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## Chapter 27

# Future trends in medical image synthesis

**Ninon Burgos<sup>a,\*</sup>, Sotirios Tsafaris<sup>b</sup>, and David Svoboda<sup>c</sup>**

<sup>a</sup>Sorbonne Université, Institut du Cerveau – Paris Brain Institute - ICM, CNRS, Inria, Inserm, AP-HP, Hôpital de la Pitié-Salpêtrière, F-75013, Paris, France

<sup>b</sup>School of Engineering, University of Edinburgh, Edinburgh, United Kingdom

<sup>c</sup>Centre for Biomedical Image Analysis, Faculty of Informatics, Masaryk University, Czech Republic

\*Corresponding author: [ninon.burgos@cnrs.fr](mailto:ninon.burgos@cnrs.fr)

The contributions of this book demonstrate a wide variety of image synthesis and simulation methods, from parametric modeling to deep learning, and their application to diverse tasks such as image enhancement or data augmentation. The ultimate goal when developing methods is to design a simulation system that can produce realistic anatomical or biological images for diverse acquisition conditions and that is fully controllable, accurate, robust, simple to use, fast and easily accessible to all. This would ideally lead to simulated/augmented data of high quality, high variability and high fidelity (both spatially and in time). However, several challenges remain. This chapter will highlight current limitations and identify possible future research directions.

Methods used for the processing and analysis of medical imaging data often come from the computer vision field. However, medical images have different characteristics than natural images and therefore standard computer vision methods cannot be directly used for image synthesis. This is for example the case of deep learning methods as many imaging modalities are intrinsically 3D, meaning that networks built for 2D images must be redesigned, and the amount of data samples available to train networks is far below that of natural images. Without sufficient training samples, the results are thus suboptimal. This is accentuated by the fact that training still often requires paired data (i.e. pairs of images from different modalities but also pairs of images and annotations), which are difficult to gather, for instance because of the invasiveness of a modality or the difficulty to obtain annotations. The development

of approaches able to exploit unpaired data, but also of weakly-supervised or unsupervised methods, comes as a natural solution. But such approaches face difficulties due to the residual mismatches or shifts that often exist between domains. For example, generative adversarial networks with cycle-consistency loss allow non-unique unpaired image translation as a one-to-many mapping exists between the source and target domains in the forward cycle, and a one-to-many mapping exists between the target and source domains in the backward cycle. Data-related difficulties are not the only obstacles in medical image synthesis, computational complexity is also of concern.

The attentive reader has surely observed between the lines that computational complexity is indeed an Achilles heel in the world of simulations. The problem of complexity can also be viewed as a scale bar where each tick mark uniquely expresses how difficult it is to design and develop a new simulation engine. On the very left tip of the bar are the complex simulation engines that try to properly model all the physical phenomena, which makes the engines rather complex. Typically such a kind of simulation can require days or weeks. These methods include for example Monte Carlo based approaches. In the middle of the scale are image-based parametric models. These models are significantly simpler because their objective is to offer a good visual imagination of the studied objects whereas the detailed description is intentionally omitted to reduce the amount of parameters. These simulation engines are nevertheless still quite complicated and require a good expert knowledge during the initial design. Finally, deep learning based simulation methods, that occupy the right most part of the bar, do not require as much expert knowledge as the learned model tends to replace it. This however comes at the cost of limited controllability. Regardless of the choice of the simulation or synthesis method, we must be aware of high demands for hardware performance. The simulations stand and fall together with the availability of high performance computing. However, the computational complexity of Monte Carlo and living system simulations or of deep learning should become less of an issue with the increased availability of highly-parallel architectures (GPU).

While generative models continue to improve, naturally the utility of synthetic data depends on how they are intended to be used. For example, if synthetic will be used to augment real data, one expects that the synthetic do not merely replicate what they have seen in the training set but are able to synthesise new and unseen samples. This ability of generative models to generalise remains a topic of active investigation. In fact, there is broad consensus now that generative models tend to faithfully be able to reproduce regions of the underlying distribution that contain the majority of the mass, whereas they find difficulty to learn how to generate rare data (closer to the distributional boundaries and tails). Of course the ability to generate only the mass and thus replicate what is frequently encountered in the training data may

have suitable applications as well. For example, in settings where data cannot be distributed due to privacy concerns, synthetic proxies can (and have been shown to) be suitable stand-ins.

This highlights another limitation preventing the wider use of synthetic images: the lack of extensive validation and comparison of the methods proposed. Synthetic data must be validated qualitatively and quantitatively as well as for their usability for particular medical or biomedical tasks. The first two are gradually becoming a standard. Usability, however, appears very rarely and has to be tailored to the intended use for the synthetic data. Usability remains hard to demonstrate. One can show that with synthetic data similar decisions can be made or show that by adding synthetic data models can be trained better, but perhaps this is not enough to convince clinical users downstream.

Readers will have noticed that, for many applications, deep learning has supplanted the approaches in place. However, classical methods must not be forgotten. Their combination with deep learning might improve the overall performance. Hybrid solutions combining deep learning and systematic modeling, or deep learning and sparse representation would exploit the advantages from each approach. If we have physical models that we know how to mathematically describe, spending data and deep model parameters to capture these degrees of freedom is not efficient use of resources. Thus, one can imagine the marriage between physical systems capturing degrees of freedom we know with learned (from data) models capturing degrees of freedom that describe physically/mathematically we either do not know how to describe or are intractable. Future methodological developments could also focus on systematic modeling to eliminate magic constants and ad-hoc parameters. The model should be well mathematically and biologically based. The still wider availability of performant computing resources will enable the larger development of synthesis of longitudinal/temporal data. Finally, future simulation frameworks need to be flexible and continually develop as current systems are too task- or data-specific. Harmonization may help reach this goal.

Overall, despite the limitations we identified and the trends which we observe, we are optimistic that synthetic and simulated data will continue to play a considerable role in medical image analysis and beyond.

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