability of novel chemical components has not been covered by these calls and will bring together more technically oriented scientists with their more theoretical counterparts to allow a technological breakthrough towards a mainstream evolvable and self-repairing technology for ICT. In this regard, there is an increasing community of scientists and companies involved. One of the objectives... is, precisely, to locate all these partners and to promote the interest on this new technology and foundational biological science in Europe."

They also highlight some of the possible disciplines that could contribute to such an effort:

"...Existing communities in evolutionary and genetic algorithms and programming, evolvable hardware, reconfigurable computing, nano-bionics, DNA and Membrane computing and self-organizing systems need to be brought together with materials scientists developing simpler self-assembling materials for increased information density and with molecular biologists who understand natural processes of assembling complex information processing structures."

Topics that we therefore consider to be within the scope of bio/chem IT include (but are not limited to:)

- Molecular, membrane and chemical computing
- Evolvable hardware
- Protocells and synthetic cells
- Molecular robots
- Integration of information processing with (bio-)chemical production
- Nano-bio-info interface
- Cellular engineering and synthetic biology
- Artificial neurons
- Programmable information chemistry
- Unconventional computing substrates (eg. ameboid organisms)

and associated computational and/or mathematical studies.

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[2] Available at http://cordis.europa.eu/fp7/ict/fet-proactive/chemit_en.html

4. Possible Approaches

Over the past few years, technological advances in chemistry, molecular biology, functional materials and engineering have brought biological and chemical information processing within our reach. The ability to build, design and grow ICT systems that can exploit these processes will lead to revolutionary advances in the future. The fundamental challenges facing bio/chem IT revolve around the evolution, construction and control of collections of individual elements, such as bacterial/neural cells, proto/artificial/minimal cells, or functional molecular complexes. These components will be capable of "intelligent" and designer-independent functioning, and be able to respond via self-assembly and/or self-regulation. In order to harness these systems, we require the ability to engineer and control chemical reaction and molecular self-assembly at the micro-level, as well as being able to understand and control macroscopic, population-level behaviour. This will require a deeper understanding of the extraordinary natural engineering processes by which living cells operate, and how bio-chem elements interact with a MEMS matrix, as well as fundamental insights into the dynamics of large numbers of interacting agents.

5. Expected Impact

The potential payoff from this field will be information processing and production systems that are evolvable, self-replicating, self-repairing and responsive to their environment (as well as having local intelligence), whilst also being capable of interfacing with existing silicon based ICT systems. Such capacity will open up a radically new form of technology that couples information processing with physical control and production at both the micro- and macro-levels. Such integration is currently only seen in natural, living systems, and this achievement may well trigger a seismic shift in ICT. Our vision of computation as something that deals primarily with *information* will be transformed into a view in which it is also intimately linked to hardware changes that influence a system's *material structure*, and therefore its future processing potential. A breakthrough in this area would allow ICT specialists programmable algorithmic entry to the world of nanoscale chemical processes, as well as the self-organised power of cellular assemblies. In the future, we will require not top-down, directed assembly of structures, but the utilisation of interactions between components to *self-assemble* functional information processing materials of immense complexity. The impact will be a major increase in the complexity and programmability of engineered nano- and micro-systems in all areas of application.

6. Case Studies

In this section we provide brief overviews of various projects or proposed projects (three of which form the core membership of the COBRA project). These are chosen to represent different aspects of bio/chem IT in terms of their objectives, methodologies and outcomes.

6.1 ***BACTOCOM*** (contributed by Martyn Amos)

The main objective of the BACTOCOM project is to build a general-purpose platform for synthetic biology. Parts of the internal ”program” of a bacterial cell (encoded by its genes, and the connections between them) may be ”reprogrammed” in order to persuade it to perform human-defined tasks. By introducing artificial ”circuits” made up of genetic components, we may add new behaviours or modify existing functionality within the cell. Existing examples of this include a bacterial oscillator, which causes the cells to periodically flash, and cell-based pollution detectors that can spot arsenic in drinking water. The potential for bio-engineering is huge, but the process itself is made difficult by the noisy, unpredictable nature of the underlying material. Bacteria are hard to engineer, as they rarely conform to the traditional model of a computer or device, with well-defined components laid out in a fixed design.

BACTOCOM: Bacterial Computing with Engineered Populations.

http://www.bactocom.eu

We use the inherent randomness of natural processes to our advantage, by harnessing it as a framework for biological engineering. We begin with a large number of simple DNA-based components, taken from a well-understood toolbox, which may be pieced together inside the cell to form new genetic programs. A population of bacteria then absorbs these components, which may (or may not) affect their behaviour. Crucially, the core of our bacterial computer is made up of engineered microbes that can detect how well they are performing, according to some external measure, such as an oscillation period. By performing massively-parallel bacterial random search, we quickly obtain functional devices without “top down” engineering.There are many potential benefits to this work, from both a biological and computing perspective. By uncovering new functional structures, we gain insight into biologicalsystems. This, in turn, may suggest new methods for silicon-based computing, in the way that both evolution and the brain have already done. In building these new bio-devices, we offer a new type of programmable, microscopic information processor that will find applications in areas as diverse as environmental sensing and clean-up, medical diagnostics and therapeutics, energy and security.

6.2 ***NEUNEU*** (contributed by Peter Dittrich)

This project will develop and produce a robust and adaptable substrate for computing. Droplets containing a chemical reaction system enclosed in a lipid membrane are the basic computational units. These units can store chemical energy and can repeatedly respond to input signals with a change in their chemical state. The droplets communicate by exchanging signalling molecules that diffuse across membranes or move through transmembrane channel proteins, much like cells in a tissue. Architectures of interconnected droplets can emulate the switching networks of conventional information technology,albeit at a much slower speed. Their natural mode of operation, however, is fundamentally different from semiconductor-based technology, and more akin to nature's information processing mechanisms. The analogy with biological architectures extends beyond information processing, to their chemical energy supply, and also to the production of the units (for example, self-organisation of lipids at a water-oil interface constructs a self-healing membrane around the droplets).

Currently the NEUNEU project studies the properties of basic droplets in the wet-lab. This study has identified configurations and parameter ranges suitable for information processing. Furthermore, novel microfluidic devices are built by rapid prototyping for automatic generation of droplets. In silico, simulators are constructed for different levels of abstraction.

These facilitate modelling of the internal dynamics of droplets, in order to study approaches that make use of wave propagation within droplets. For droplets with homogeneous internal activity and self-assembly processes, a novel rule-based approach is developed, which allows the simulation of relatively large architectures in three-dimensional space.

NEUNEU: Artificial Wet Neuronal Networks from Compartmentalised Excitable Chemical Media.

http://neu-n.eu

6.3 ***ECCell*** (contributed by John McCaskill)

ECCell is an EU sponsored project funded in the ICT Future Emerging Technologies by the FET-Open program (2008-2011). The aim of the project is to establish a novel basis for future embedded information technology by constructing the first electronically programmable chemical cell. This will lay the foundation for immersed micro- and nanoscale molecular information processing with a paradigm shift to digitally programmable chemical systems (Figure 1).

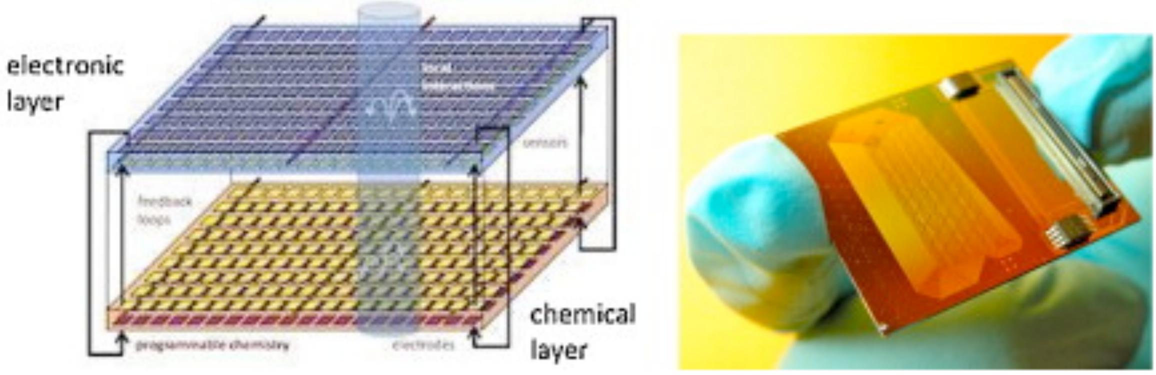


Fig. 1. (Left) Tight local coupling of electronic and chemical layers in the ECCell project as proposed by McCaskill (2008). Spatially localized cells can grow and proliferate in the hybrid plane. Through the symmetric local feedback coupling, the role of the two layers can be made symmetrical, not just electronics controlling chemistry but also the chemistry controlling the electronics. Electronic chemical cell functionality is divided between the two layers: with both electronic and molecular genomes. (Right) Physical realization of programmable environment for electronic chemical cells. Microfluidic channels at the rear supply a continuous flow of chemicals and the system is connected via CCD cameras and FPGA chip to a monitoring computer. Chemical cells must combine self-replication, self-containment and self-regulation of resources (metabolism) enabling evolution to qualify as alive. Electronic chemical cells will do this in conjunction with a reconfigurable electronic system.

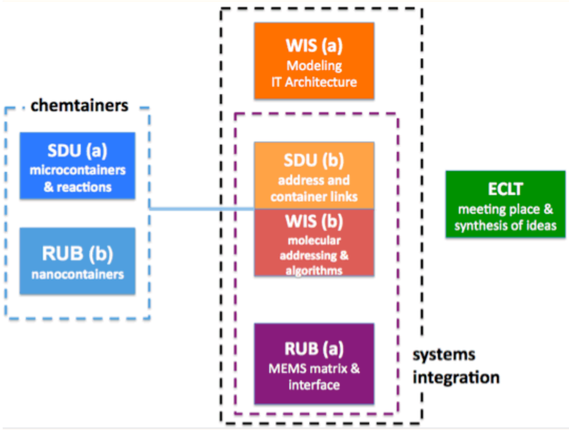
ECCell is employing novel families of fully synthetic hybrid informational polyelectrolyte copolymers (not simply DNA), which simultaneously support all three cell functionalities. Their self-assembly under electric field control is the primary information processing mode of this technology. Electrochemical reactions at digitally controlled electrodes regulate pH, microfluidic flow and metabolite concentrations. The research will establish an effective IT interface between microelectronic and molecular information processing, by demonstrating its use to achieve a hard chemical synthetic systems objective (an artificial cell) opening a platform for programming a novel chemical Living Technology at the microscale.

ECCell: Electronic Chemical Cell.

http://www.ruhr-uni-bochum.de/ECCell

6.4 ***MATCH-IT*** (contributed by Steen Rasmussen)

The full integration of programmed chemical synthesis and complex nanoscale function is a hallmark of information processing in living systems. In eukaryotic cells, the subcellular matrix involves a highly modular chemistry in which membranes delimit dynamic chemical containers of various sizes and functionalities. Functional units are actively transported by a protein assembly system throughout the cell, depending on the recognition properties of molecules on their surfaces, and the energy that fuels all these processes is embedded within the system. This project will abstract such a high-information-density and modular self-organizing chemical system and realize it in a more programmable way, as an interface connected to traditional computers, making novel use of MEMS technology and chemical addressing via DNA. DNA address tags can be synthetically attached to other chemicals, and hence to a variety of containers. Like computer addresses, they can then be processed, as research in DNA computing has demonstrated.



MATCH-IT: Matrix for Chemical IT.

http://fp7-matchit.eu/

Self-organizing container addressing allows micro- and nanoscale processing of any collection of chemicals that can be packaged in the containers. DNA-addresses can be used to bring containers together spontaneously exploiting parallel physical self-assembly. Addresses may be resolved with respect to an external address space (e.g. via immobilized DNA on surfaces or in gels) or by specifying binary or higher- order inter-container docking and thence content processing. In the design and analysis of such interactions we will derive inspiration also from membrane computing, a formal framework for information processing via package release chemistry. We aim to show that this concept can be applied to make chemical material processing programmable in a broad range of chemical systems, both in aqueous solution and in hydrophobic solvents. This will lay the groundwork for general addressable-container-based information and production chemistry.

7. A possible grand challenge: Sustainable Personal Living Technology (SPLiT) and Constructive Molecular Information Processing (contributed by John McCaskill, Steen Rasmussen and Norman Packard)

The grand challenge we focus on is the *personal fabrication* of molecular information processing devices and systems. We contend that the molecular level is where construction can and should be dynamically entwined with information processing. The two pressing questions are (i) is there a fundamental difference between molecular information processing and normal computation, and (ii) why personal fabrication?

The first question is not just about information processing density, where molecular systems arrive at the end of Moore's law. The distinguishing feature of what we will refer to as "strong" molecular information processing is that it combines the production of new molecular structures with the information processing by existing structures. This is also the key distinguishing feature of living systems as we know them, providing the technological platform for sought after self-X and consequently adaptive properties of life: including self-assembly, self-reproduction, homeostasis or self-maintenance, autopoeisis or self-production, self-encoding, self-repair, self-organization, self-recognition, self-defense, self-optimization and many others up to self-awareness. By contrast, "weak" molecular information processing uses molecules as fixed switches in parallel processing applications and conforms to the traditional separation of hardware and software in silicon computers.

Chemistry provides a rich substrate for information processing. As a result of the complex, reciprocal and collective modulation of local structural properties and dynamics by the surrounding molecular structures, creativity in chemistry is not simply at the level of novel large-scale pattern formation but also at the level of the discovery of novel local configurations and local processes with special properties. Life masters the interfacing of embedded DNA-encoded combinatorics with this complex world of possibilities, and demonstrates both the enormous potential and complexities of a programmable interface to molecular information processing. Increasing attention is being given to the adaptive dynamical combinatorial processes in non-biological systems, including, for example work on dynamic combinatorial libraries. The self-imposed restriction of the full range of chemical creativity to combinatorial work with a limited number of local modules is enabling a more rapid exploration and programmable mastery of this subspace of chemical possibilities. It also provides, through subsequent transformation (as exemplified in the genetic encoding of biological metabolism) a route to *programming* the full complexity of chemistry. Mastering the combinatorial programming of such systems provides an alternative, *bottom-up* route to that of synthetic biology, towards achieving programmable molecular information processing that links computation with fabrication. We contend that interfaces can now be developed that will make this technology available to individuals for personal molecular-scale fabrication.

Now, for the second question: why personal fabrication? We believe, together with the broader scientific community in SPLiT, this is both the only route to a truly sustainable economy and a natural development beyond the personal computer. It is also the way to make the transition from a mass-production society of inanimate artifacts to a technology-enhanced human society. The personal computer, along with the world-wide-web, has revolutionized personal productivity of informational content. The next giant leap is to the personal production of the complex things we need: this requires a combination of personal computation, networked information and programmable functional device fabrication. Personal fabrication becomes necessary because of both diverse personal needs (once we embrace influencing the processes that keep us alive) and diverse local environments and goals (including the complexity of the local technological world). Changing individual, social and environmental requirements can come first, even for those with special needs missed by mass-production. With the help of a personal fabricator network (PFN), information processing and material production can coevolve under all of the constraints and opportunities of local deployment.

The general grand challenge is to integrate ICT with dynamic ICT-Construction. So far only living systems are able to seamlessly integrate ICT and production. We contend that this can be achieved with an appropriate research investment using biological information encoding principles at the molecular level, bootstrapped by electronically programmable local manipulation systems that combine the advantages of 3D printing with self-assembly and autonomous electronic functionality. We believe that personal fabrication will open the door to a sustainable and fundamentally human technology, because it respects the needs and goals of individuals and local environments. A concentration on this will also inspire and harness the creative potential of society at all ages, by enabling individuals to share in the economic creative process, and thereby also serve to alleviate some of the social injustices of industry in our society. We also believe that research on this topic will foster both progress with and the acceptance of nanotechnological advances and increasingly autonomous ICT in the community.

Concrete applications will be far ranging, and stretch from supporting our daily infrastructure at home, in education and the work-place to personalized systems for local health monitoring and medication. More generally, it will support the transition to an information-rich biological evolution of technical devices and systems under strong, creative and local human control.