Supporting Adaptability in Agent-Based Digital Healthcare Ecosystem

Victor Rentea[a], Fabrizio L. Ricci[b], Luca Dan Serbanati[c], Andrei Vasilateanu[d]
[a,c,d] Faculty of Engineering Taught in Foreign Languages, Politehnica University of Bucharest
Bucharest, Romania
[b,c] Institute for Biomedical Technology, National Research Council
Rome, Italy
[a] victorrentea@gmail.com, [b] fabrizio.ricci@itb.cnr.it, [c] luca@serbanati.com, [d] andrei.vasilateanu@upb.ro

***Abstract*—The paper describes a new direction towards supporting a continuity of care by using the more natural and expressive paradigm of digital ecosystems. We introduce the conceptual model and architecture of the Digital Healthcare Ecosystem focusing on the reflection of the real to the virtual in healthcare followed by a "contamination" of the virtual in the real. We also propose a nature-inspired, agent-based approach to an adaptive mechanism supporting the evolution of the e-health services in the ecosystem. The mechanism is based on aggregation, migration and selection strategies inspired from biomimicry and distributed evolutionary computing.**

Keywords-virtual healthcare record; digital healthcare ecosystem; biomimicry; multi-agent systems; virtual organisms; adaptability

I. Introduction

The paper presents the conceptual model of a system supporting the following objectives with applicability in the e-health domain: to ensure a continuum of care on managerial, informational and relational dimensions, and to offer new opportunities to the stakeholders in the health system by introducing an evolution mechanism for the e-health services. Building towards these goals, we take inspiration from nature's mechanisms and shift the paradigm to a *Digital Healthcare Ecosystem* (DHE).

Like any other IT-supported domain, e-health also faces the gap between the business and IT, with domain specific peculiarities. An important concern of the stakeholders is the continuous alignment to norms that will probably increase in complexity due to the current trends towards wide interoperability. A rising number of e-services will be required from part of the e-health organizations, some of which will be also available for e-enabled healthcare actors. DHE attempts to provide a solution to this issue by disseminating and evolving the local human creative energy to meet future needs for e-services.

We start by an overview of the current healthcare and e-health context then introduce the theoretical background for our new direction based on biomimicry, digital ecosystems and multi-agent systems. Section III holds the description of our concept of Digital Health Ecosystems. After an overview of the base principles, we investigate how to achieve a seamless integration between the real and the virtual worlds in healthcare by relying on intertwined control loops. Starting with reflecting the real in the virtual, we introduce an evolutionary mechanism to produce better or locally innovating solutions that can influence back the reality in a positive way. Section IV resumes our current research and sets directions for future steps.

II. The State of the Art

A. Healthcare context

In the past two decades, much of the growth in health expenditures has been attributable to chronic conditions in the context of global population ageing. Future health reform should address changed health needs through care coordination and support for patient self-management [2]. It is clear that efficiency and effectiveness of the health system and healthcare management of aged population become prime issues in the attempt of mobilizing the full potential of all people of all ages. The solution requires a shift of paradigm in healthcare towards patient-centric care provided by multidisciplinary teams in different settings along the continuum of a disease. To support the continuity of care for chronic pathologies, Information and Communications Technology (ICT) needs to address different dimensions of business modeling: informational, managerial and relational.

B. E-Health context

Supported by ICT, the management of chronic conditions, home recovery, patient empowerment and coordination of clinical pathways with multiple actors become possible [16]. IT adoption allows innovating or re-engineering healthcare sectors to promote the economic sustainability of healthcare services and improve their quality.

The existing healthcare information systems are not suitable to meet these requirements because they are oriented to acute disease care, emphasize short encounters of patients with their caregivers, favor diagnosis and treatment of only the current symptoms and usually support the caregiver's activity in solitude. Following the patient-centric trend, we consider that a solution should go along three directions:

1. Integration of healthcare systems in order to share common information health state of each individual;

2. Support of all various business processes in the health system ranging from patient care provision to health

governance with coordination, control, alert, and monitoring services;

3. Promotion of the collaboration between caregivers, organizations and patients by creation of ad-hoc teams of stakeholders involved in one patient's care.

C. Biomimicry

Biomimicry is the science that studies nature, its systems, processes and elements and takes creative inspiration from them for the design of modern technology [3]. In computer science, biomimicry produced Nature Inspired Computing with several branches of which we are interested in Biologically-Inspired Computing. BIC takes inspiration from nature for the development of complex problem-solving techniques such as Evolutionary Algorithms (EA), neural networks and swarm intelligence.

The method employed by using biomimicry tends to be ad-hoc and un-formalized [3] and generally involves an engineer or scientist observing an area of biological study which seems applicable to a research problem they are currently tackling. The biological mechanisms need then be well understood, abstracted and applied to the non-biological system whilst also being aware of its particularities.

An ecosystem is a natural unit made up of living (*biotic*) and non-living (*abiotic*) components, from whose interactions emerge a stable, self-perpetuating system [11]. In Computer Science, [20]Digital Ecosystems are a new research area that builds upon Multi-Agent Systems, Service Oriented Architectures and Evolutionary Computing.

D. Multi-Agent Systems

A software agent is a piece of software that acts autonomously in an environment to achieve its design objectives. A Multiple-Agent System (MAS) is a system composed of several software agents collectively capable of reaching goals unachievable by an individual agent or a monolithic system [4].

Healthcare is and has been a field of interest for the use of software agents [5] because the agent-based paradigm is a natural way of representing many recurrently occurring situations in medical environments such as: absence of a central control, bounded resources of a caregiver, and knowledge and data distribution. Research projects have targeted specific use-cases of healthcare, such as workflow-oriented care plan monitoring or the establishment of agent-based virtual organizations around a patient [6]. Also, recent research in agent development has stressed the need for collaborative environments such as e-health to focus also on organization- and artifact-based agent environment [18].

When mapping natural ecosystems in the virtual intelligent agents can conceptually represent organisms despite their lack of mobility and evolution. Even if mobility is added in Mobile Agent Systems, the lack of evolution limits the resemblance with their biological counterparts.

E. Service-Oriented Architectures

Trying to support adaptability in DHE, we need a modular reusable paradigm to software development that allows us to modify the virtual to comply with the changing reality. Often considered as developing the concepts of modular programming and distributed computing [7], SOA is the best choice. This encompassing paradigm is an approach to organizing software in the form of independent, interoperable services. A service is the encapsulation of some related software functionalities accessible by clients in network. It is exercised consistent with constraints and policies as specified by the service description and can be discovered using some interpretable metadata. The same service can have multiple implementations. It can be composed and recomposed from other services or participate in service compositions to fulfill multiple business requirements. SOA does not take into account evolutionary semantics and context-awareness for services. This is why it has been suggested [9] that the SOA approach is not adequate to face the dynamic interactions between evolving organizations and a shift of paradigm towards an Ecosystem-Oriented Architecture is required. However, we believe that any attempt to change the paradigm should build upon the current largely embraced technologies and one of the goals of our research is to investigate how such a shift can be achieved.

Our work builds towards the great promise of SOA that the marginal cost of creating the n^{th} application is virtually zero, as only the combination of existing software is required [8]. Taking into consideration the complexity of e-health, the approach should build upon the latest technologies in interoperability, such as Semantic Web Services.

F. Digital Ecosystems

The term *digital ecosystem* (DE) is being increasingly used for describing the future developments of ICT in e-business towards the so-called *digital business ecosystems* [17]. According to [1], we consider a DE as "an open, loosely coupled, domain clustered, demand-driven, self-organizing and agent-based environment within each species is proactive and responsive for its own benefit and profit".

A rigorous and somewhat revolutionary approach referring to digital ecosystems is that of [10] that aims to establish a novel form of Distributed Evolutionary Computing by creating a digital counterpart of biological ecosystems. The basic idea is to combine an Evolutionary Algorithm with the migration of solutions to face a dynamic stream of requests for software from a heterogeneous *User* base. The "organism" and the basic building block is the *Agent* that represents a software service or a SOA-style aggregation of services. In the envisioned distributed system, Agents move around Users to find the environments in which they prove most useful to subsequent requests for applications. Applications are assembled on-demand using a *Genetic Algorithm* (GA) seeded with the Agents "living" in a *Habitat* associated with that User. Our approach takes great inspiration from this work to which adds several innovating features, highlighted in the last section.

III. THE DIGITAL HEALTH ECOSYSTEM

A primary goal of our research in Digital Ecosystems is to explore the possibility to employ in the e-health domain the strengths of biological ecosystems, such as self-organization, adaptability, self-manageability and the ability to provide hierarchical solutions to complex problems [20]. In front of complex information-intensive decision tasks in e-health, we are attempting to move the control process in the virtual world, where information is fast and efficiently accessible. For doing this, we need to increase the permeability between the two worlds through bridges that must be added in the form of sensors and actuators, which bring in the virtual the state of the reality and act upon it, respectively. Due to the increased complexity of coordinating the processes in e-health, the traditional software controller responsible for this task is replaced in DHE with a mechanism that relies on evolution. The decisions are no longer taken based on an implicit or explicit rule set, but derive from a process of evolution that runs in a context reflecting the reality. Evolution mechanisms in the virtual operate both retrospectively, to align the virtual to changes sensed in the reality, and prospectively, to generate different models to propose or impose, depending on the case, to the real world. To be useful, the virtual must always remain in close contact with the real, such that any autonomous evolution of one of them must rapidly be followed by the other. In essence, the DHE tries to speed up the evolution process at a different level, by mapping the real to the virtual, evolving a solution or a proposition and then using it to influence back the real world.

Until now, the digital had to react to changes in the uncontrolled reality, but due to the recent advances in pervasive computing it is now becoming possible for the virtual to act upon the real in its turn and to achieve goals emerging from virtual.

The entities inhabiting the DHE are partitioned in two groups (Figure 1): entities that map a real entity into the virtual world and purely virtual entities without any real counterpart. The latter are further distinguished into passive *virtual artifacts* and proactive *virtual agents*, such as those that will perform monitoring and maintenance tasks in DHE. When mapping the real into the virtual, we recognize between mapping in an agency relationship or in a pure representational purpose. In this sense, an *avatar* is a proactive agent working towards the goals of the stakeholder it represents, but also following additional objectives related to the virtual environment in which it lives. On the other hand, an *artifact* is a passive or reactive entity, defined as a "first-class abstraction introduced to model and engineer general-purpose computational environments for multi-agent systems" [18]. An artifact is the virtual projection of a real entity, either physical (e.g. device, drug, operation room) or digital (e.g. software application, resource, database).

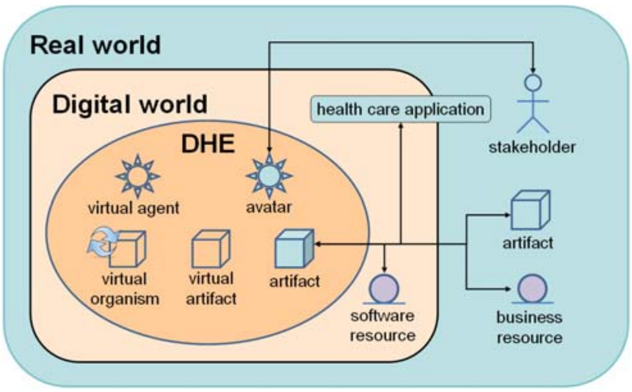

Figure 1. The Digital Health Ecosystem

Following a discussion on the control mechanisms in action, the rest of this chapter presents the system by following the natural flow, from real to virtual and back to real, focusing on the DHE distinctive features and the new evolution mechanism residing in the virtual world.

A. Control loops

In the real world the patient's health care is a typical control loop process where activities of human analysis (observation and diagnosis), planning (care plan delivering), and execution (treatment) must be completed by evaluation in order to measure the progress in the care.

DHE can support this process in its various activities but only being aware that the reality has been and will be the origin and destination of any immersion in the virtual. The virtual itself appears due to a need in the reality and therefore is subordinated to it. As a consequence, for the virtual to be helpful it must be able to influence the real world, thus closing the main control loop of DHE.

Both worlds aim at improving the current situation by inspiring one from another and evolving creative solutions.

The virtual should accurately reflect the most relevant aspects of the reality and be kept in tight contact by continuous update processes. In DHE, evolution processes take place in a context that mimics the real situations. Feedback information to assess the alignment between the two worlds is needed. In this way a second control loop is identified.

The evolution processes in DHE produces a creative energy that can be used for the benefit of the reality. Sometimes the evolution in the virtual may anticipate changes in the real and new ideas in virtual may accelerate the evolution of the real world by "osmosis". The proposals the DHE issues may be presented to stakeholders that can decide for restructuring the actual systems. Information about the success or failure of the solutions is reported back in the DHE and constitutes the feed-back for controlling future evolutions.

The three control loops are presented in Figure 2.

B. Virtualization

In DHE, the avatars live in an environment populated by artifacts (abiotic components) and governed by norms and laws inherited from the real world. Avatars are able to organize themselves in hierarchical structures mimicking the real organizational structures. Their proactivity follows some goals that are derived from the roles, goals and concerns of those real stakeholders that they represent and act as vectors for the self-conscious initiative of the humans.

Mapping the real to the virtual in this case is addressed differently depending on the role each stakeholder plays. In the case of the patient's avatar we are interested in an accurate reflection in the virtual of his/her health state, while for the doctor's avatar his/her medical knowledge is important to be reflected. For the former, we rely on our past research on the *Virtual Healthcare Record* [19], a complete

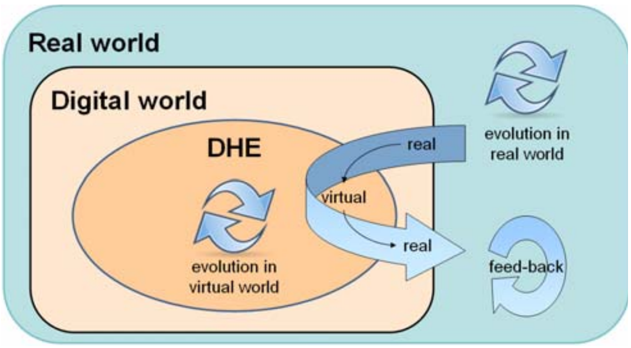

Figure 2. Real to Virtual to Real

and authoritative representation of the patient's current health state, clinical history and ongoing care processes, including information on demographics, past medical history, normal values of vital signs, medications and treatment plans. We designed our conceptual model for the virtual health state of the patient, by applying successive abstractions to the reality. The health state concept is an ideal, as we can never reach a perfect match between the real situation of the patient's health and the digitally represented health state. However we can strive towards it by multiplying the observations resulting from a diagnostic investigation process where additional investigations are needed to build a useful, reliable health information set that can be further used in decisions.

Activities in the ecosystem may be initiated by certain situations in the environment and in turn modify it. Such a situation is a *MedicalAct* and can be a condition found in the health state of the patient or a lack of knowledge thereof. An activity in the health ecosystem is transmitted through the stakeholder avatars in the digital ecosystem as an event or as a data flow. Subsequently, this will favor some activities to be executed by the digital ecosystem agents and may also change the knowledge about the real world. This means that activities inside the DHE are indirectly and partially determined by actions and events in the real world.

Clinical events, changes in the health state of the patient arrive through the information flow inside the digital ecosystem and can change the state of the patient avatar. A need in the real world is transformed into a care goal in the DHE. Reacting to this change in the environment, avatars representing different healthcare providers are assembled into an ad-hoc multidisciplinary team, having a structure generated by the process of solving that care goal.

In the paper, the focus is on the living environment of the avatars in DHE, filled with artifacts among which projections of the applications used by stakeholders. The digital part of the healthcare ecosystem reflected in DHE must be flexible and adaptable to support the dynamic stakeholder activity and organization.

C. *The virtual organisms*

We will refer to *virtual organisms* (VO or, hereafter, in short, *organism*) as a kind of virtual artifacts that can evolve autonomously, that is, change internal structure according to changes in their living environment. Although they lack proactivity, the collective behavior of the avatars regarding those reproduces the mechanisms we observe in the natural ecosystems, allowing them to evolve in ways similar to physical organisms. A VO can be used for various types of structured solutions, but in the paper we will focus on evolving software applications in a SOA meaning.

The VOs live near avatars that own and support their existence by providing them with living *Habitats*. The abiotic environment for VOs is a set of interconnected Habitats, each with its particular living conditions. The avatar uses the population in its Habitat for solving local requests for applications and effects explicit control on this population through new VO addition and removal. In this way the relations between avatar, Habitat and organism were defined. The following will further address the evolution of the organisms in the network of Habitats (Figure 3).

The living conditions of the Habitat change according to the application requests received, allowing potentially useful VOs to live longer and forcing the non-fitting to emigrate or die. Focused not only on software creation but also on its adaptation, we believe that after an application was generated similar requests will follow, due to the continuous change in the e-health domain. In order to gather more VOs for subsequent software changes, we set the environment of our Habitat stateful by storing every new application request. Based on the past requests, a fitness landscape can be calculated for the evaluation of incoming organisms and the estimation of their future usefulness and survival. In our approach, the avatar has full control over the parameters of the bio-mimicked processes in its Habitat, although recommendations will be formulated.

Virtual organisms represent software components or applications and carry a *semantic description* of their functionality and an *executable component* consisting in either a service or a service aggregation, in a SOA-style. On-demand software assembling and modification requires a component-oriented model of which SOA is the current state of the art [7] and a great degree of interoperability, featured

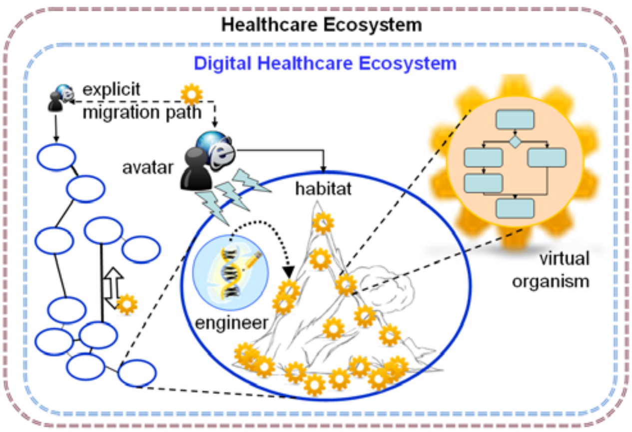

Figure 3. Virtual Organisms in the network of Habitats. The picture represents, from left to right: the weighted network of Habitats, each with its own avatar; the 2 types of VO migration; the structure of a Habitat with a specific landscape fitness; the meaning of an VO.

by the use of semantic descriptions for services [12]. The executable component of a composite VO is an encoding of the entire SOA workflow and represents its genetic material (*genotype*). Unlike other entities in DHE, autonomic evolution of VOs is possible by applying recombination and mutation on their genotype.

Special attention should be addressed to the distinction between *genotype* and *phenotype*, because it takes more than a genotype to produce a phenotype. In biological terms, the *phenotype* of an organism is the manifestation of its genotype in a given environment [13]. Similarly, we consider the phenotype of a VO to reflect the actual behavior of its executable component when operating in deployment environment. Examples of phenotype attributes include response time, availability, cost, quality and security. The same individual, carrying the same executable component, that is, the same genotype, expresses a different behavior in different environments, that is, a different phenotype [13]. Even though the distinction between genotype and phenotype is generally not present in today's EAs [14], it cannot be overlooked in our scenario, as the execution of a distributed SOA application depends on a variety of factors including different configuration parameters, geographical location, local resources, legacy systems and usage pattern.

When offering a software solution to an application request, we are interested in knowing not just the genotype but also the phenotype, i.e., the future actual behavior. Unfortunately, the entire phenotype cannot be known at generation time and querying, deductive, inductive or recommendation-based strategies could be employed to gather as many information as possible. We must also admit the multi-purpose optimization nature of the task, the variety of algorithms that can be employed and the difficulty to build a proper fitness function. Thus emerges the need of decoupling the application generation task and allowing various implementations to coexist in the form of *engineer agents* (as in "genetic engineering"). Whatever their implementation may be, these agents start with the population within the Habitat, localized and probably useful to the user, on which then apply an EA and derive a solution to produce the application requested. Although we admit the need of a type of EA, we do not commit ourselves to a genetic algorithm as [10] nor to any other particular algorithm. Instead, we only require that in each Habitat an engineer agent is in function. At this point, evolution has been added to our system, as an essential component of an ecosystem's stability.

There are additional key features that enable the strength of biological ecosystems: population dynamics, local interactions and spatial distribution. A natural consequence of the distinction between genotype and phenotype is the possibility that a solution inefficient in Habitat *A* may be of great help in Habitat *B*, operating within other conditions. On the other hand, the organism with a strong genotype has high chances of being useful in other Habitats in response to similar requests. In order to produce the best individuals, a mechanism for migration is required, that is, moving in the former case and copying in the latter case. While copying is intuitively best used for highly fit individuals and enable fast

```
deploy_agent(ag)
ag.max_cycles = ∞
for each h in ag.friendly_habitats
  send_success_feedback(h)
for each conn in this_h.connections
  if randomTrue(conn.strength) and
      not conn.remote_h in ag.visited_habitats
    copy(ag,conn.remote_h)
```

Figure 4. Successful agent usage algorithm

`ag` is set to "perpetuating", links are established or strengthened with the habitats in which `ag` was used, and `ag` is randomly migrated to connected Habitats

dissemination of quality software, moving weak organisms to other Habitats helps in maintaining diversity throughout the digital ecosystem and escaping the local optima locking [14]. Mechanisms such as organism's life duration should be enforced in order to limit the dissemination process when copying and to force low-quality solutions to eventually disappear after several migrations.

The feed-back produced by the *migration success* on the *migration path* is a simple improvement to Distributed Evolutionary Computing that eventually leads to self-organization of the Habitat network based on similar application requests [10]. Links between Habitats are weakened or strengthened by the migration *success*, i.e., when the organism proved useful in the remote Habitat (Figure 4). This represents a form of Hebbian learning [15] in which Habitats are seen as neuronal cells.

The migration mechanism represents a paradigm shift from pull-based, currently used with SOA, to push-based mechanisms, in which avatars collaborate on their own will, proactive for the society's benefit, to provide the real world with the best possible software with the lowest possible cost.

D. *Influencing the reality*

The final purpose of the DHE is to influence the reality by proposing a new or updated model, obtained through evolution. The virtual organisms produced in DHE lead to the creation of new e-health services in the reality, contextualized and adapted to the requirements, better or even completely new in that context. If such a proposal is accepted and deployed, it leaves the virtual world and becomes an artifact in the real world, that is, deployed software. Given a VO is a solution with applicability in the reality, its constituting elements must also be elements brought from the real world, i.e., artifacts representing software entities. As such, the responsibility of the DHE is not to invent new software from scratch but to evolve solutions by combining real components, seen as the manifestation of the human creative power in front of different problems. From this point of view, DHE is an enabler of global evolution based on local human creativity.

In DHE, the healthcare organizations will probably benefit most from evolving software e-services to conform to the norms, best practices and local specific requirements. For better understanding, the software adaptation to a change in the healthcare norms is presented next. The change in legislation is pushed in the DHE where subsequently threatens the compliancy of the current software applications. The avatar senses the situation and tries to adapt each impacted application deployed within its organization. For each of them, the previous request is edited accordingly to the change in norms and re-issued in the local Habitat. The decisions of the avatar may rely on a Belief-Desire-Intention model following the preferences and goals of the individuals in a community. Within several limits, the reality need not even be notified about the event, being shielded or at least helped in front of the continuous change.

The adapting of software services can prove useful also for those people that run locally deployed software, for their own use, most probably software clients. The evolution of the applications may offer a richer interface, self-adaptability to changes in provider-side and even support contextualization of e-health services. A form of evolution, context adaptation relies on ad-hoc connections between avatars in DHE that enable the migration of virtual organisms towards the local Habitat to support in context-dependent applications.

For both use-cases, the specific interests and preferences for software are reflected by the connections of the local Habitat within the Habitat network, gathering the most useful selection of software available.

IV. Conclusion and Future Work

Our research in Digital Healthcare Ecosystems is part of the project “An innovative approach to health care by a seamless integration of real and virtual worlds” which is now in the inception phase. This phase consists in defining the conceptual model of the DHE and in interviews with the involved stakeholders in order to achieve an accurate view of the business processes. The paper presents our research on evolutionary processes in DHE that is inspired from [10] to which adds the following contributions. The genotype of a virtual organism in DHE is not just an unordered set of genes but fully encodes the workflow it represents. The evolution is not strictly based on a genetic algorithm but various EAs are allowed, as different evolution mechanisms will help improve diversity of the VOs. Another improvement is the explicit specification that the evolved virtual organisms do not manifest proactivity in a MAS way. Instead, they follow nature-mimicked processes without being able to interfere, and therefore are seen as virtual artifacts in DHE.

In the paper, e-health services are created to support the evolution of software in a dynamic environment reflecting the reality. Our approach relies on a self-organizing network of localized Habitats that provide a scalable approach towards automatic composition from among numerous distributed services, therefore building towards the SOA great promise [8]. A great potential of DHE is to become an enabler of global evolution based on local human creativity manifested as disparate distributed services. The results of initial simulations of the evolution mechanisms are very promising but, to be relevant, must rely on an estimated usage profile, which we plan of building next. On the other hand, other applications for the evolution mechanisms are possible and will be analyzed in further work, including evolving and adapting treatment plans and wellness assistance for a patient having a monitored health state.

References

[1] E. Chang, M. Quaddus, and R. Ramaseshan, “The vision of DEBI Institute: digital ecosystems and business intelligence”, DEBII, 2006.

[2] K. Thorpe, L. Ogden, and K. Galactionova, “Chronic conditions account for rise in medicare spending from 1987 to 2006”, Health Aff, Feb. 2010, doi:10.1377/hlthaff.2009.0474.

[3] C. Hastrich, "Biomimicry: A tool for innovation" [online], 2007. Available from: http://www.biomimicryinstitute.org/about-us/biomimicry-a-tool-for-innovation.html [14.05.2011].

[4] M. Wooldridge, “Introduction to MAS”, Wiley, 2002.

[5] A. Villar, A. Federici, and R. Annicchiarico, "Agents and Healtcare: A Glance to the Future", Birkhauser, Agent Technology and e-Health, pp. 141-148, 2008.

[6] G. Leonardi, S. Panzarasa, S. Quaglini, M. Stefanelli, van der Aalst W.M.P. "Interacting Agents through a Web-based Health Serviceflow Management System", Journal of Biomedical Informatics, vol. 40(5), pp. 486–499, 2007.

[7] D. Krafzig, K. Banke, and D. Slama, “Enterprise SOA: Service-Oriented Architecture Best Practices”, Prentice Hall, 2004.

[8] G. Modi, "Service oriented architecture & web 2.0”, Technical report, Guru Tegh Bahadur Institute of Technology, 2007. Available from: http://www.gsmodi.com/files/SOA_Web2_Report.pdf [14.05.2011].

[9] P. Ferronato, “Architecture for digital ecosystems, beyond SOA”, IEEE Digital EcoSytems and Technologies Conference, 2007

[10] G. Briscoe, M. Chli, and M. Vidal, “Creating a Digital Ecosystem: Service-oriented architectures with distributed evolutionary computing” in JavaOne Conference. Sun Microsystems, 2006. [online]. Available from: http://arxiv.org/abs/0712.4159 [14.05.2011]

[11] M. Begon, J. Harper and C. Townsend, "Ecology: Individuals, Populations and Communities", Blackwell Publishing, 1996.

[12] P. Rajasekaran, J. A. Miller, K. Verma, A. P. Sheth, "Enhancing Web Services description and discovery to facilitate composition", First International Workshop on Semantic Web Services and Web Process Composition (SWSWPC 2004), LNCS 3387, pp. 55-68.

[13] E. Lawrence, "Henderson’s dictionary of biological terms", Pearson Education, 2005.

[14] M. Shackleton, R. Shipma and M. Ebner, “An investigation of redundant genotype-phenotype mappings and their role in evolutionary search”, Congress on Evolutionary Computation, pp. 493–500, IEEE Press, 2000.

[15] D. Hebb, “The Organization of Behavior”, Wiley, 1949.

[16] G. Demiris, et. al., “Patient-centered applications: use of information technology to promote disease management and wellness” Journal of the American Medical Informatics Association (JAMIA), vol. 15, Jan. 2008, pp. 8-13.

[17] F. Nachira, P. Dini and A. Nicolai, “Digital Business Ecosystems”, European Commission, 2007.

[18] A. Ricci, M. Viroli and A. Omicini, "CArtAgO: An Infrastructure for Engineering Computational Environments in MAS", 3rd Workshop “Environments for Multi-Agent Systems”, E4MAS 2006.

[19] L.D. Serbanati, F.L. Ricci, G. Mercurio, A. Vasilateanu Steps towards a digital health ecosystem.”, Journal of Biomedical Informatics”. in press, doi: 10.1016/j.jbi.2011.02.011.

[20] S. Levin, "Ecosystems and the biosphere as complex adaptive systems", Ecosystems, vol. 1, pp. 431– 436, 1998

