How to map billions of short reads onto genomes

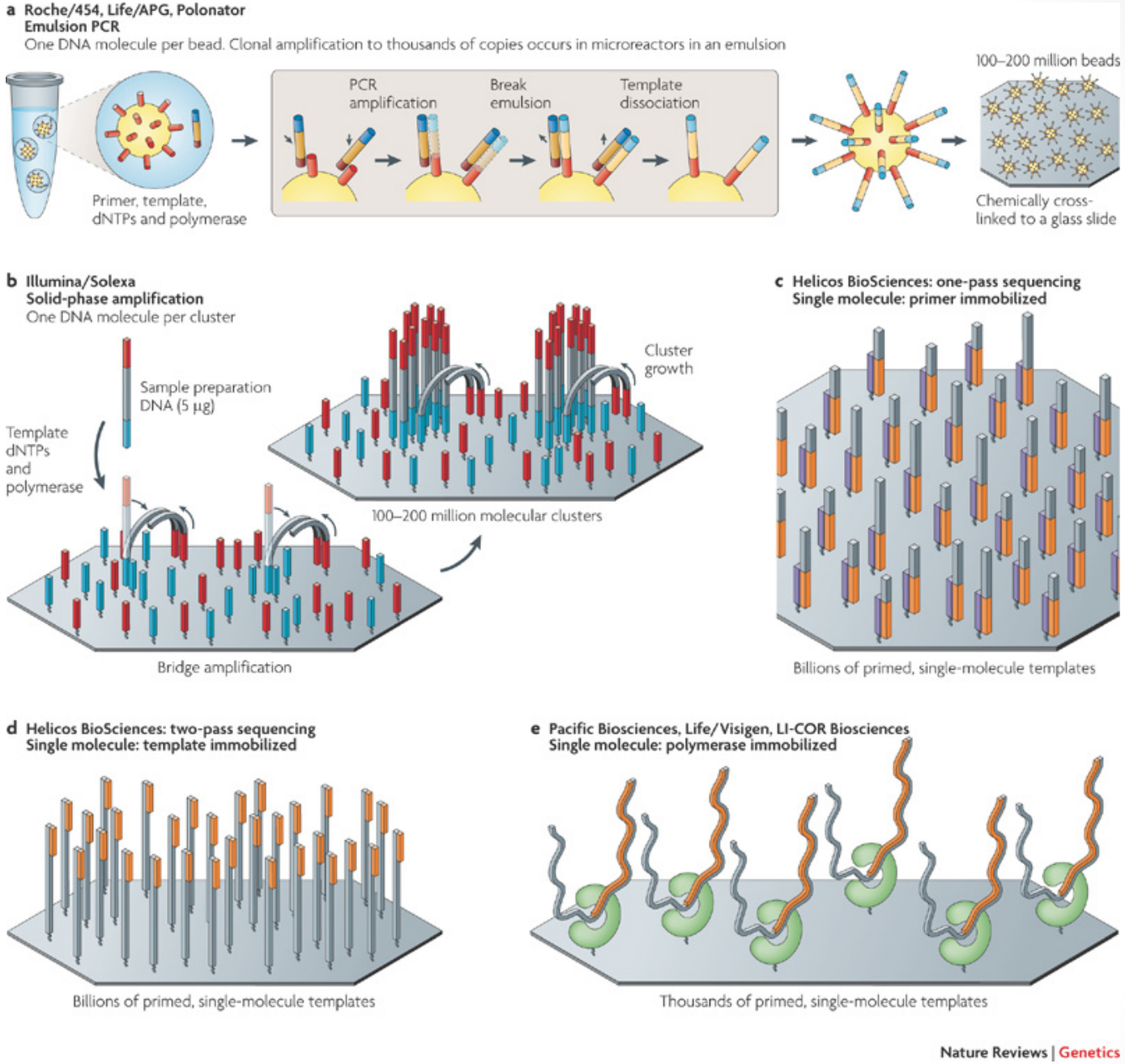
Methods in Bioinformatics

Student Presentation Group 4

October 30th, 2013

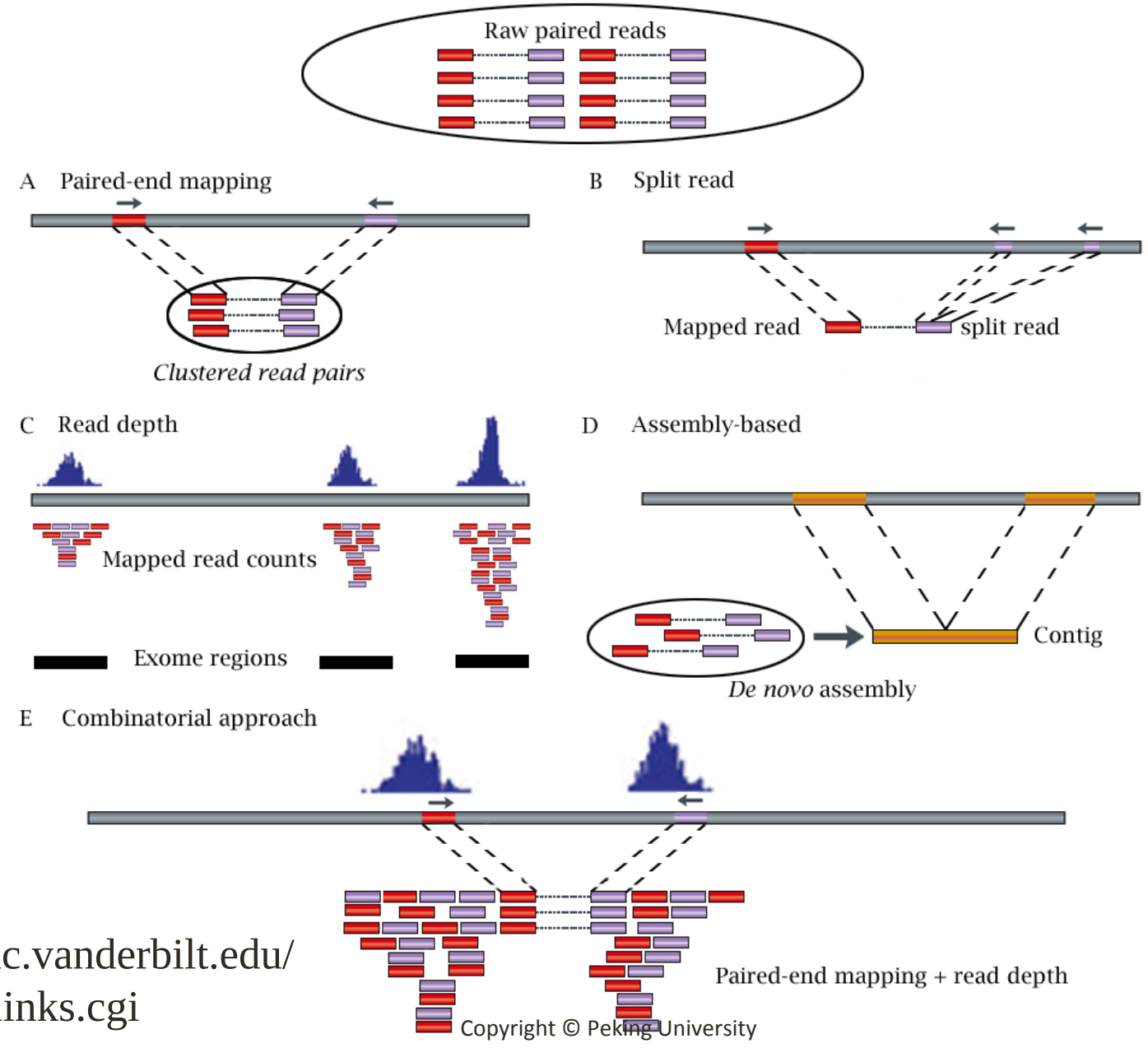
Next-Generation Sequencing

- A variety of sequencing-based assays:
  - gene expression
  - DNA-protein interaction
  - human re-sequencing
  - RNA splicing studies
- Examples: RNA-Seq, ChIP-Seq



Metzker. *Nature Reviews* 2010 Volume 11: 31-46

Genome Assembly



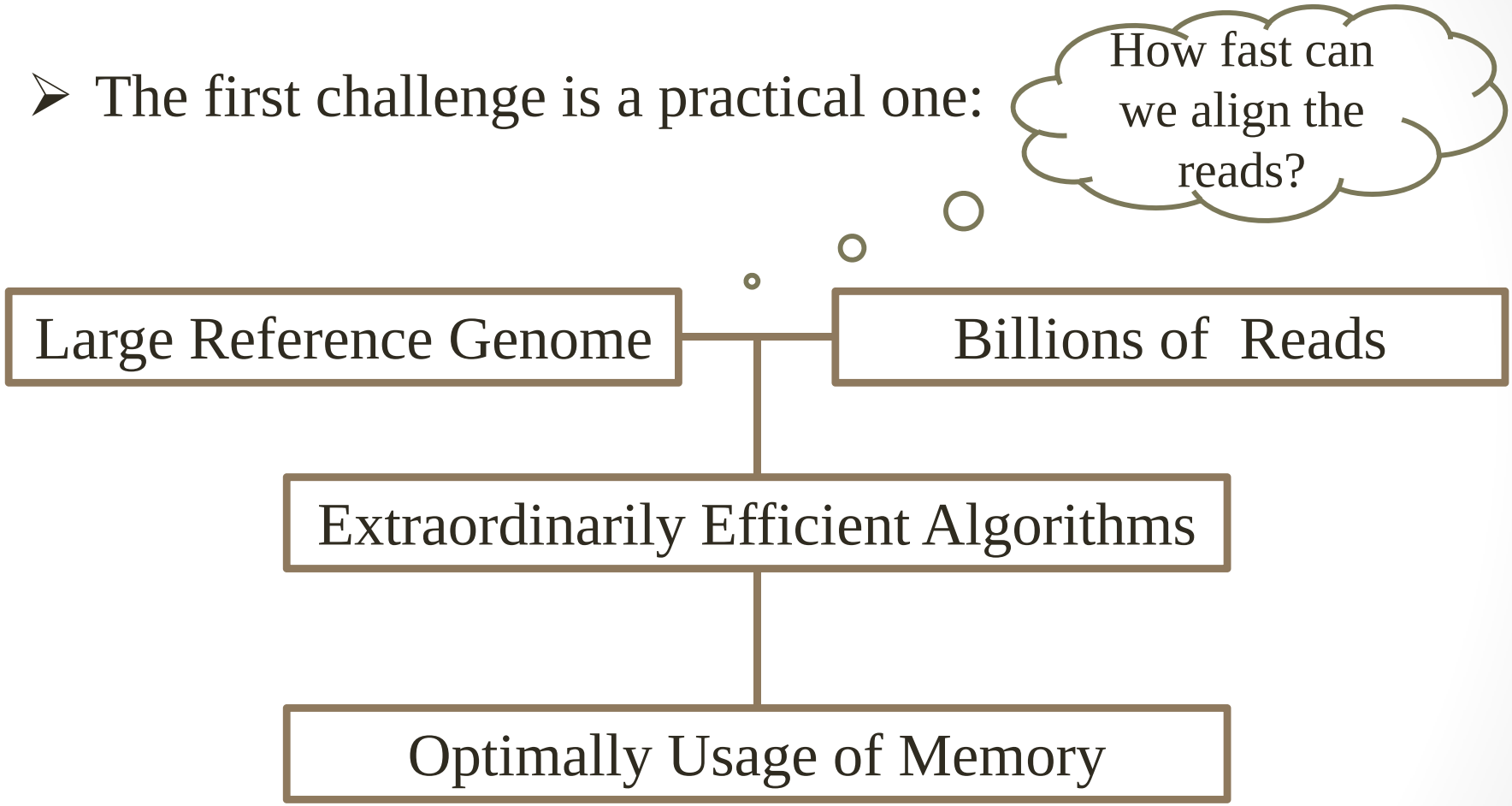
http://bioinfo.mc.vanderbilt.edu/CNVannotator/links.cgi

Scientific Question

- Short sequence fragments produced by next-generation sequencing platforms are quite large.
- Mapping the vast quantities of data is a challenge.
- ‘read mapping’ problem
- What programs are available and how do they work?

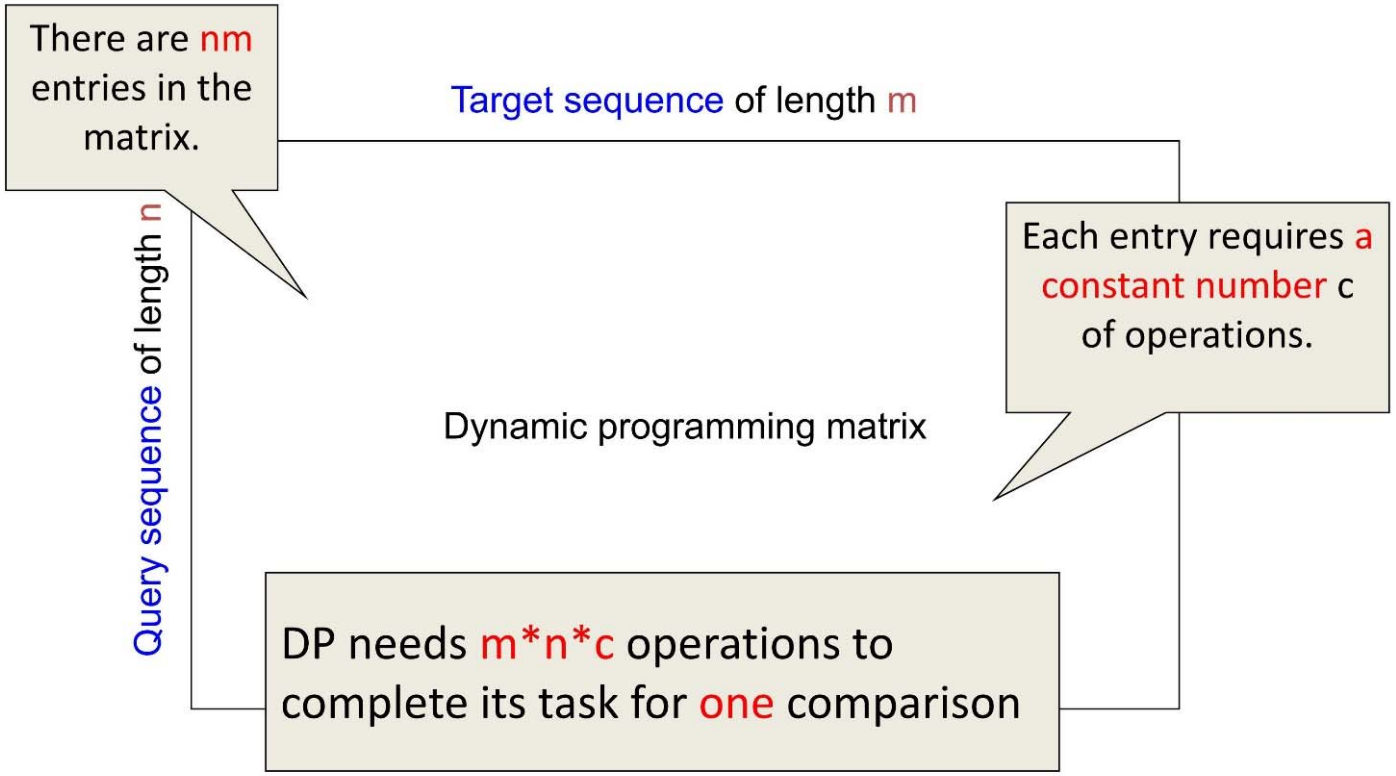
Challenges of mapping short reads

- The first challenge is a practical one:



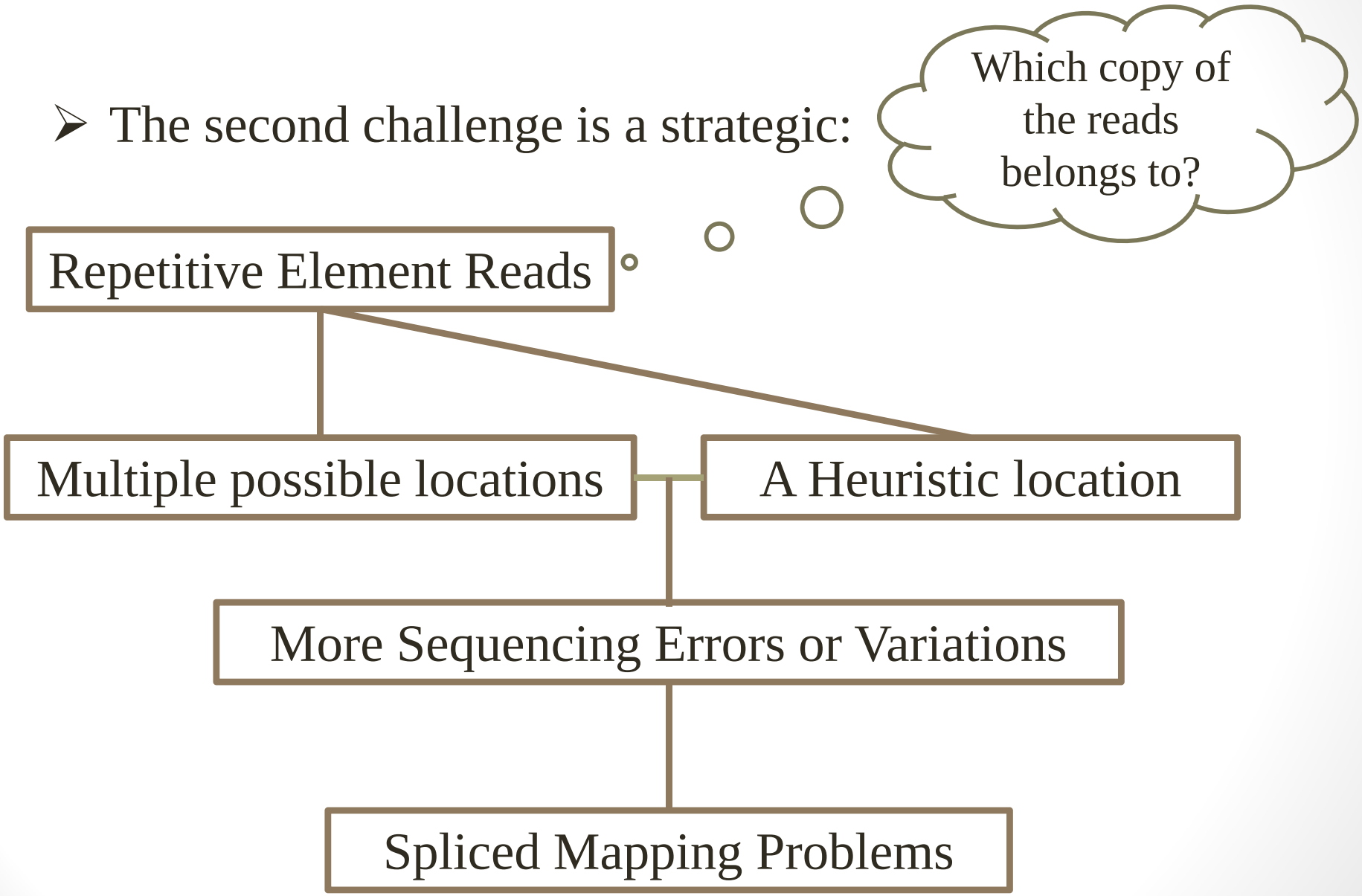
Genome Assembly & Mapping Problem

Sometimes, size does matter!



Challenges of mapping short reads

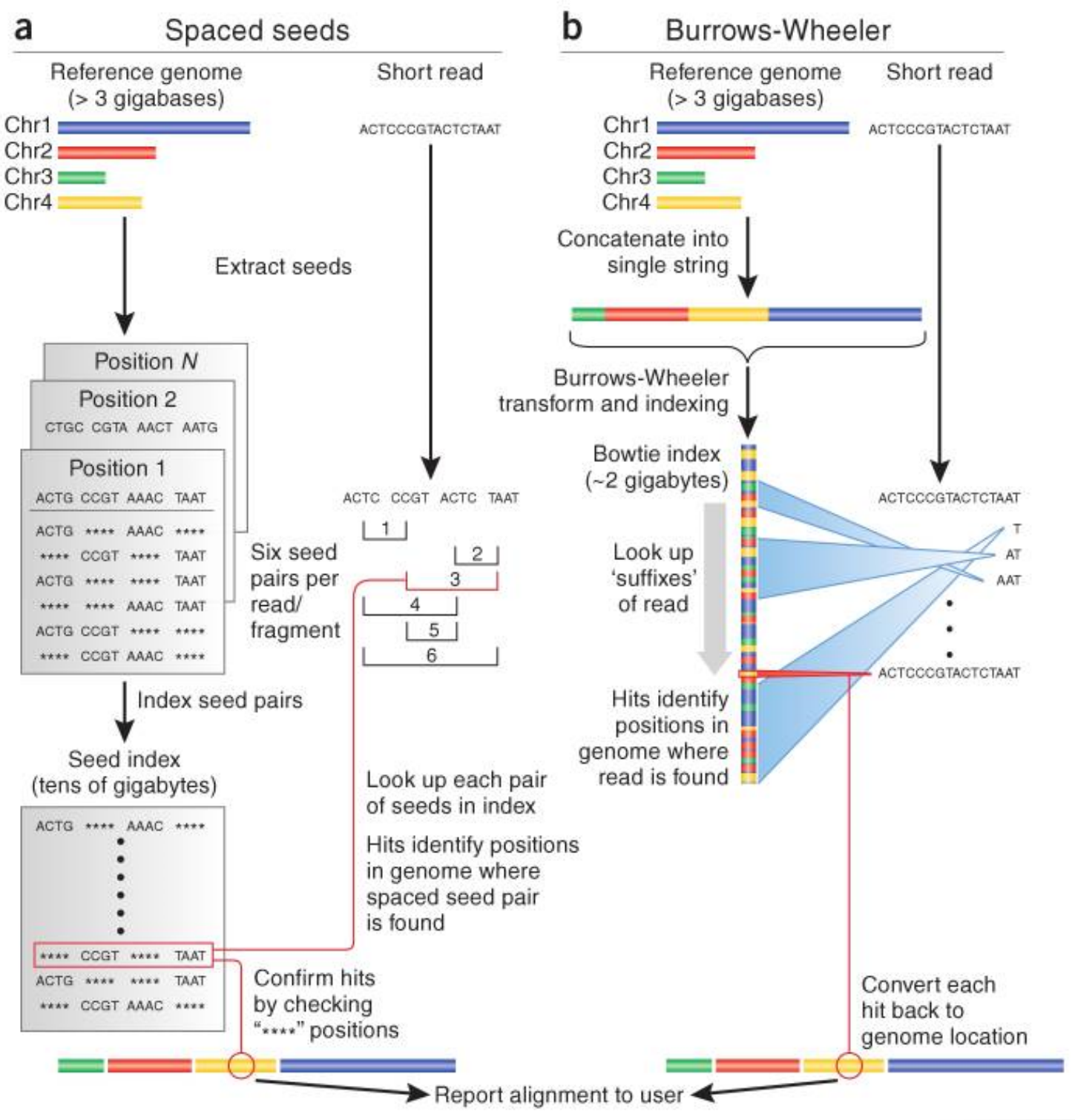
- The second challenge is a strategic:



Alignment Programs

- **Traditional alignment algorithms:**
  - BLAST (Basic Local Alignment Search Tool)
  - BLAT (The BLAST-Like Alignment Tool)
- **New generation alignment programs:**
  - E.g. ELAND program from Illumina
- **Third-party software packages:**

Program	Website	Open source?	Handles ABI color space?	Maximum read length
Bowtie	http://bowtie.cbcb.umd.edu	Yes	No	None
BWA	http://maq.sourceforge.net/bwa-man.shtml	Yes	Yes	None
Maq	http://maq.sourceforge.net	Yes	Yes	127
Mosaik	http://bioinformatics.bc.edu/marthlab/Mosaik	No	Yes	None
Novoalign	http://www.novocraft.com	No	No	None
SOAP2	http://soap.genomics.org.cn	No	No	60
ZOOM	http://www.bioinfor.com	No	Yes	240



Limitations and Open Problems

- The current solutions for short-read mapping all have limitations.
- Many challenges and questions remain for developers of read mapping software:
  - Will the short-read mapping programs scale well as the reads get longer?
  - How should a program's parameters be adjusted, and can that adjustment happen automatically?
  - How useful is mapping quality in downstream analysis, and should it be computed while aligning reads, as Maq does, or later?

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