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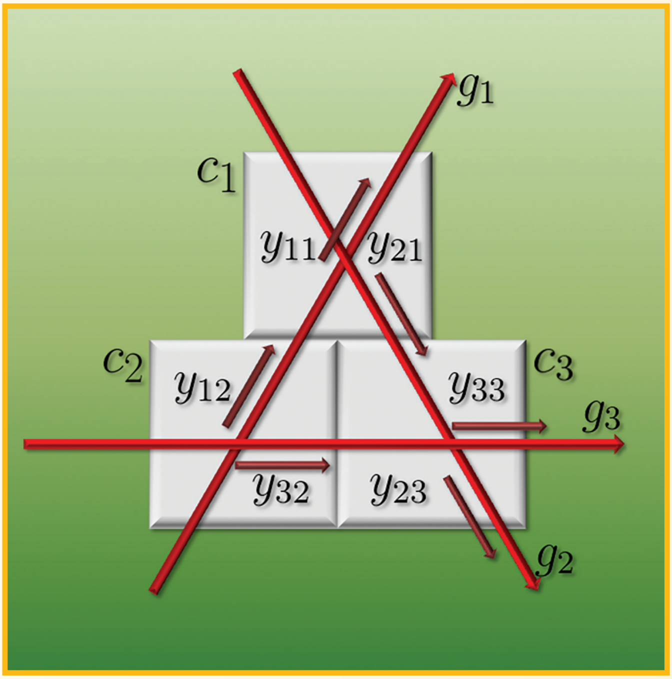

Arkadiusz Sitek

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Series in Medical Physics and Biomedical Engineering

Statistical Computing in Nuclear Imaging

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Dedication

To Sylwia and Pascal Jan

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Preface

My main reason for writing this book is to introduce Bayesian approaches to analysis of randomness and uncertainty in nuclear imaging. Bayesian methods used in imaging research and presented in many imaging texts do not reflect the Bayesian spirit of obtaining inferences about uncertain phenomena, which is quite unfortunate. Most users who utilize statistical tools in their research consider the probability as the frequency of occurrence of some random phenomena. The word "random" indicates that if an identical experiment is performed repetitively the results may be different and unpredictable. We all have gone through examples of frequentist[1] coin flipping and die rolling way too many times. However, the interpretation of probability as a frequency makes practical applications of drawing inferences quite limited. Anyone who uses computing to analyze experiments and to model uncertainty will certainly encounter serious limitations and complexity of the frequentist techniques. At this point, many of us reach toward Bayesian methods because the Bayesian techniques are overwhelmingly simple to implement to a wide variety of scientific problems.

However, there is a caveat. When we adopt Bayesian methods we often still carry a heavy baggage of misconception of the probability being a frequency. This misapprehension leads to misuse, confusion, and certainly to misinterpretation of results of our analyses. I've heard often conjectures stating that "Bayesian results are biased." For a Bayesian, this statement sounds like "The weather today is yellow"—nonsense! In an effort to explain many of the misconceptions, I introduce Bayesian statistics and present the Bayesian view on uncertainty in the first two chapters of the book. These two chapters are probably the most important because in order to fully embrace Bayesian methods, one needs to purge his or her mind of the concept of probability being a frequency.

Another objective of this book is to introduce Bayesian computational techniques in nuclear imaging. I introduce the statistical model in Chapter 3. Many will find the model unorthodox, as I deviate from the routinely used Poisson statistics in order to derive computationally efficient numerical implementation of Bayesian methods. The Poisson distribution of nuclear imaging hinges on the assumption that the generative process of events is described by an independent event rate. Such a rate is a mathematical construct that helps simplify the description of the decay laws. The gamma radiation, however, is the result of the decay of radionuclei, and I build the statistical model from the ground up based on this simple assumption. Then, I demonstrate how the

[1] A frequentist is someone who interprets probability as a frequency of occurrence.

derived decay laws can be approximated by Poisson independent rates and Poisson distribution. Although the goal of Chapter 3 is to provide a statistical basis for algorithms developed in Chapter 6, the theory may also be useful for a better understanding of the counting statistics in general.

With the advent of readily available and inexpensive computing, Monte Carlo methods based on Markov chains became a workhorse for Bayesian computing. They can be used to approximate multi-dimensional distributions (e.g., posteriors) that are otherwise very difficult to characterize. I introduce these techniques in Chapter 4. A short introduction to nuclear imaging and several concepts used in analysis of nuclear imaging data are provided in Chapter 5. The final chapter, Chapter 6, provides derivations of Markov chain algorithms applicable to analysis of nuclear data. It contains demonstrations of calculations of estimators, intervals, Bayes factors, Bayes risk, etc. These examples of Bayesian analysis are provided with the hope that they will inspire readers to use presented methods in problems they face in their work. A sample C++ code that was used in Chapter 6 is provided in Appendix F.

Who should read this book? The book is addressed to a wide spectrum of practitioners of nuclear imaging. This includes seasoned scientists who have not been exposed to Bayesian paradigm as well to students who want to learn Bayesian statistics. I believe that many may benefit from reading Chapters 1 and 2 in understanding of the Bayesian methods in general. My description of the counting statistics in Chapter 3 will also benefit practitioners of nuclear data analysis because they provide complete in-depth derivation of the statistical model of nuclear decay and photon counting. The chapter dedicated to Monte Carlo methods (Chapter 4) and the introductory chapter dedicated to nuclear imaging (Chapter 5) are intended for readers who are not accustomed with basic ideas of Monte Carlo methods and nuclear imaging. These chapters can be skipped by someone familiar with these topics. Chapter 6 is intended for readers looking for alternative methods to nuclear data analysis. The chapter is short and intended to be an inspiration for investigators to discover new ideas and methods of advanced Bayesian data processing in nuclear imaging. My hope is that this chapter will promote new ideas and support development of the field of nuclear imaging data analysis in the future.

I had the privilege and was fortunate to work with many great imaging scientists and I am very grateful to my mentors, collaborators, postdocs, and students who, in one way or another, contributed to this book. I want to acknowledge Anna Celler and Grant Gullberg for early discussions that eventually led to many concepts discussed here. I received many useful and thoughtful comments about this manuscript from Anna Celler, Mellisa Haskell, Joaquín López Herraiz, Sylwia Legowik, Peter Malave, Stephen Moore, and Hamid Sabet, and I would like to thank and acknowledge them for their input and help.

Arkadiusz Sitek

About the Author

Arkadiusz Sitek, Ph.D., is an associate physicist at Massachusetts General Hospital in Boston and an assistant professor at Harvard Medical School. He received his doctorate degree from the University of British Columbia, Canada, and since 2001 has worked as a nuclear imaging scientist in the Lawrence Berkeley National Laboratory, Beth Israel Medical Center, and Brigham and Women's Hospital before joining Massachusetts General Hospital in 2012. He has authored more than 100 scientific journal and proceedings papers, book chapters, and patents, and served as a principal investigator on nuclear imaging research projects. Dr. Sitek is a practitioner of the Bayesian school of thought and a member of the International Society for Bayesian Analysis.

1 Basic statistical concepts

1.1 INTRODUCTION

This chapter and the next chapter are essential for understanding the content of this book. By design, the chapters present statistics from a quite different perspective as usually the statistics is introduced and taught. The theory of statistics is presented from the pure Bayesian perspective where we attempt to make sure that concepts of the classical statistics are not mixed in the exposition of the theory. In our experience, the Bayesian statistics is frequently introduced in image and signal analysis texts as an extension of the classical treatment of probability. The classical treatment of probability is based on the interpretation of probability as the frequency of occurring of some phenomena based on repeated identical trials. The classical approach is often referred to as the *frequentist* statistics. From the Bayesian point of view, the probability describes the strength of beliefs in some propositions. One of the most frequently used terms, the probability distribution, in frequentist statistics means the "histogram" of outcomes of the infinite number of repetitions of some experiment. In Bayesian statistics, the probability distribution quantifies beliefs or in other words measure of uncertainty. Unfortunately, these two concepts of probability, Bayesian and frequentist, are not compatible and cannot be used together in a logically coherent way. What creates confusion is that both approaches are described mathematically by the probability calculus and because of that they can be intermingled and used together which, to us at least, is incomprehensible.

In this book we decided not to introduce classical concepts at all. To help the reader who is accustomed to thinking about the probability as a frequency, we intentionally do not use the term *random variable.* This is because the random variable is strongly associated with the concept of frequency. To avoid any unwanted associations, the term random variable is replaced in this book by the term *quantity.* The classical term *parameter* is not used in this book either. In the classical statistics, parameters describe unknown values and inference about those parameters is obtained in classical statistical procedures. Instead of the term "parameter" the term *quantity* is used as well. Both the "random variable" and the "parameter" are put on the same conceptual level and are referred to as *quantities.* Finally, in the classical statistics the term *data* is used to describe the outcome of experiments. Based on the data, inferences about parameters are made in frequentist statistics. In the Bayesian view utilized here, the term data is another *quantity* which is conceptually the same as quantities corresponding to random variables or quantities corresponding to parameters. For this quantity we relax our naming rule and use interchangeably the data and the quantity to describe outcomes of the experiments.

It may appear that such convention creates confusion because there is a single term "quantity" to describe so many phenomena. There is more to gain than lose as we believe that this naming convention helps considerably with understanding of Bayesian concepts. In order to help differentiating different quantities, we will use adjectives *observable* and *unobservable* added to the term quantity that identify which quantities are revealed in the experiment (correspond to "data" in classical treatment) and which are never revealed (correspond to parameters in classical statistics).

1.2 BEFORE- AND AFTER-THE-EXPERIMENT CONCEPTS

In this chapter, a specific view on processes that involve uncertainty will be considered. The author hopes that the approach will allow to smoothly introduce concepts that are frequently poorly explained or misunderstood. The content of this book is concerned about knowledge of *quantities* that can, or cannot, be observed directly in an experiment. Such quantities will be referred to as observable and unobservable quantities, respectively. Interchangeably, we will refer to knowledge about quantities as beliefs. We will also use uncertainty about the quantity which is the opposite term to knowledge. For *unobservable quantities* (UQs) the true value of the quantity is unknown (uncertain). For example, suppose we are interested in a true weight of some object. This quantity cannot be observed (determined) directly and the true weight is unknown. By unobservable directly we mean that there is no experiment that can reveal the true value of that quantity. The *observable quantities* (OQs) will be those where the true values are revealed by the experiment. For example when weighing an object the reading from the scale is an observable quantity. Obviously, the true weight of the object (unobservable quantity) and the reading from the scale (observable quantity) are two different quantities and are not necessarily equal.

> **Important:** Here an important distinction has to be made. The weight of the object and the result of the measurement are two different quantities. The weight is uncertain before and after the experiment; however, the measurement is uncertain before the experiment (we do not know what the reading on the scale will be), but it is known exactly after the experiment. Therefore the quantity which is the measurement is revealed and known exactly. The true weight remains uncertain.

The quantities that we will be interested in are going to be referred to in this book as the *quantities of interest* (QoIs) which include UQs and OQs. Sometimes quantities that are known will be required to fully describe a problem at hand (when considering the radioactive decay such quantities can be the half-life or decay constant for given radiotracer). These quantities will be referred to as *known quantities* (KQs). The values of all QoIs constitute the objective truth that will be referred to as the "state of nature" (SoN). Obvi-