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Chapter 1

Introduction to medical and biomedical image synthesis

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*The human brain is the best **image synthesizer** ever!*

When storing our photos using the most popular image file format called jpeg, a vast amount of information in the image, to be compressed, is intentionally thrown away to markedly reduce the file size. Afterwards, when viewing the compressed image, the missing parts are surprisingly not disturbing us as those are either too tiny for our eyes or automatically completed by the human brain due to our previous experience with real world scenes.

***Image synthesis** is nothing more than an attempt to mystify the human visual perception!*

Each image synthesis process is naturally followed by an obvious, and often obligatory, question whether the artificially generated image is plausible enough or whether the difference between the artificial and real image is so small or negligible that the human eye is not able to recognize it. Answering no to this question clearly shows that our eyes do not accept the generated image as the naturally acquired one.

Every day, millions of images are created using various acquisition devices starting from the smallest ones like smartphones or compact cameras and ending with the large ones, typically including expensive imaging devices located in hospitals or observatories. Taking photos is mostly cheap, fast, and repeatable. This is however not true in the case of medical imaging where the acquisition process might be long, expensive, dangerous, or too scarce to be repeated if even possible. A simple example of such a real life situation is scanning the patient's body with computed tomography or positron emission tomography. Regardless of the fact that the scanning process is not comfortable, time demanding, and expensive, one should keep in mind that each exposure of the patient to X-rays increases the probability of getting cancer in the future. On the other hand, more scans would bring more information needed for proper diagnosis or prognosis of the illness for which the patient currently undergoes the examination. Here comes the obvious question: how to reduce time, price, and allow repeatability? A similar issue is apparent also in microscopy, where for proper analysis of cells and subsequent diagnosis, one needs to know the correct shape and location of such cells. This is however a difficult task as no one knows the exact shape and location of the observed cells and cell compartments, as we are able to observe them only using the optics that naturally introduce some blur and artifacts. One can rely on standard image restoration methods to improve the images to some extent but the question of possible shift or misalignment still persists.

The discipline that tries to answer the above-mentioned questions has been studied for years by many research groups and is called simply "image synthesis". One can find many adjectives that anticipate this phrase. These might be "medical", "biomedical", "deep learning based", "model-driven", or "data-driven" but all of them have the same objective – to synthesize some image or its part that is missing. One can even complicate the task and try to synthesize time-lapse image sequences, but this is nothing more than increasing the dimensionality of the image that one wants to artificially generate. In this book, we will try to answer the questions that are narrowly connected to challenges in medical and biomedical imaging and how to answer them using image synthesis.

Currently, image synthesis methods in medical and biomedical imaging are able to augment image datasets, increase image resolution, fill missing or incomplete data, derive data in one modality using another modality, prepare perfect annotation, etc. This is definitely not a small amount and we can expect that the possibilities will rise in the future. All the given use cases listed above (and not only those) are mentioned in the second part of this book which is dedicated to success stories and how individual image synthesis

methods were employed in particular situations. The first part of the book, on the other hand, is more theoretical and shows and explains the basic principles of image synthesis methods, how they work and how to implement them. Both parts together form a book that gives the reader insight into the technical background of image synthesis and how it is used, in the particular disciplines of medical and biomedical imaging.

It is not a secret that this book emerged from the narrow cooperation of the experts in the field of image synthesis in medical imaging. Most of them are more or less connected to the international workshop on Simulation and Synthesis in Medical Imaging (SASHIMI), organized as a satellite event of the International Conference on Medical Image Computing and Computer Assisted Intervention – a vivid platform for sharing knowledge and experience in this field.

The aim of this book is to present the already well established image synthesis approaches as a family of methods that together form a puzzle game where each tile has its own meaning, position and is unreplaceable. We hope that the reader will find this puzzle game solvable, interesting and enjoyable. The book is splitted into two main parts – Methods & Principles and Applications – each consisting of several chapters written by the specialists and experts in the given fields of medical and biomedical imaging. The first chapter that immediately follows this introduction is focused on traditional systematic modelling, which is also called model-driven approach. We consider this chapter and its position at the very beginning of the book as important because it presents the basic principles of image synthesis that were valid before deep learning appeared and became a de-facto standard. Currently, the deep learning approaches dominate but before we start enjoying their strength, we should understand the cornerstones that are not visible at first sight but still form the fundamentals on which the deep learning methods are also built. The first part of the book thus presents the methods that have been developed for image synthesis in chronological order: first systematic modeling, including parametric modeling, Monte Carlo simulations and image synthesis methods using segmentation and registration, and then data driven machine learning approaches including dictionary learning, convolutional neural networks, generative adversarial networks and (variational) autoencoders. The second part of the book is dedicated to the applications of image synthesis, first to medical and then to biomedical imaging. The medical applications start with a chapter dedicated to the use of a framework that simulates magnetic resonance images relying on the acquisition physics principles, i.e. the simulated image is not obtained from another image as will be the case in the following. This chapter precedes a series of modality-agnostic chapters covering image harmonization

and enhancement, and how these can help subsequent image processing steps. Follow applications specific to a task, e.g. anomaly detection, or a modality, e.g. positron emission tomography. After the medical applications, the focus is put on biomedical applications, covering different scales, from single cells to whole histological slices, both static and changing in time. The book ends with a third part on perspectives that includes three chapters. The first one summarizes the different options that exist and should be considered when validating image synthesis approaches. The second one explains the crucial role that uncertainty quantification plays in medical image synthesis. The last one concludes the book with research directions that should be worth exploring in the future.

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