

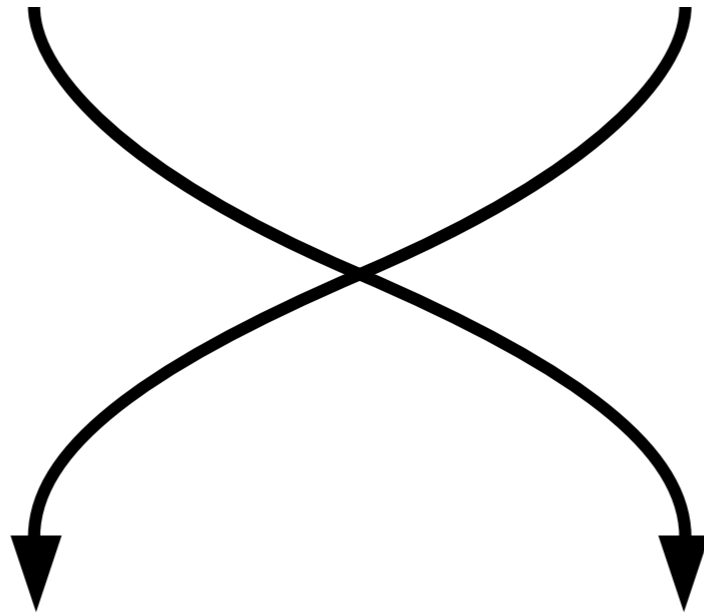
REPRESENTING MICROBE COMMUNITIES WITH SYNTHETIC DNA SPIKE-INS

TIM MERCER | NIST 08/14/17



Human Genome

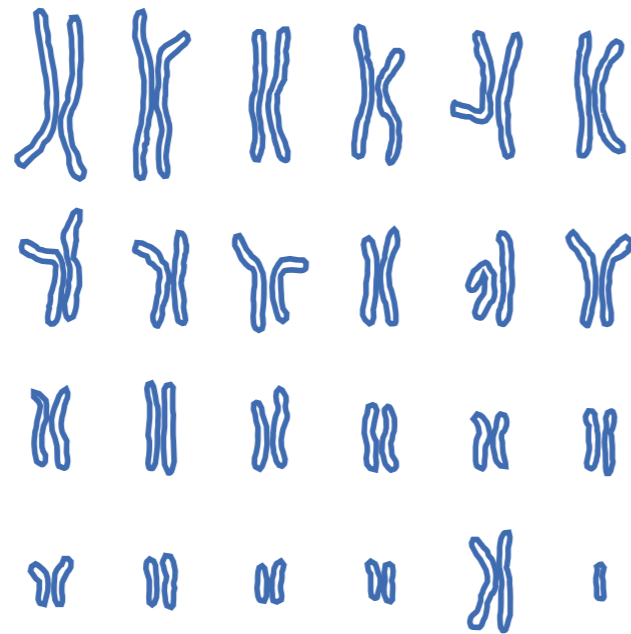
5 - G A C T G A - 3



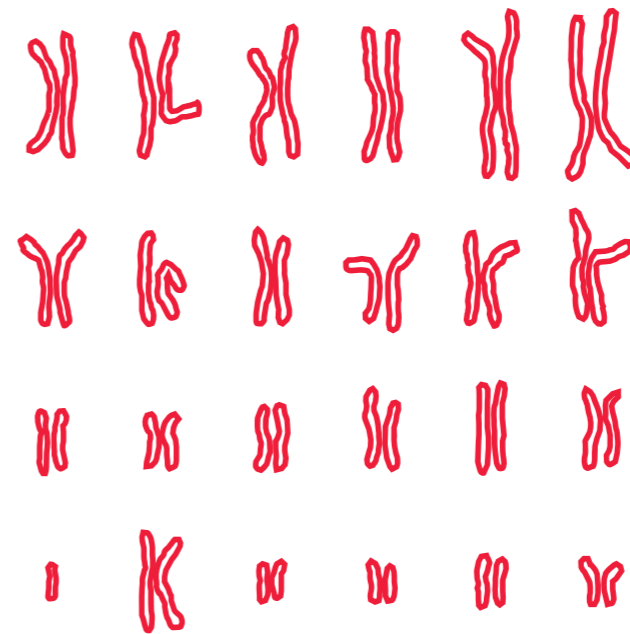
3 - A G T C A G - 5

'Mirror' Genome

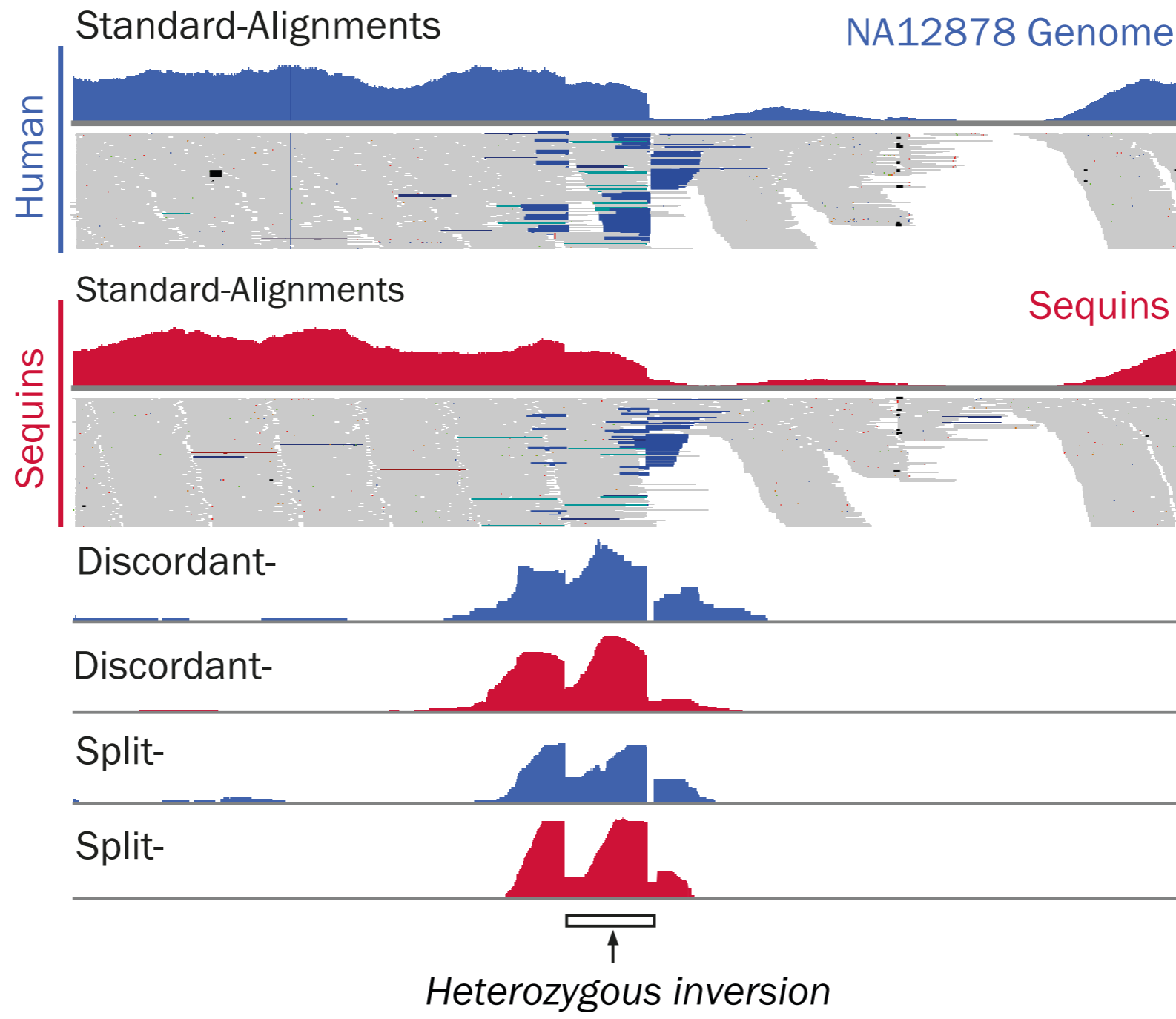
Human Genome
(5' - 3')



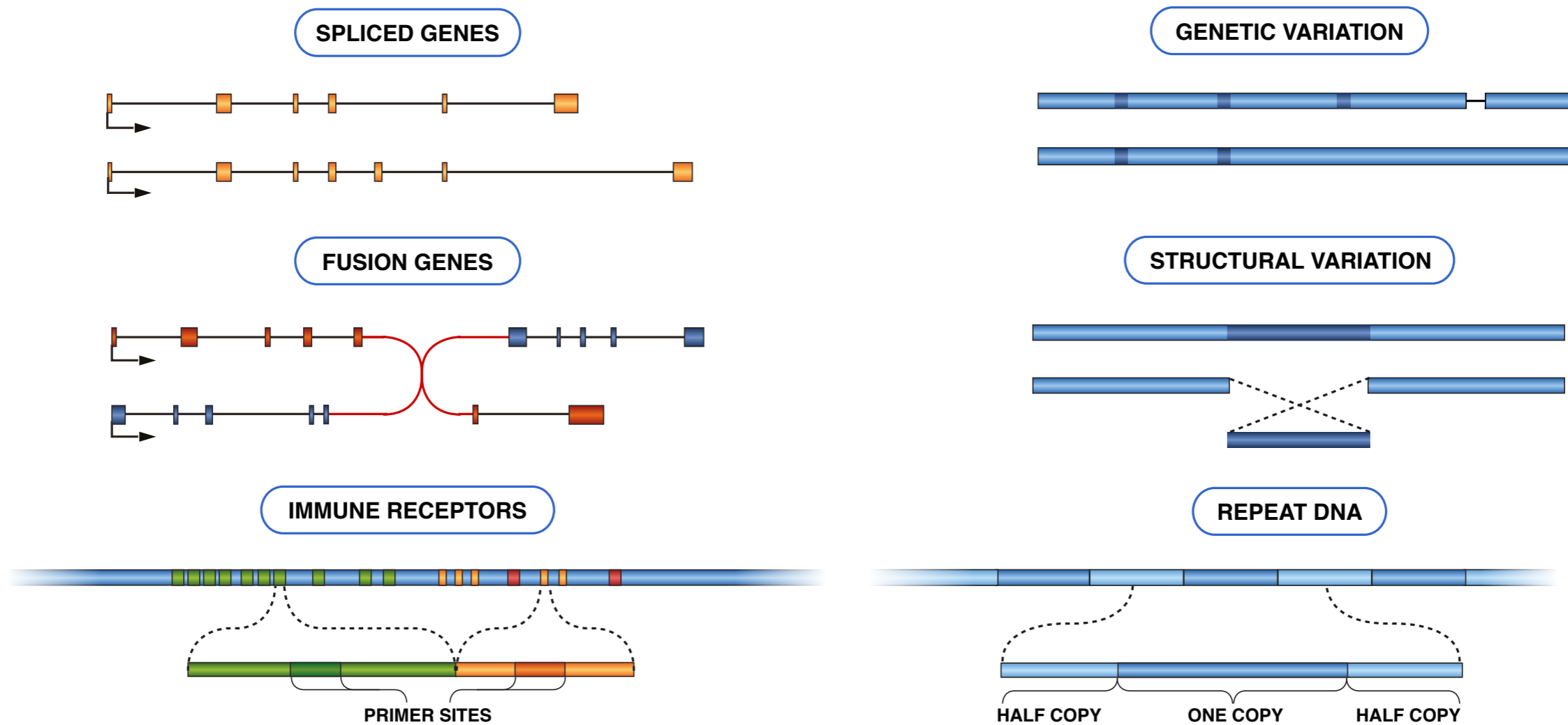
Mirror Genome
(3' - 5')



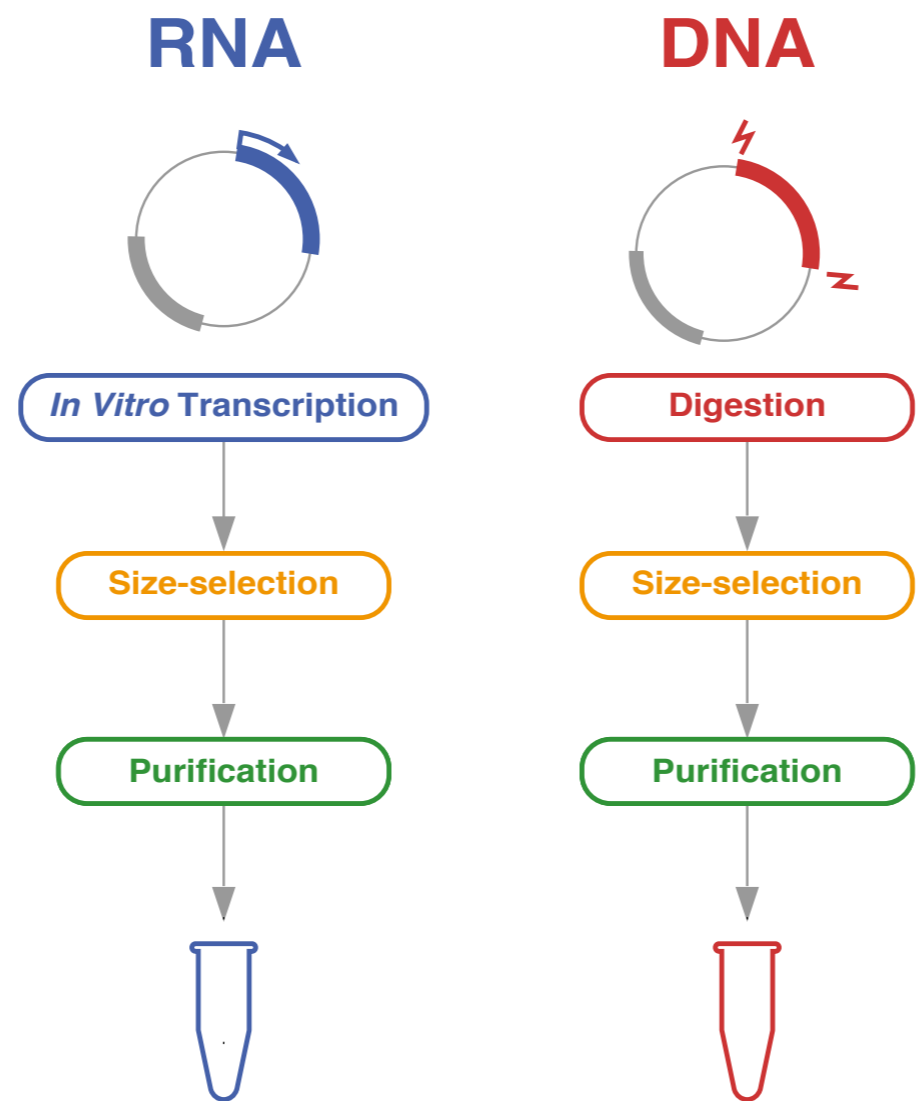
Reads from the **human** genome
do not align to the **mirror** genome,
and vice versa (ie. chiral).



Human and mirror sequences have same hybridization, sequencing, and alignment properties (enantiomer).

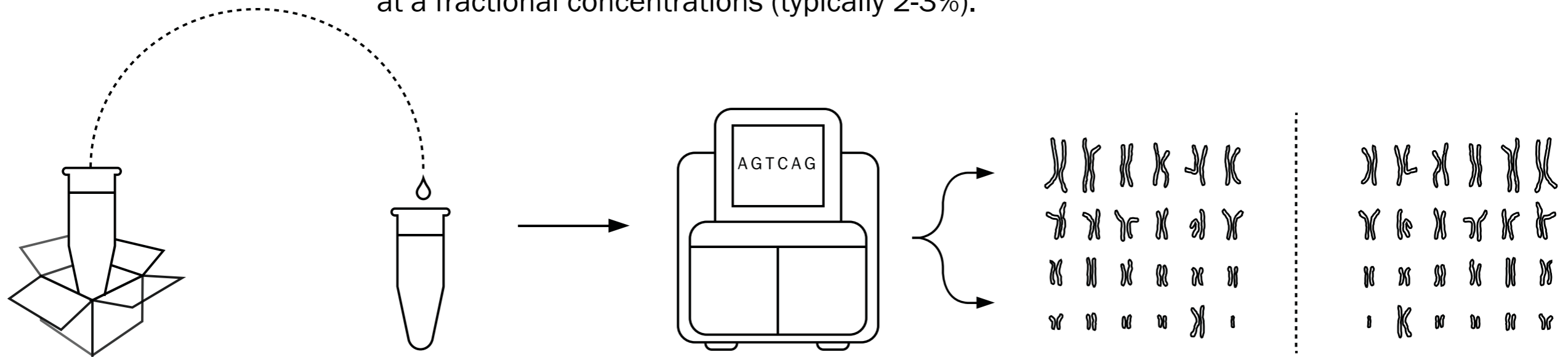


Can mirror almost any feature of the genome, transcriptome or metagenome using RNA/DNA sequencing spike-ins (*sequins*)

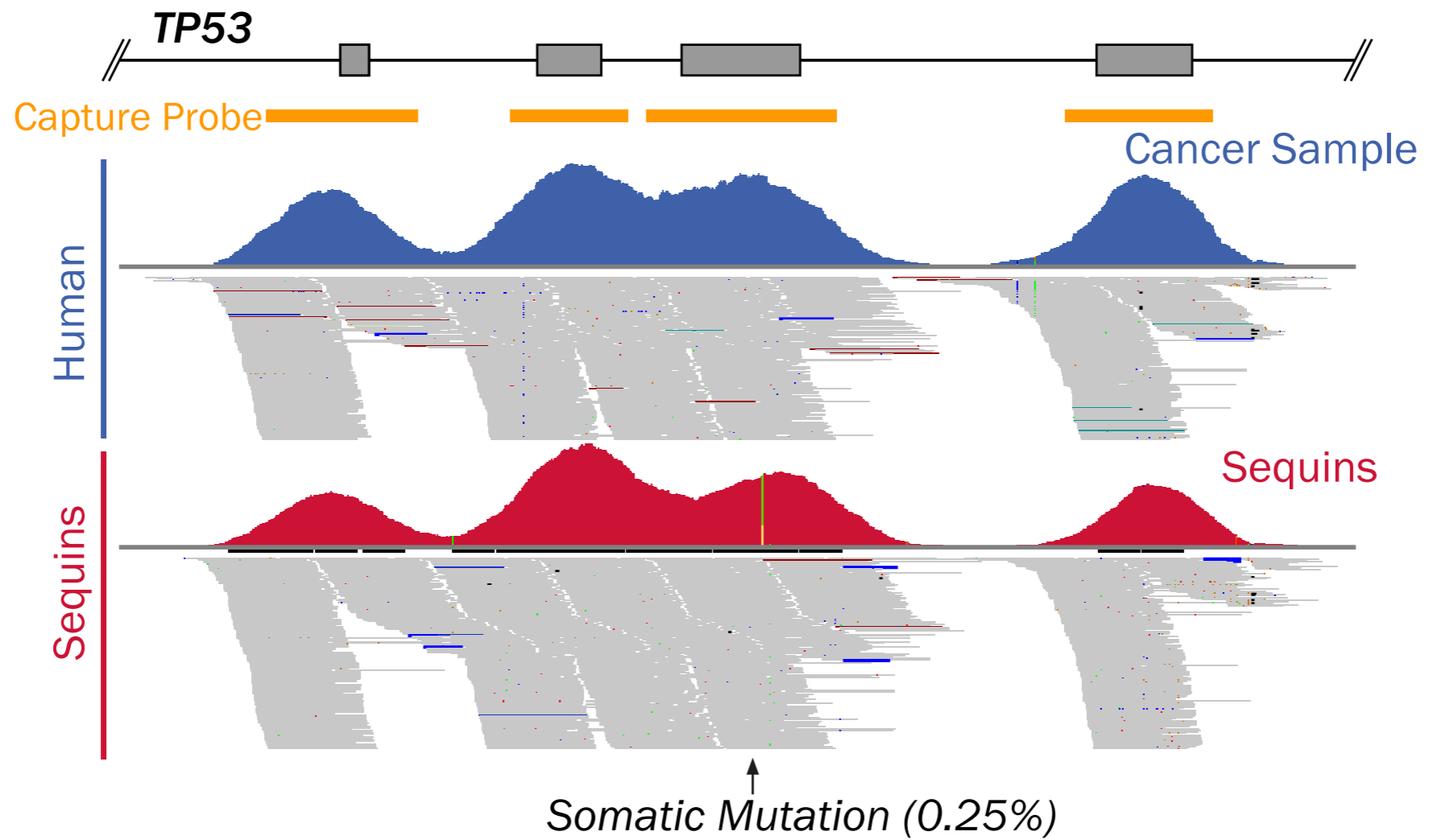


Mirrored sequences are synthesised to form **RNA** or **DNA** sequencing spike-ins (sequins; typically between 1-15kb)

Sequins are added to a RNA/DNA sample
at a fractional concentrations (typically 2-3%).



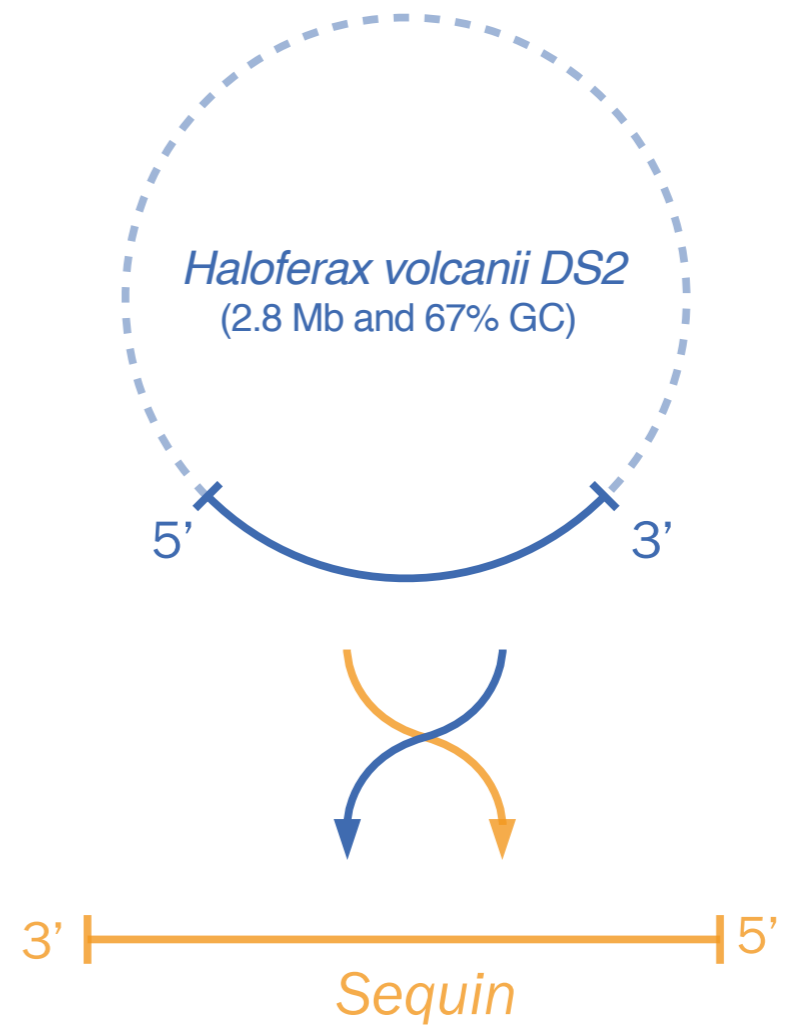
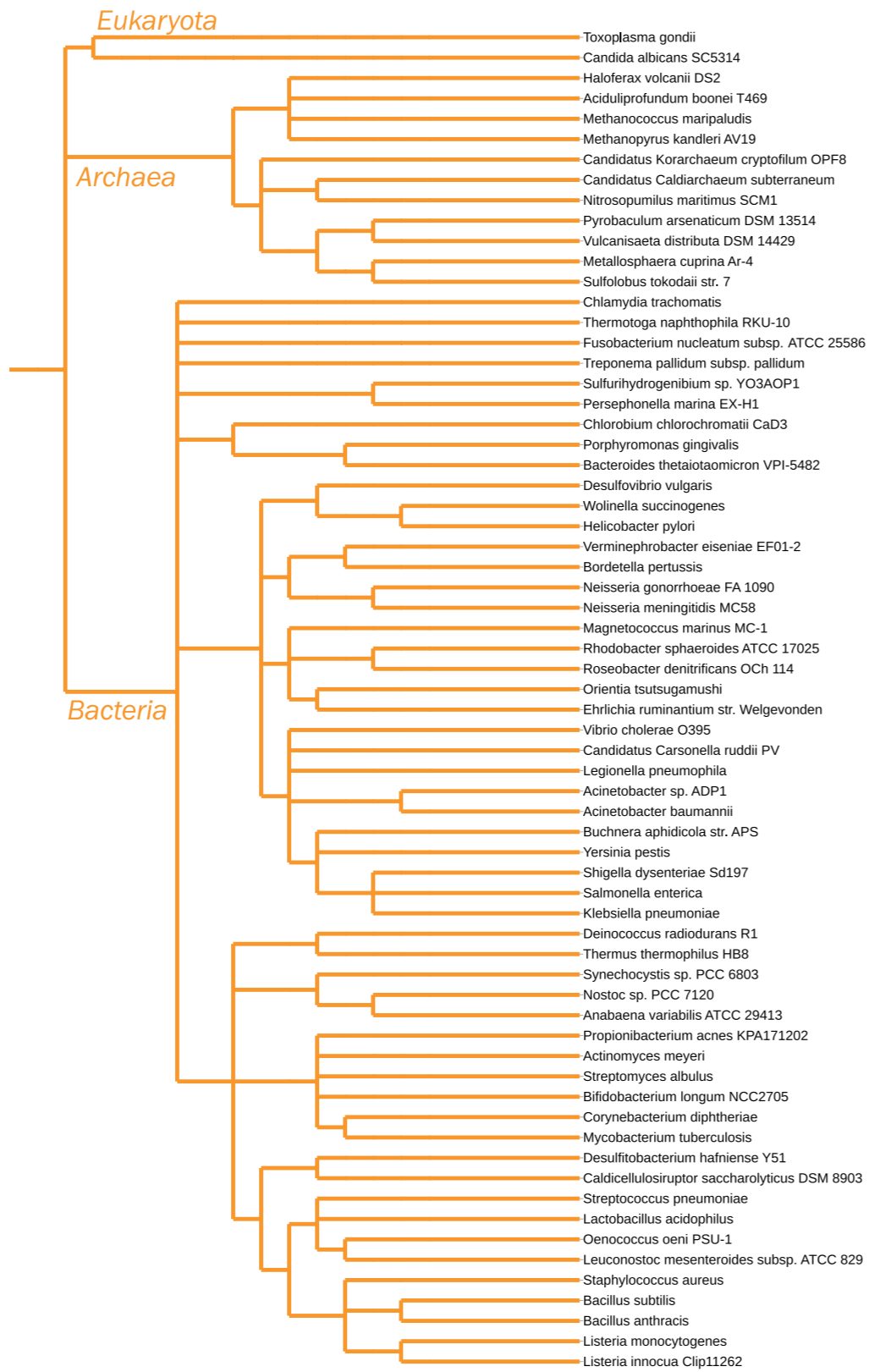
The library is simultaneously aligned to the human genome (+)
and mirror genome (-) to distinguish the sample from the sequins.



Sequins act as qualitative and quantitative internal controls throughout the NGS workflow.

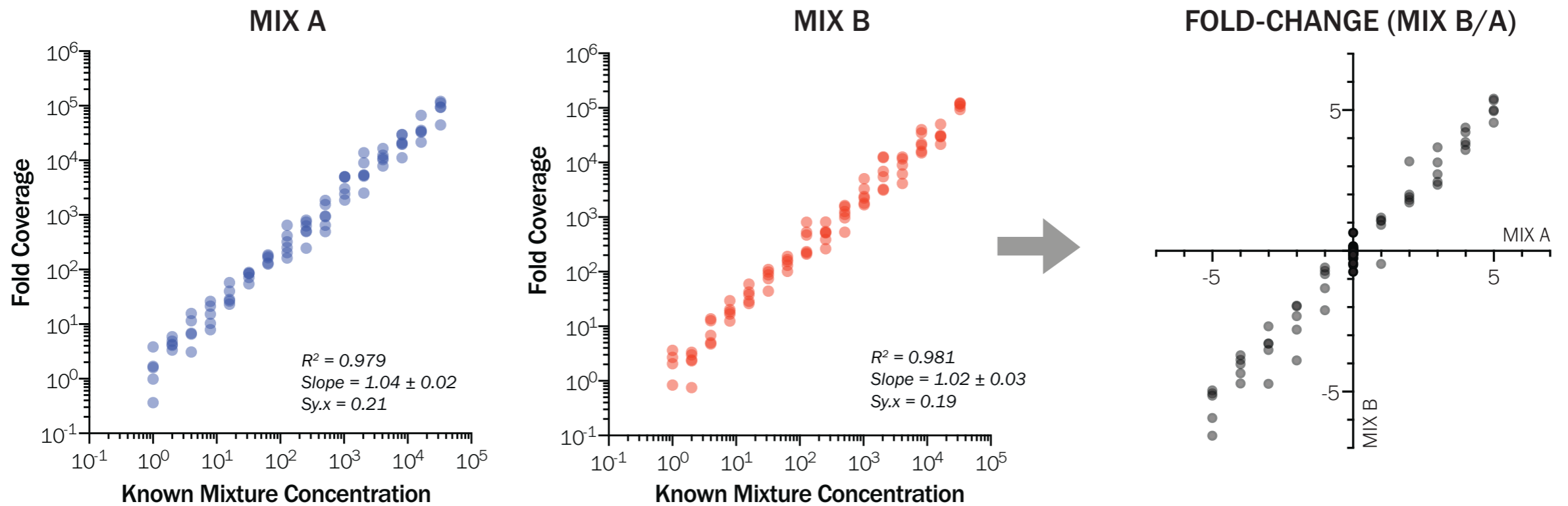


METAGENOMICS



86 sequins mirror a diversity of microbe genomes
(GC% 24 - 74% and length 1 - 9kb)

Sequins are titrated at different concentrations to form reference ladder.

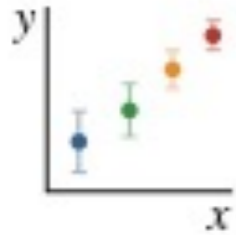


Alternative mixture formulations can assess fold-change differences between samples.

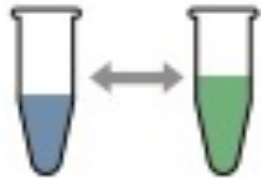
Sequins can be analyzed as internal control throughout the NGS workflow:



Diagnostic performance – assess the sensitivity and specificity for detecting pathogens in a sample.



Quantitative accuracy – measure quantitative performance of a NGS library, and the impact of sequence coverage on analysis (see over).



Normalization – sequins can act as scaling factors to normalize between multiple samples for more accurate comparisons.



Quality control and troubleshooting – calibrate and optimize library preparation, sequencing and analysis steps.

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