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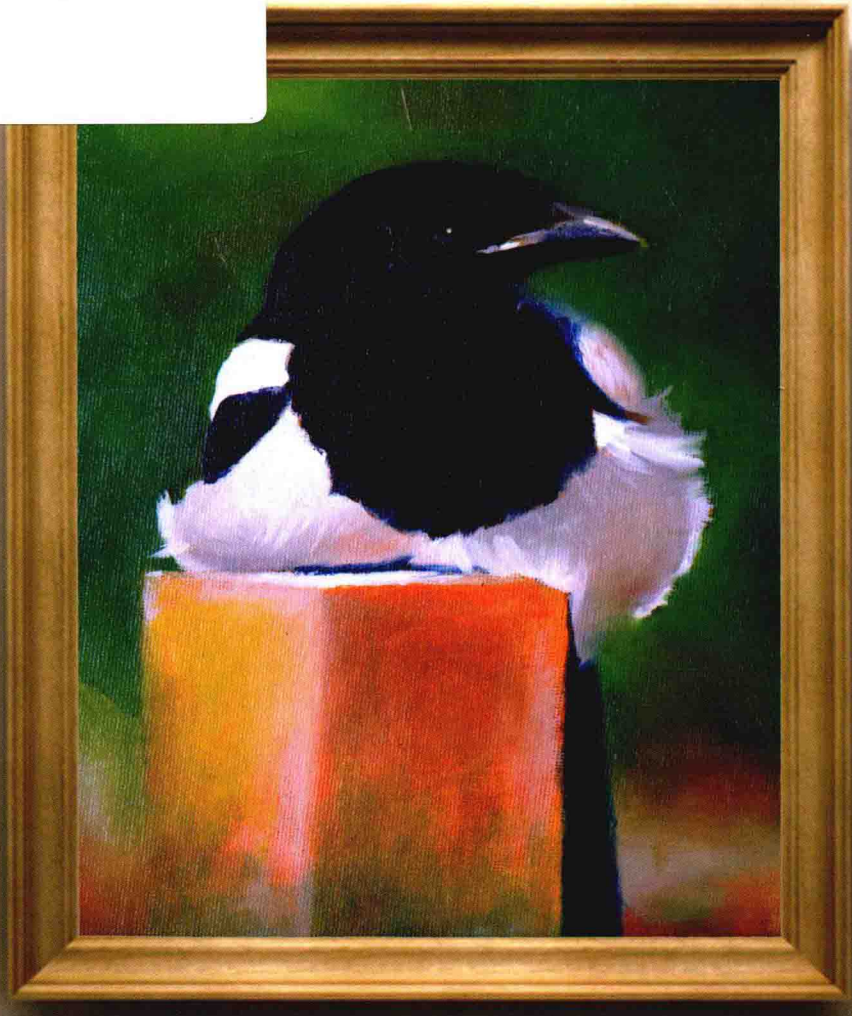
Mathematical and Computational Biology Series

Genome Annotation

Jung Soh, Paul M.K. Gordon,
and Christoph W. Sensen



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Genome Annotation

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Mathematical and Computational Biology Series

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Preface

The year 1995 saw the arrival of the first completed microbial genomes, *Haemophilus influenzae* and *Mycoplasma genitalium*. Several years of struggle for a complete genome was ended by the group at The Institute for Genomic Research (TIGR). From today's point of view, 16 years and more than a thousand completed genomes later (including, of course, the human genome), it may be hard to understand how much of an accomplishment this was. At the time, however, most laboratories around the world were still sequencing on slab gels using radioisotopes as the label for the fragments, which represent the DNA sequence.

When we sit down to "browse" genomes today, we do not often remember the days before e-mail and the Internet, or the days before automated DNA sequencing became a commodity. But it is certainly worthwhile to take a look back, as many of the design decisions that were made in the last 16 years influence the way we deal with genomic information today.

When the first genomes were presented at a by-invitation-only meeting in Worcester, England, in 1995, the only tool that was capable of handling such a large file was a word processor. Therefore, the sequence was first presented to the scientists at the meeting as a character file, which was scrolling on the screen behind the speaker. One of the major problems with handling a large DNA sequence file at the time was that most bioinformatics software was only tailored for DNA fragments of a size much less than a complete microbial genome, typically no more than approximately 100 kilobase pairs. The first automated genome analysis and annotation systems were barely emerging in 1995, and thus the handling of a complete genome with a size of more than a million base pairs all at once was impossible.

The Web was a fledgling entity in 1995, with not much power and entirely based on the Hypertext Markup Language (HTML). It became clear very quickly that only large communities of scientists with a diverse

background could really make sense of the genomic information, provided that they were enabled to collaborate, and thus the Web quickly became the vehicle by which genome annotations were created and exchanged among scientists. The first automated genome analysis and annotation systems, which were Web-based, initially produced tabular output that listed the location of potential genes and gene functions, which were predicted mostly by database comparison. It became obvious very early that this was not sufficient for biologists, therefore graphical subsystems were added, which are today part and parcel of all genome analysis and annotation systems and are probably the only part of an automated genome analysis and annotation system that most users ever encounter.

Over time, the Web developed into the massive entity it is today, with many additions to the Web technologies, which were utilized in turn by the developers of today's genome analysis and annotation tools. The three most useful tools in this context were probably (1) the creation of the programming language Java by James Gosling, which allowed the development of truly platform-independent applications; (2) the introduction of Extensible Markup Language (XML), which could adequately be used for the description of biological and medical objects; and (3) the creation of Web services (for example, the BioMOBY system), which made distributed computing simple and easy, and allowed the transparent and seamless integration of new bioinformatics tools into Web-based bioinformatics applications.

DNA sequencing technology has progressed in several iterations to today's level, which is called "next-generation sequencing," but really represents the third or fourth generation of DNA sequencing technologies, with yet another generation just around the corner. The sheer amount of DNA sequence, which can be produced on a single device today, is mind-boggling. It has literally become possible to resequence genomes the size of the human genome within a few hours in a single laboratory and the $1000 human genome is on the horizon. At the time of this writing (2012), very few genome annotation pipelines are capable of dealing with this information volume and new strategies need to be developed to accommodate the needs of today's genome researchers.

In the near future, everyone will be able to carry their genome sequence on some kind of data storage device and diagnostics might become largely based on the results of genomics screens, which will be cheaper than today's advanced imaging technologies (MRI and CT scans, for example). Thoroughly annotated genomic information and the integration

of all information into a single model will be a prerequisite to successful approaches to individualized medicine, the development of advanced crops and the sustainable production of food, medical research and development, and the development of new and sustainable energy sources.

This book attempts to introduce the topic of automated genome analysis and annotation. The initial chapters take the reader through the last 16 years, explaining how the current analysis strategies were developed. This is followed by the introduction of up-to-date tools, which represent today's state of the art. The authors also discuss strategies for the analysis and annotation of next-generation DNA sequencing data. This book is intended to be used by professionals and students interested in entering the field.

We would like to thank Hershel Safer and the editorial team at CRC Press/Taylor & Francis for their patience while creating this book.

Authors

Jung Soh is a research associate at the University of Calgary, in Alberta, Canada. He was born in Seoul, Korea, and received a Ph.D. in computer science from the University at Buffalo, State University of New York, where he worked at the Center of Excellence for Document Analysis and Recognition (CEDAR). From 1992 to 2004, he worked as a principal research scientist at the Electronics and Telecommunications Research Institute (ETRI), Daejeon, Korea, in areas such as biometrics, human–computer interaction, robotics, video analysis, pattern recognition, and document analysis. Dr. Soh moved to Calgary in 2005. His current research interests include bioinformatics, machine learning, and biomedical data visualization.

Paul Gordon is the bioinformatics support specialist for the Alberta Children's Hospital Research Institute at the University of Calgary. He was born in Halifax, Nova Scotia, Canada. He received his bachelor of science (first class honors) and master's of computer science from Dalhousie University (Halifax). He worked at the Canadian National Research Council's Institute for Information Technology and at its Institute for Marine Biosciences

(1996–2001) before moving to Calgary. From 2002–2011, he was a lead programmer on several genome Canada-funded projects, supported by the University of Calgary. In the new era of the $1000 genome, Gordon's current work focuses on developing bioinformatics techniques for personalized medicine.

Christoph W. Sensen is a professor of bioinformatics at the University of Calgary, in Alberta, Canada. He was born in Oberhausen-Sterkrade, Germany, and studied biology in Mainz, Düsseldorf, and Köln. From October 1992 to November 1993, he worked as a visiting scientist at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. At the beginning of 1994, he moved to Canada. Until his move to Calgary in February 2001, he worked as a research officer at the National Research Council of Canada's Institute for Marine Biosciences (NRC-IMB). His research interests include genome research and bioinformatics.

Contributor

Stephen Strain was born in Szeged, Hungary. He studied visual arts and music in Debrecen, Szeged, and Budapest. In 1981, he emigrated to Calgary, Alberta, Canada, where he lives and works as an artist. He is known for his interpretation of flamenco music (www.flamencoelegante.com) and as a painter.

His painting *Magpie* is used as the cover design.

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