Preface

This book brings together a selection of papers by George Gerstein, representing his long-term endeavor of making neuroscience into a real science inspired by physics, where he had his roots. In this, George was many years ahead in the field, consistently striving for quantitative analyses, mechanistic models, conceptual clarity, and, foremost, true understanding. In doing so, George pioneered Computational Neuroscience, many years before the term was even born.

The overarching goal of George Gerstein's research program throughout his productive career was to understand the functional organization of neuronal networks in the brain. How do neurons in these networks interact to make the network accomplish a certain function, e.g., in sensory perception, while providing the neurons with the stimulus–response properties they reveal when recorded in experiments? To quote from his own writings (Gerstein et al. 1989): *"Long before emergence of all the current complexities of single neuron anatomy and physiology, it was recognized that the computational processes constantly carried out by the nervous system could not be explained by the properties of single neurons alone. Sherrington, in the 1930's, verbalized the idea that neurons must cooperate in fulfilling a complex task. This concept has been completely assimilated into neurobiological thought and explanation, but only in the most general way. Experimental access to the properties of real neuronal assemblies has largely been impossible until quite recently. Thus, the development of the assembly concept has been somewhat unfettered."*

In this research effort, George Gerstein played an active role, both as an experimenter and as a theoretician. Thus, he was quite aware of the pros and cons of both approaches and of the limitations of either one. To quote from his own writings once more (Gerstein and Turner 1993): *"Over the years, the relationship between experimenters and theoreticians in the study of brain function has been at best uneasy. Fault can be found on both sides; in part there is a communication difficulty. The principal problem is the lack of direct confrontation: theories are rarely couched in terms amenable to experimental testing, while experiments are rarely aimed at theoretical issues. Theoreticians often use large populations of elements and implied observation times that are wildly unrealistic for the measurement possibilities of the laboratory. Conversely, even those experimenters*

who are observing a population of neurons are all too often thinking in terms similar to single neuron stimulus designs."

Yet, George, being a staunch pragmatist and optimist, consistently endeavored to connect the two approaches, in a constructive effort to join forces and, thereby, optimizing the chances of success (Gerstein and Turner 1993): *"At this point in time, the confrontation we are seeking might therefore come at an intermediate, less global level, involving modest numbers of elements. Here we may be able to seek emergent properties of neuronal assemblies from both the experimental and the theoretical point of view."*

George never liked to write a book. Despite many requests, he consistently refused. His response invariably was: *"Books are about old papers. I prefer to write new ones."* And so he did, until the very end. Thus, we found ourselves with the task of collecting a selection of George Gerstein's many seminal contributions to neuroscience, be they experimental, theoretical, or computational, into a single, comprehensive volume. Our aim, in doing so, was also to provide the readers, especially the younger ones who may not even be aware that there was ever a time in neuroscience without the PSTH, the cross-correlation approach, or stochastic neuron models, with the fresh introduction of these various concepts in the original literature.

We organized the material in a series of chapters by subject, ordered in time, each one containing one or more of George Gerstein's papers. References to the included papers throughout this volume are highlighted in boldface type. Several of George's former students and collaborators kindly contributed an Introduction to these various chapters, intending to put the reprinted papers in their historical and present context and to add the personal touch of their involvement in generating these papers. Thereby, each of these chapters introduces one (or more) of George Gerstein's seminal contributions to the Neurosciences, be it in the domain of neuron and network modeling or in the area of neuronal data analysis techniques, ordered by their publication date. Specifically, the various chapters highlight the following innovative computational approaches and their applications in neurophysiological experiments first introduced in George Gerstein's papers:

Chapter 1: the first stochastic model of a neuron's spiking activity

Chapter 2: the introduction of statistical techniques from stochastic point process theory (e.g., inter-spike interval histogram, serial correlation, Peri-Stimulus Time Histogram (PSTH), auto- and cross-correlation) to the analysis of neuronal spike train data

Chapter 3: setting up a lab for single neuron recordings in the inferior temporal cortex of the awake behaving monkey and demonstrating the effect of attention on neuronal responses to visual stimuli

Chapter 4: demonstrating plasticity of neuronal interactions in small neuronal networks upon stimulation

Chapter 5: designing novel methods for finding repeating spike patterns in single- and multi-neuron spike recordings and for identifying cooperating groups of neurons (gravitational clustering)

Chapter 6: using gravitational clustering analysis to identify neuronal assemblies in the respiratory brain stem and their reconfiguration with breathing phase
Chapter 7: characterizing the dynamics of spike correlations and neuronal interactions (Joint-PSTH) and their dependence on sensory stimuli and behavior
Chapter 8: introducing different measures for statistical significance of spike train correlations
Chapter 9: detecting recurrent spatiotemporal firing patterns in multi-neuron spike train recordings
Chapter 10: interpreting cross-correlations between unresolved multi-neuron recordings
Chapter 11: demonstrating plasticity in receptive field properties and neuronal interactions in auditory cortex upon intracortical microstimulation
Chapter 12: demonstrating appetitive conditioning-induced plasticity of receptive fields and state-dependent modulation of stimulus-evoked responses and their across-trial variability in auditory cortex
Chapter 13: improving the signal-to-noise ratio in multi-neuron recordings and the sensitivity of gravitational clustering in measuring neuronal interactions
Chapter 14: detecting higher-order correlations and other signs of neuronal assembly activity in network model simulations and experimental data from large-scale multi-neuron recordings

We hope that, taken together, these various chapters and their Introductions will help the reader appreciate how much our current thinking on brain function owes to George Gerstein's research and the insights gained from it. George was not only an innovative thinker in theory, experiment, and analysis methodology, he also inspired by his mode of thinking science. Thus, in a way, this book is both a product of this inspiration and a tribute to it.

The volume closes with two separate contributions: a commemoration of the first Nencki Award being awarded in 2008 to George Gerstein, including a summary **CV of his education and scientific career**, written and published by Andrzej Wróbel, and an **Epilogue**, presenting an Obituary to George Gerstein, written by his colleagues Ad Aertsen and Moshe Abeles.

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