
Preface

“Rule IV. There is need of a method for finding out the truth.

Rule V. Method consists entirely in the order and disposition of the objects toward which our mental vision must be directed if we would find out any truth. We shall comply with it exactly if we reduce involved and obscure propositions step by step to those that are simpler, and then starting with the intuitive apprehension of all those that are absolutely simple, attempt to ascend to the knowledge of all others by precisely similar steps.”

—Rene Descartes, *Rules for the Direction of Mind*

“...Perhaps he would sooner satisfy himself by resolving light into colours as far as may be done by Art, and then by examining the properties of those colours apart, and afterwards by trying the effects of rejoining two or more or all of those, and lastly by separating them again to examine what changes that rejoining had wrought in them. This will prove a tedious and difficult task to do it as it ought to be done but I could not be satisfied till I had gone through it.”

—From Newton’s letter, quoted in *The Life of Isaac Newton* by Richard Westfall. Cambridge University Press, 1993.

As much as the progress of a discipline depends on the progress of methods it uses, the overall goal of *Renal Disease: Techniques and Protocols* is to provide a comprehensive and balanced account of adequacy, advantages, and potential pitfalls of various modern approaches to study renal function in health and disease. Toward this end, any possible hesitation in selecting the shortest, safest, and most picturesque path to one’s research summit should be alleviated by the expert contributors, who have already taken a similar road and are keen to share their observations. It is our sincere hope that this collection of technical approaches should become a *vade mecum*, which will be both a user-friendly guide for the uninitiated and a thoughtful counselor for the experienced scholar of fluid–electrolyte homeostasis and kidney function.

The last few years have witnessed the completion of the human genome project, development of high-throughput techniques for the screening of expressed genes, and the emergence of technological platforms for the next major enterprise—proteomics research. Yet, the basic tenets of approaching the problem at hand have not undergone transformation since the time when

Rene Descartes formulated them. Simplified models, devoid of the complexities and “obscurities” of reality, remain the bedrock of investigation. Lessons learned are further tested in more complex models, ascending ultimately to the organismal level. Therefore, the flow of chapters in this book has been designed to reflect upon this process—from simple models to integrative physiology.

With this in mind, *Renal Disease: Techniques and Protocols* is subdivided into five sections: (I) Optimizing the Usage of Models of Renal Disease, (II) Choices of Imaging Techniques, (III) Studies of Embryonic Development of the Kidney, (IV) Approaches to Study Molecular Mechanisms of Disease, and (V) Technical Means to Assess Functional Correlates of Disease. Though intricately interconnected, such a subdivision should provide an investigator with a possible path to follow in the course of investigation.

Certain technological areas are not represented in this volume (i.e., gene therapy). This does not reflect this editor’s negligence, but rather acknowledges that it has become a subject for another volume published in this series and the interested reader is referred to that edition (*1*).

Methods per se are not science, but mere tools to achieve scientific goals. And yet in this process new techniques are being born or the old ones modified to satisfy the precise goals of a researcher. The intelligent use of the technological armamentarium is a valuable assistant in our inquiries. It is for this reason that philosophers and thinkers of all times have developed a body of literature that summarizes the diversity of scientific approaches. In addition to the reductive and inductive methods, illustrated by the above quotations from Descartes and Newton, approaches to a problem that are based on theoretical predictions initially unsupported by the facts (“dogmatic method”), reliance on a chance discovery (“haphazard experiment”), as well as the “method of contradiction” and the “method of recodification,” searching for known patterns in unknown situations (or vice versa), all enrich the repertoire of strategies to be selected by an investigator (*2*). The advent of high-throughput screening technologies provides, at least at the first glance, a typical example of a shifting paradigm of research strategies. In contrast to the “dogmatic method,” these screening approaches are, basically, unbiased and unenlightened by a hypothesis—perfect examples of what one would call “a fishing expedition.” When successful however, they offer the researcher a previously concealed and entirely unexpected set of data. These in turn require the engagement of a “reductive method” to try sorting out potential pathways that have led to the fact(s) disclosed in an unbiased fashion and their consequences. Thus, starting with the Newtonian stance of *hypotheses non fingo* (I don’t make hypotheses), these high throughput approaches require just the opposite at the stage when the output from the technological platforms reaches the desk of an astonished investigator.

With more than 50,000 scientific periodicals published worldwide that in toto print weekly more than 40,000 scientific articles, the level of informational barrage to which an investigator is exposed has become almost unbearable. No matter which strategic decisions for attacking the problem at hand have been made, the next challenge of selecting the correct tool set confronts every investigator. Under the stress of informational overflow, this selection turns into an overly complex process. Therefore, a manual, guiding investigators among the thicket of available techniques and providing them with expert insights into the advantages and bottlenecks of each, should serve to strengthen the scientific backbone and save time. With these goals in mind, we offer the reader *Renal Disease: Techniques and Protocols*.

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References

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2. Moles, A. "La Creation Scientifique," Geneva, 1957; quoted from J. Barzun "Science: The Glorious Entertainment," Harper & Row, New York, 1964.



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