Emerging Opportunities in Medical and Healthcare Simulation

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***Abstract*—This position paper provides a high-level overview of recent trends in the research landscape that portend of new opportunities in medical and healthcare engineering. These trends arise from myriad resources potentiated by the Internet, in particular the current emphasis on open-source software contributions, both in well-designed toolkits and GitHub repositories, and the emergence of high-throughput techniques based on graphical processor units on the hardware side and on deep neural networks on the algorithmic side.**

Keywords-open source; deep neural networks; segmentation; meshing; therapy models; haptics.

I. INTRODUCTION

Medical and healthcare (M&H) simulation span a variety of areas where medicine converges with Modeling and Simulation (M&S). Computer-based medical simulation emphasizes the application of computers to synthesizing the response of tissues to therapy, which represents a trade-off between fidelity to real tissue response and computational efficiency. High-fidelity medical/surgical simulation is typically used to provide experienced clinicians, including surgeons, with insight on how to optimize treatment of the patient, while high-efficiency simulation emphasizes real-time interactivity for haptics, typically used in conjunction with Virtual Reality (VR) visualization for skill acquisition and training.

In both cases, a computer visualization of the anatomy is needed, however in the interactive case based on VR, this visualization must be also responsive in real-time, which presupposes highly efficient therapy models (e.g., cutting models) as well as relatively sparse anatomical models and collision models, where the latter determines where the therapy takes place, in conjunction with the pose of the haptic device. A related research area is the segmentation of medical images that map intensities to tissues and discretization (meshing) that converts tissues to elements.

Healthcare simulation is used to denote two areas that complement the above-described medical simulation. One the one hand, it is used to designate mannequin-based training systems and part-trainers, whose physical implementation is intended to develop proprioceptive understanding of therapies. On the other, this term also represents medical processes at a large scale, such as emergency rooms, and hospitals, to formulate an understanding of bottlenecks in patient treatment and improve efficiencies.

This paper describes some trends that broadly apply to the academic landscape and that are particularly relevant to the M&S community, in a manner that could trigger the emergence of simulators that are much more descriptive that the current state of the art. Many of these trends arose as a result of the wide impact of the Internet, though they also built on a climate of goodwill on the part of researchers. In particular, there is a substantial ecosystem of open-source tools that make it possible for a researcher with suitable interests to ramp up a project in spite of a lack of prior footprint in that area, simply by leveraging existing source code and publicly available data. In addition, the emergence of deep neural networks (DNNs) has led to important advances in both anatomy and therapy modeling. In parallel, hardware advances include graphical processor units of ever-improving performance characteristics, as well as haptics support that includes a bimanual 7 degree-of-freedom device as well as bimanual haptic gloves with both finger-centered tactile as well as force feedback loops.

The rest of this paper is organized as follows. Section II describes limitations of the current state of the art in medical simulation. Section III addresses a survey of open-source tools in anatomy modeling. Section IV proposes a survey of therapy and function modeling. Section V draws conclusions and summarizes the findings of the paper.

II. CURRENT LIMITATIONS AND PROMISE OF INTERNET-BASED ECOSYSTEM

It can be argued that much of existing medical practice is still unrepresented in the current state of the art in M&H simulation. For example, if one were to peruse the bookshelf of a neurosurgeon, with a substantial coverage of techniques applicable to the skull base, where care must be exercised around cranial nerves and cerebrovasculature, while comparing this colossal literature with the state of the art in neurosurgery simulation, arguably less than 1% of neurosurgical practice is accounted for in simulation. The same can be said of most areas of medicine: orthopedic surgery, obstetrics, and so on. M&S engineers are just beginning to scratch the surface, in part because so few of us have carried out a meaningful conversation about the requirements of M&H M&S. It may also be that we fall in love with a technology and strive to make it fit to a given situation, which to a degree is putting the cart before the ox. Regardless of the cause, our methods have change for this relative irrelevance of H&M M&S to give way to significant penetration of the technology.

Fortunately, there is some cause for optimism, through the disruptive impact of Internet-based trends on M&S research. The first emerging trend that has potentiated the work of M&H M&S practitioners is the broad dissemination of both algorithmic information and source code through the Internet. This phenomenon serendipitously has also enabled us to build collaborations that would have been infeasible in the past. In this ecosystem, a suitably inclined researcher simply needs to find out about existing work in a conference or journal paper, which is increasingly available publicly in pdf form, determine the relevant keywords and apply them to a Google or Engineering Village search, track down the relevant open-source software tools and publicly available data repositories, possibly initiate a collaboration that builds on the authors of the paper or the architects of the open-source tools (or both), generate some preliminary results that may leverage examples embedded in the open-source platform, and finally publish the new application that can then lead to funding. This cycle can take place in 1-2 years, which would otherwise have been infeasible or taken a decade or more to replicate in pre-Internet times. This ecosystem also makes it feasible to identify early adopters among clinicians who are willing to collaborate; while funding bodies may have a preference for a compact team, geographically distributed efforts do get funded.

III. HIGH-LEVEL SURVEY OF ANATOMICAL MODELING

Broadly speaking, unlike healthcare simulation that often builds on a single model such as a discrete-event design, continuous medical simulation is typically founded on at least two types of models: the patient's anatomy and the therapy. Moreover, haptics-driven interactive simulators must also imbed a third, a contact model, which informs the simulation where on the anatomy the user interaction is taking place. The French open-source platform Simulation Open Framework Architecture (SOFA) [1] [2] typically labels these three as the Deformation, Visual and Collision Models, while prescribing the precise nature of the real-time interactions between any pair of models. Kitware's Interactive Medical Simulation Toolkit (iMSTK) platform has a similar approach [3] [4]: it also decouples the surface rendered visualization from the therapy model and the anatomical mesh.

In the nascent period of interactive medical M&S in the early 2000s, the emphasis in the literature was mostly on therapy models and the algorithmic infrastructure that emerged as foundation for SOFA and iMSTK. At the predictive end of the spectrum, tools like FEBio also emerged [5]. During this time, and even prior to it, much the medical image analysis community has proposed several segmentation techniques that map intensities of MRI and CT volumes to tissue classes. Classically, we can mention voxel, boundary and digital atlas-based techniques [6]. In the past decade, the medical image analysis community has undergone a revolution in embracing deep neural networks for much of this activity, which generally speaking emphasize voxel-based techniques [7]. Specifically, convolutional neural networks have been developed, where the spatial organization of the digital image is best suited to a network with several hidden layers and with operators based on spatial convolutions. Leading architectures include U-Net and ResNet [8] [9]. Leading open-source tools for medical image analysis include ITK [10], while emerging tools for DNNs include TensorFlow, Caffe and PyTorch [11] [12] [13].

The plurality of the medical image analysis literature, including DNN-based techniques, emphasizes voxel-based segmentation, but this has a number of limitations in relation to medical M&S. This literature tends to restrict the image analysis problem to a narrow subproblem, which is typically concerned with a small, manageable number of tissues, such as determining the tumor tissues (active and necrotic) as well as edema in an MRI dataset. However, from the standpoint of the M&S developer, that narrow problem definition is often insufficient to represent the totality of the anatomy that must be modeled for clinical relevant, high-validity simulation. To further complicate matters, some tissues are inconspicuous in the medical image. For example, in our work on scoliosis surgery simulation, whose end-goal is to specify which ligaments must be cut in order to make the spine sufficiently compliant, we must deal with the inconspicuity of these ligaments in CT and MRI. Our solution involves leveraging the conspicuous tissues like vertebrae and intervertebral discs to anchor a multi-surface model-to-image warping to the patient's dataset [14].

To mitigate these limitations of prevailing segmentation techniques, a high-level set of specifications must describe which aspects of the anatomy are needed in the simulation. In particular, it is vital to know which critical tissues are at risk and should be preserved in the intervention, even if they are relatively inconspicuous in most images. If indeed such tissues are not visible, then the anatomical modeling approach should either be hand-drawn by an anatomist, in the form of a multi-surface atlas of the patient or use such an atlas and warp it to the target image, possibly in a manner that exploits a DNN-based voxel segmentation.

In some cases, the anatomy must factor in some anisotropic aspect of tissue orientation, such as the MR Diffusion Tensor Imaging (MR-DTI)-based tractographic reconstruction. Leading tools in this area, which my team uses, include Diffusion Imaging in Python and DSI Studio.

Either way, it is essential to have a high-level representation of the main steps of the medical intervention, which is termed a medical ontology or a medical workflow in the literature [15] [16]. This workflow will typically make explicit the main steps of the procedure, in a manner that can be described at various levels of resolution. As depicted in figure 1, a workflow for a neurosurgical procedure typically is defined as a function of the choice of approach: pterional, transnasal, and so on. This approach prescribes the precise configuration of the craniotomy, which then leads to expectations about the typical surgical corridor. Having this knowledge will then enable the M&S designer to make informed choices about which portions of the anatomy to mesh in significant detail and which others to mesh coarsely. One of the main open-source platforms for medical ontologies is Stanford's protégé ontology editor [17].

While mapping image voxels to tissue labels is a vital stage of anatomical modeling, a collection of labeled voxels is invariably too dense for practical simulation purposes. Each tissue blob must be represented as a discretized model, whose dimensionality should be appropriate for the shape of the tissue. A 3D tissue should be discretized as a collection of tetrahedra or hexahedra, where the former is often preferable due to the unsupervised aspect of the meshing. Meanwhile, a surface-like structure such as the dura mater of the brain should be represented as surface elements, i.e. triangular shells, and a curvilinear tissue like a nerve benefits from a simple beam element representation that traces a path through its central axis. One rich open-source repository for discretization is Computational Geometry Algorithms Library, CGAL [18], which includes Alliez' variational tetrahedral meshing algorithm [19]. Surface meshing is also a challenging exercise, with support from VTK, GMSH and various GitHub repositories, such as controlled surface mesh decimation based on Approximated Centroidal Voronoi Diagrams (ACVD) [20] [21] [22]. There is also new research and GitHub support for DNN-based approach to tetrahedral meshing, termed DefTet [23]. In earlier work, my group has proposed curvilinear discretization founded on deformable Simplex contours, where every non-terminal edge linked a pair of vertices, and each vertex was attracted to the central axis of tubular structures. We applied this discrete deformable contour to identifying cranial nerves in T2-weighted MRI [24].

IV. Survey of Function and Therapy Modeling

In lockstep with progress on anatomical modeling, substantial resources have been made available for therapy and function models of various kinds.

Orthopedics, geriatric medicine and indeed obstetrics, as proposed by my group in this conference, can benefit from high-efficiency musculoskeletal M&S, which is available from Stanford's OpenSim platform [25] [26]. Our adaptation of OpenSim will involve the coupling of this musculoskeletal simulation with glove-based haptics, where the ObGyn in training can practice the Posterior Arm Release technique, which entails hooking a finger under the trailing armpit of the fetus, while cradling the head with the nondominant hand, to enable the baby to emerge from a life-threatening shoulder dystocia situation. It is also feasible to exploit OpenSim with realistic anatomical surfaces, adapted to geriatric patients, to train an DNN dedicated to Human Pose Estimation to identify imminent falls in these patients and deploy mitigating strategies [27].

As mentioned above, a significant area of open-source activity involves the deployment of haptics-driven surgery simulation platforms SOFA and iMSTK, respectively developed at INRIA (France) and Kitware (USA). The basic architecture is fairly similar, in emphasizing coupled models for surface rendering-based visualization, soft tissue deformation founded on efficient finite elements [28], and efficient collision detection for determining the portion of the anatomy in contact with the virtual tool [29].

Many simulation platforms are dedicated to one physiological system. OpenCarp [30] is an advanced in silico cardiac electrophysiology (CEP) platform which has emerged as an important staple for cardiology research, including device and drug development while also providing assistance for diagnosis. State-of-the-art modeling studies use unstructured, high resolution, image-based tomographic reconstructions to reflect individual cardiac anatomies with high geometric fidelity and avoid spurious boundary artefacts introduced by jagged surfaces of Cartesian grids. Unstructured tetrahedral meshing enables sophisticated discretization such as finite elements [31]. CEP four chamber models are emerging and can account for anisotropic tissue properties as well as high-fidelity conduction pathways in all chambers, where the cardiac conduction system consists of the sinus node, atrio-ventricular node and the His-Purkinje system. This software platform is leveraged in the cardiac simulation paper presented by Owusu-Mensah et al.

For computational neuroscience applications, neuroactivation simulation techniques can be categorized in terms of their scale: i) microscopic models, ii) mesoscopic models, and iii) macroscopic, large-scale models spanning the whole brain. Microscopic models emerged when McNeal proposed coupled electric field data to multi-compartment neuron models to predict neural activation around the stimulating electrode, in deep-brain stimulation applications. This model represented a point current source and a myelinated fiber placed near it, with both assumed to lie in a long, uniform conducting medium, which was solved with Kirchoff's law [32]. Another microscopic model was proposed by Rubin and Terman for representing the synaptic interconnections in basal ganglia as well as between their afferent and efferent structures [33]. Microscopic neural models are available in the Neuron toolkit and ModelDB [34] [35]. Mesoscopic models focus on the dynamics, size and structure of neural systems rather than on the exact morphology of individual neurons. The first models of localized populations of neurons were proposed based on an axiom [36]: all neural processes depend upon the interaction of excitatory and inhibitory cells. This network is seen as a sequence of a group of neurons connected in a feed-forward manner through divergent or convergent connections, forming a chain-like structure. Finally, macroscopic mean-field models represent the dynamics of large populations of neurons with a number of state variables [37]. A statistical description of each population is given by a probability density function that expresses the distribution of neuronal states, i.e. membrane potential, in a population. Neural dynamics are described by the evolution of the probability density function, which under simplifying assumptions is Fokker-Planck equation. A large-scale model such as this one is the foundation of the software tool The Virtual Brain [37], which is used to model epileptogenic neural circuits based on patient cortex data, in a manner driven by Diffusion Tensor Imaging tractographic and connectomic models [38].

In addition to the preceding functional and therapeutic models, there are numerous public resources in physiology simulation worth citing. In particular, single-focus physiological simulation toolkits, such as CellML and the Physiome Project are useful in providing an understanding of a physiological system, particularly at a cell level [39] [40]. In addition, integrative physiology simulation originated with Guyton, culminating in the 1970s in a model of cardiovascular physiology featuring roughly 150 distinct variables [41]. Milestones in integrative physiology simulation include Quantitative Circulatory Physiology (QCP), which reproduced several hundred functions describing cardiovascular, renal, neural, respiratory, endocrine and metabolic relationships within and across various organ systems [42]. The latter led to University of Mississippi's HumMod, and to recent open-source integrative physiology engine, BioGears [43] [44]. BioGears has spawned the fully open-source Pulse Physiology Engine, which is available from Kitware [45]. Pulse has also been shown to support coupling with haptics-driven surgical simulation based on iMSTK [46].

Last, the convergence between therapy models and deep neural networks should be brought to the attention of the reader. A U-Net-based simulation of finite elements, termed U-Mesh was proposed by Mendizabal, Cotin et al, at INRIA, France [47] [48]. U-Mesh is the one of the earliest and most effective deep neural networks of its kind dedicated to synthesizing FE computations; it is designed to run on top of the Simulation Open Framework Architecture (SOFA) open-source interactive surgery simulation platform. The original U-Mesh network is a parameterized function that accepts a {3 x nx x ny x nz} force tensor f as input and produces a displacement tensor u of the same size as output. Training data for U-Mesh are generated by solving a discretized boundary value problem (BVP) with the FE method. U-Mesh computations ran over 100 times faster than comparable FE simulations also designed for interactive processing, typically under 0.01 seconds, using graphical processor unit (GPU) hardware. An earlier implementation is the PhyNNeSS system proposed by De in 2011, which also used finite elements studies to train a neural network; PhyNNeSS has not yet been made public.

V. Summary

This paper provided a short summary on public state-of-the-art software tools now available to medical and healthcare simulation communities. There was an overview of the main approaches and corresponding tools for tissue segmentation and meshing that comprise patient-specific anatomical modeling. In addition, a high-level survey was also proposed for therapy and function modeling as well as corresponding simulation platforms, many of them with usage in both academia and industry. The prevailing theme has been the availability of these tools in the public domain as well as convergence with progress in deep neural networks.

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