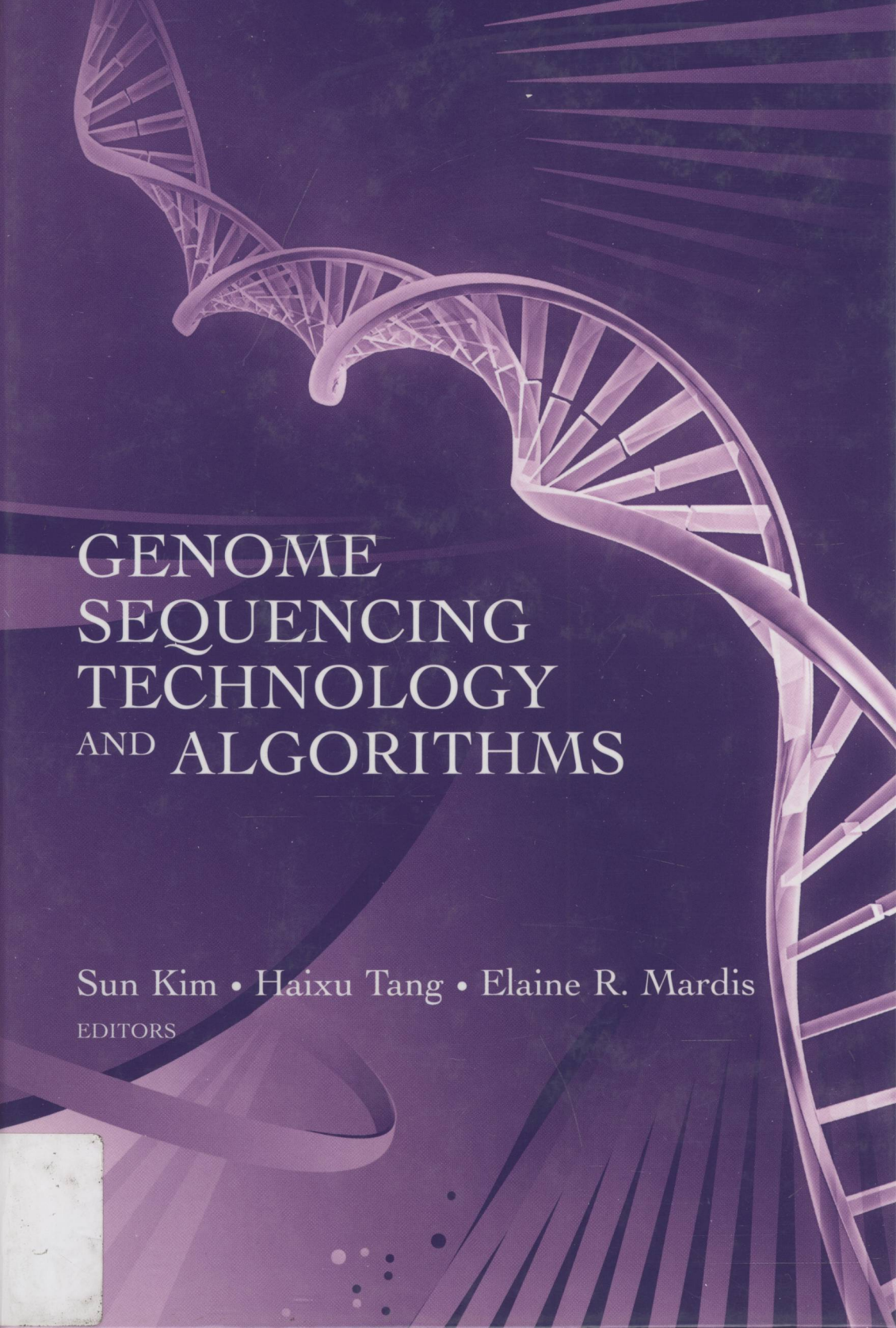

GENOME SEQUENCING TECHNOLOGY AND ALGORITHMS

Sun Kim • Haixu Tang • Elaine R. Mardis
EDITORS

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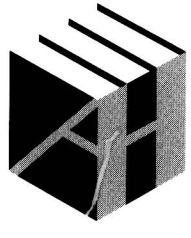

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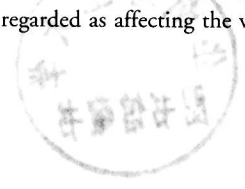

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Part I
The New DNA Sequencing Technology

1

An Overview of New DNA Sequencing Technology

Elaine R. Mardis

1.1 An Overview

1.1.1 Background

The dideoxynucleotide termination DNA sequencing technology invented by Fred Sanger and colleagues, published in 1977, formed the basis for DNA sequencing from its inception through 2004 [1]. Originally based on radioactive labeling, the method was automated by the use of fluorescent labeling coupled with excitation and detection on dedicated instruments, with fragment separation by slab gel [2] and ultimately by capillary gel electrophoresis. A variety of molecular biology, chemistry, and enzymology-based improvements have brought Sanger's approach to its current state of the art. By virtue of economies of scale, high-throughput automation and reaction optimization, large sequencing centers have decreased the cost of a fluorescent Sanger sequencing reaction to around $0.30. However, it is likely that only incremental cost decreases will continue to be achieved for Sanger sequencing in its current manifestation. This fact, coupled with the ever-increasing need for DNA sequencing toward a variety of biomedical (and other) studies, has resulted in a rapid phase of technology development of so-called next generation or massively parallel sequencing technologies, that will revolutionize DNA sequencing as we now know it. Along with this revolution will come a significant and potentially unanticipated impact