Detecting Evolutionary Inter-Gene Heterogeneity in *Borrelia burgdorferi*

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2. Conventional (homogeneous) model for likelihood-based phylogenetic inference.

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Phylogenetic likelihood methods

- Phylogenetics is the reconstruction and analysis of trees and other parameters to describe and understand the evolution of organisms.

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- Likelihood-based phylogenetic analyses start by observing the aligned DNA sequences of *s* organisms:

TCAAGCTATACCCGAT…

TATACCAGCTATAGCT…

CAAAGCTATACCCGAT…

CAAAGCTATACCCGAT…

⋮

The homogeneous model

T C AAGCTATACCCGAT…GC T
T A TACCAGCTATAGCT…GC A
C A AAGCTATACCCGAT…CA A
C A AAGCTATACCCGAT…CC T

- The homogeneous model for independent observations $y_1 = (T,T,C,C)'$, $y_2 = (C,A,A,A)'$, …, $y_n = (T,A,A,T)'$, is:

$$y_i \sim f(\cdot \mid \mathcal{X}, \mathbf{t}, Q) \quad \text{independently for } i = 1, 2, \ldots, n$$

Model parameters

$y_i \sim f(\cdot \mid \mathcal{X}, \mathbf{t}, Q)$ independently for $i = 1, 2, \ldots, n$

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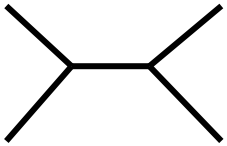
- A bifurcating tree with s leaves, 

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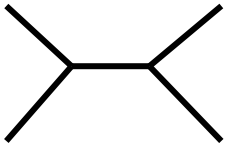
- A bifurcating tree with *s* leaves, 

- A set of positive real-valued branch lengths,

$$\mathbf{t} = (t_1, t_2, \ldots, t_5)$$

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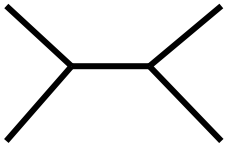
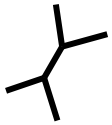
- A bifurcating tree with *s* leaves, 

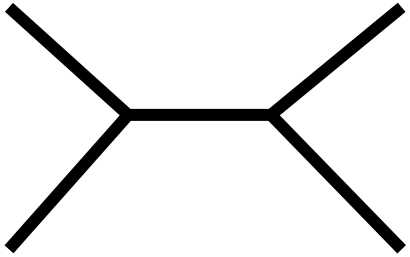
- A set of positive real-valued branch lengths,

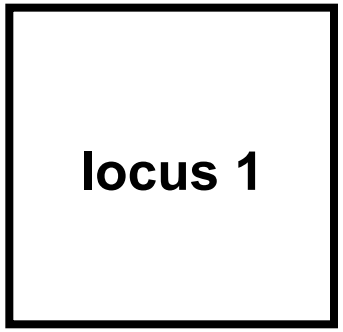
$$\mathbf{t} = (t_1, t_2, \ldots, t_5)$$

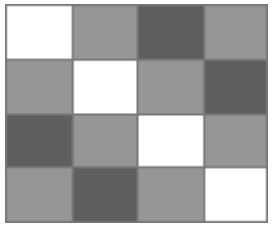
- A rate matrix Q specifying a Markov process of character substitution along 

	$r_{AC}\,\pi_C$	$r_{AG}\,\pi_G$	$r_{AT}\,\pi_T$
$r_{AC}\,\pi_A$		$r_{CG}\,\pi_G$	$r_{CT}\,\pi_T$
$r_{AG}\,\pi_A$	$r_{CG}\,\pi_C$		$r_{GT}\,\pi_T$
$r_{AT}\,\pi_A$	$r_{CT}\,\pi_C$	$r_{GT}\,\pi_G$	

DNA data may be not homogeneous







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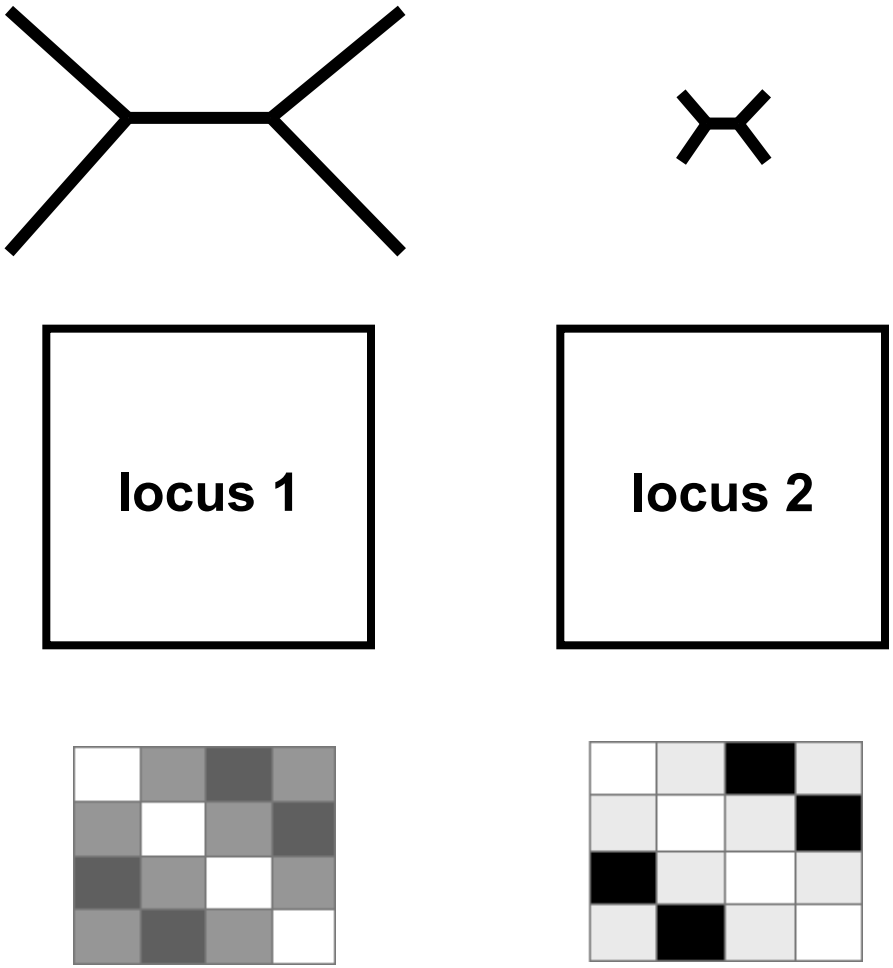

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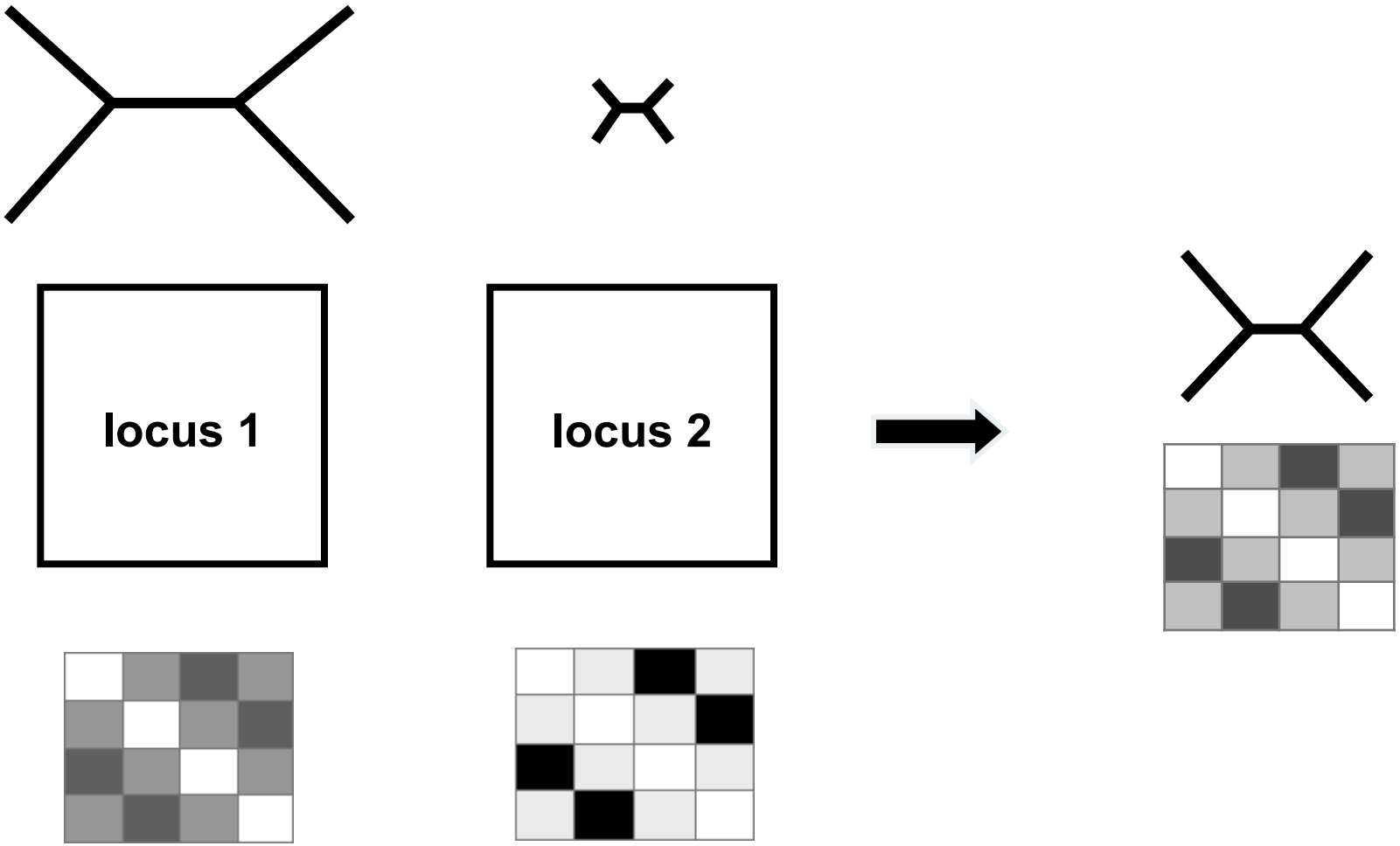

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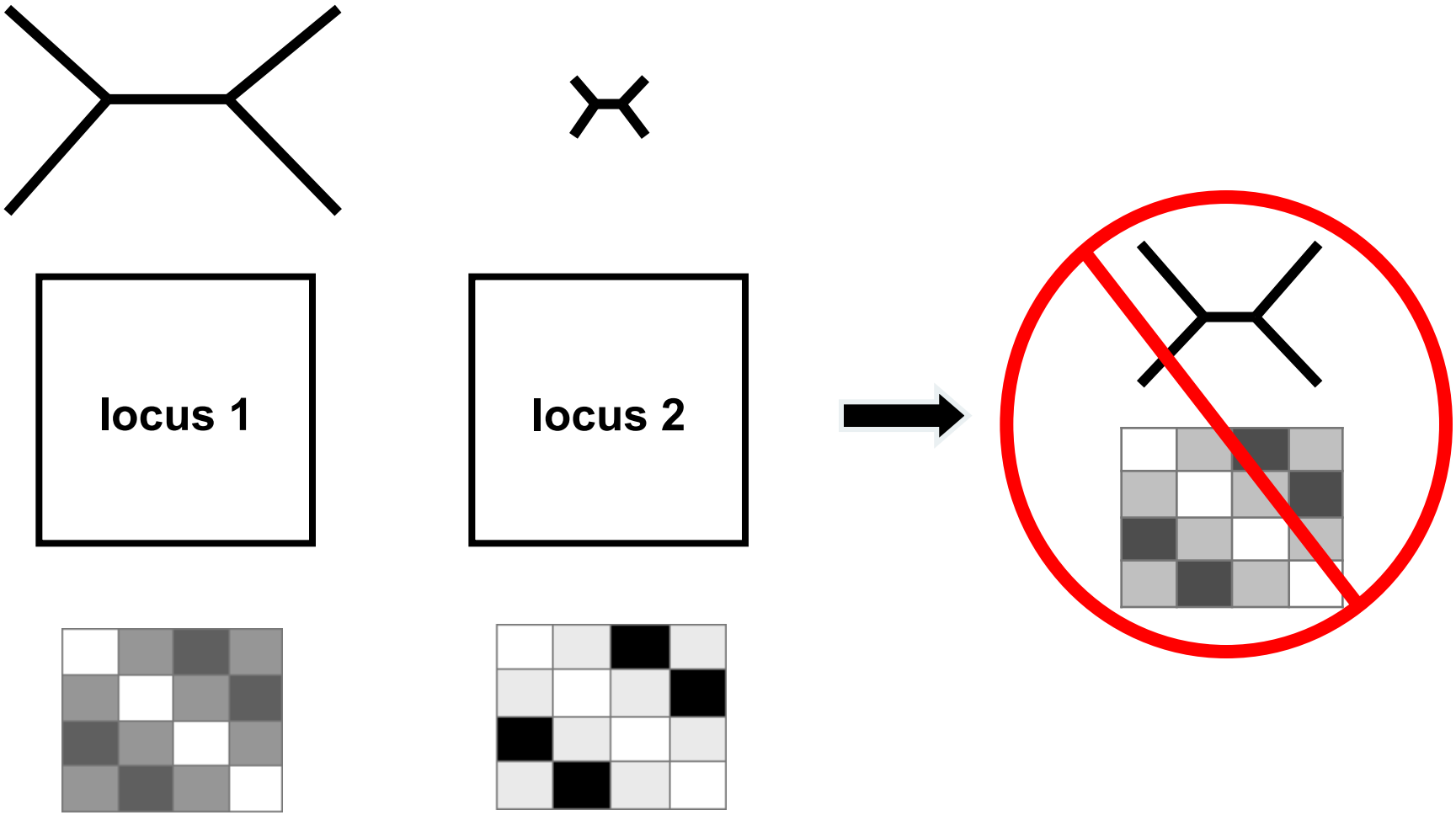

Borrelia burgdorferi

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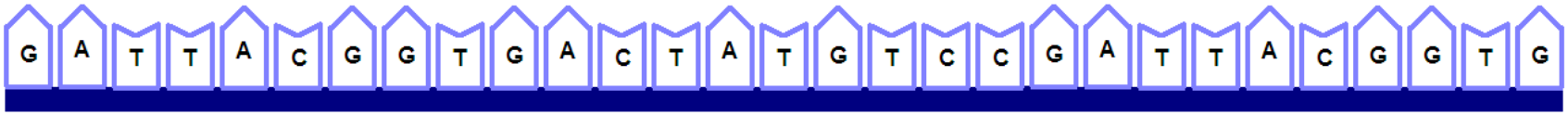
- *Borrelia burgdorferi* is one of the bacterial species responsible for Lyme disease.
- To fully understand the disease, it is crucial to unveil the evolutionary properties of its genetic variants (strains).
- Phylogenetic analysis is an essential tool.

Identification of *B. burgdorferi* strains



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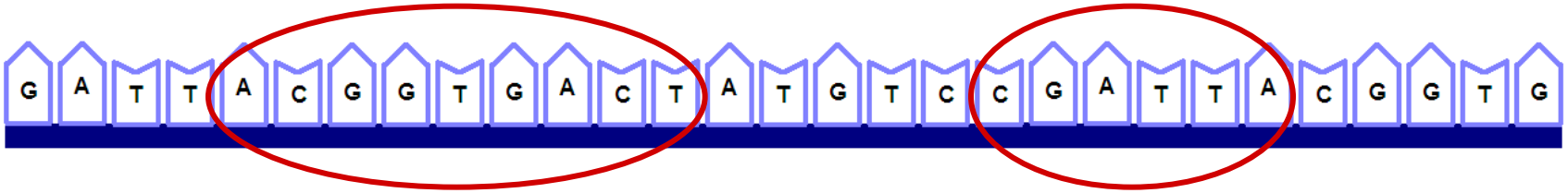

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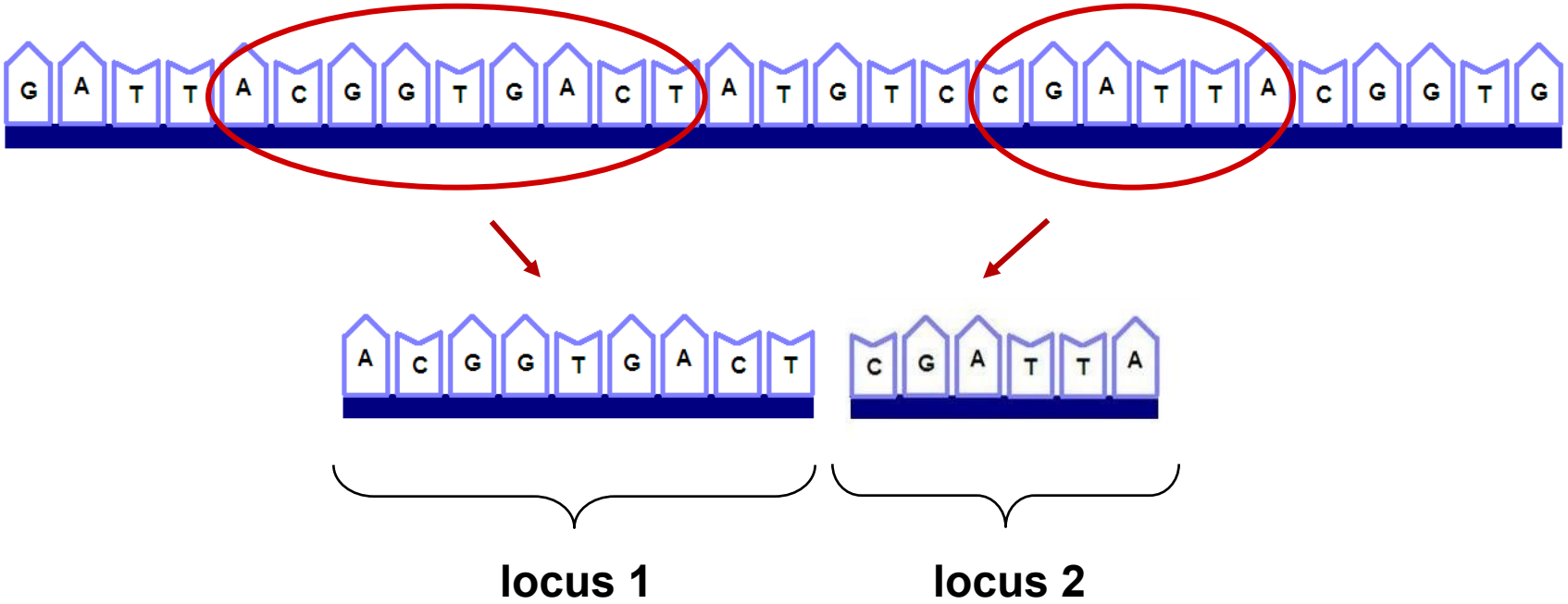

Are the loci congruent in evolution, such that valid inferences can be made under a homogeneous phylogenetic model?

The Q + *t* mixture model

- Finite mixture models provide a natural way to model heterogeneous data.

$$f(\cdot \mid \chi, t, Q)$$

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for $\mathbf{w} + \mathbf{w} + \ldots + \mathbf{w} = 1$

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and ind. for $i = 1, 2, \ldots, n$

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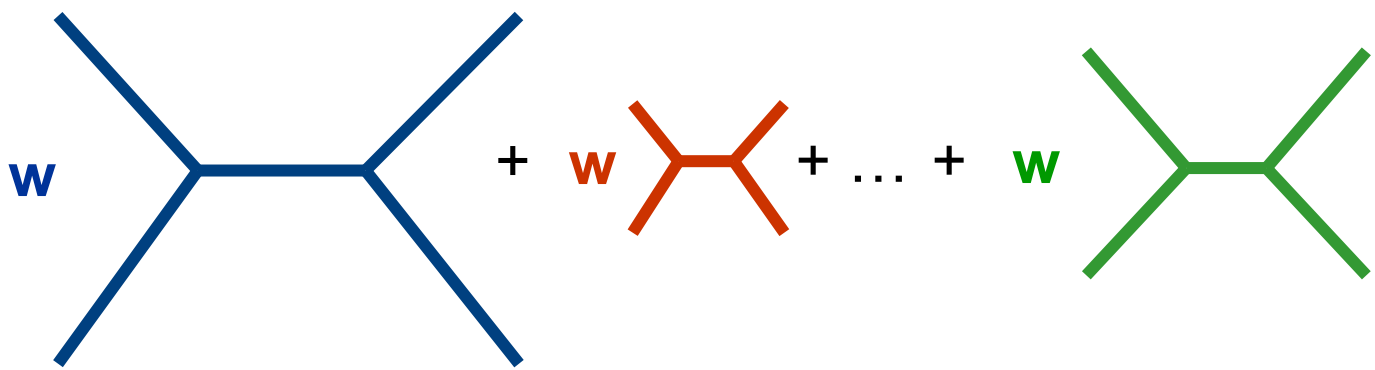

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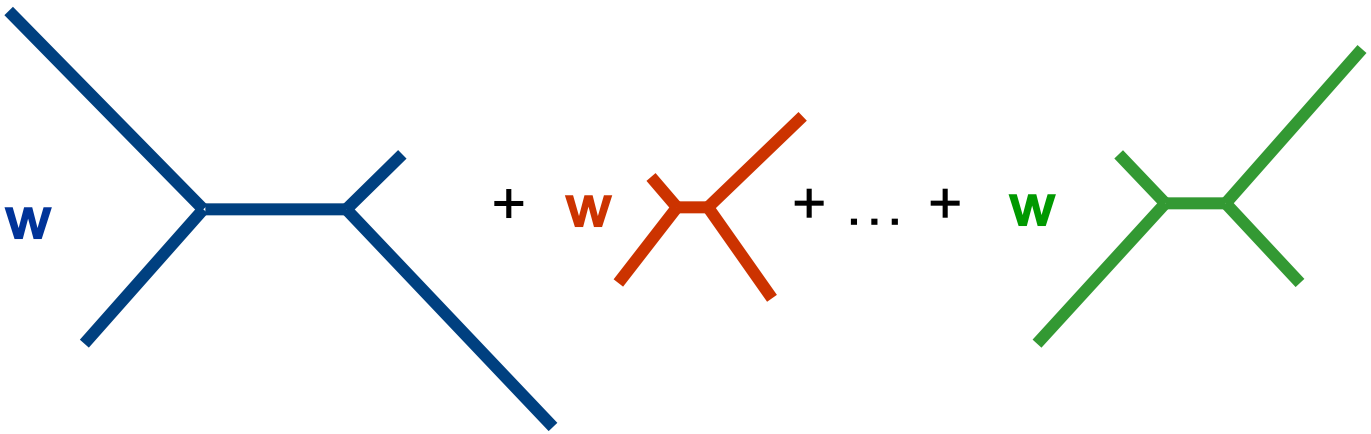

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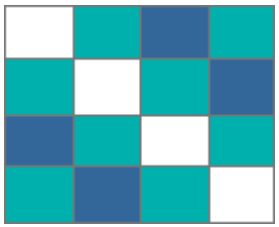
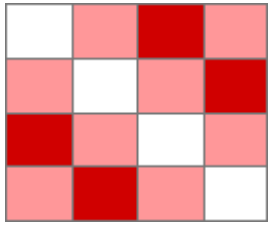
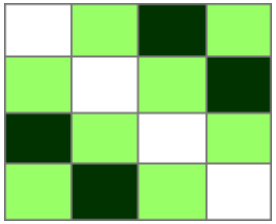
w  + **w**  + … + **w** 

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- Once the **label**$_i$ for site *i* is known,

$$y_i \mid \square \sim f(\cdot \mid \lambda, t, Q)$$

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The Q + *t* mixture model: an example

- Consider a DNA alignment:

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The Q + *t* mixture model: an example

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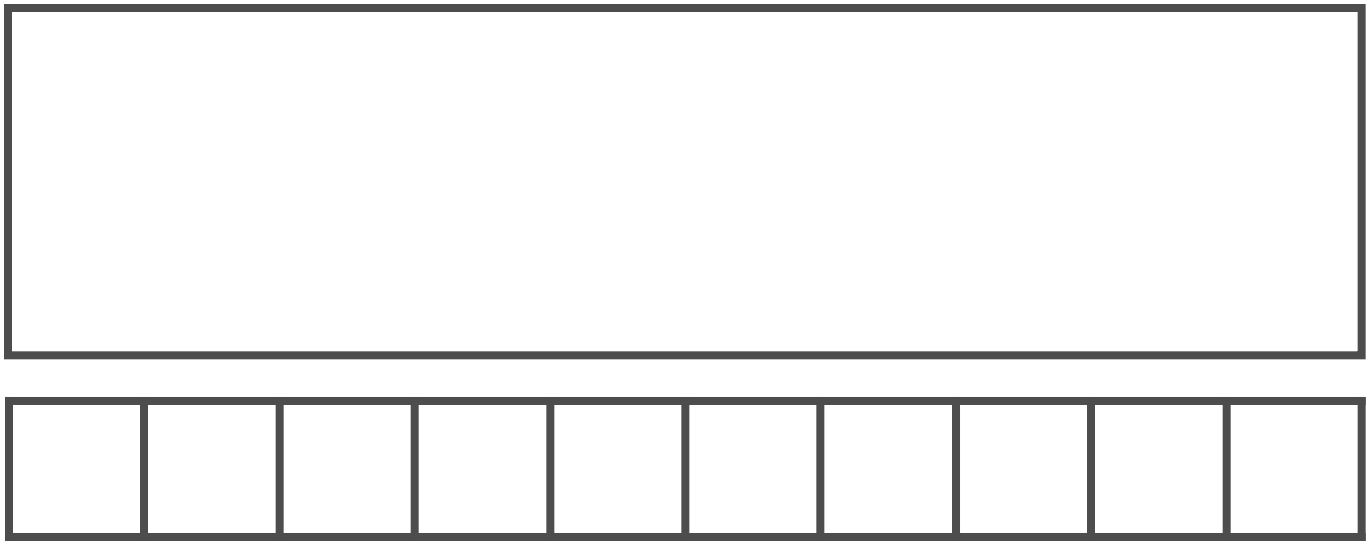

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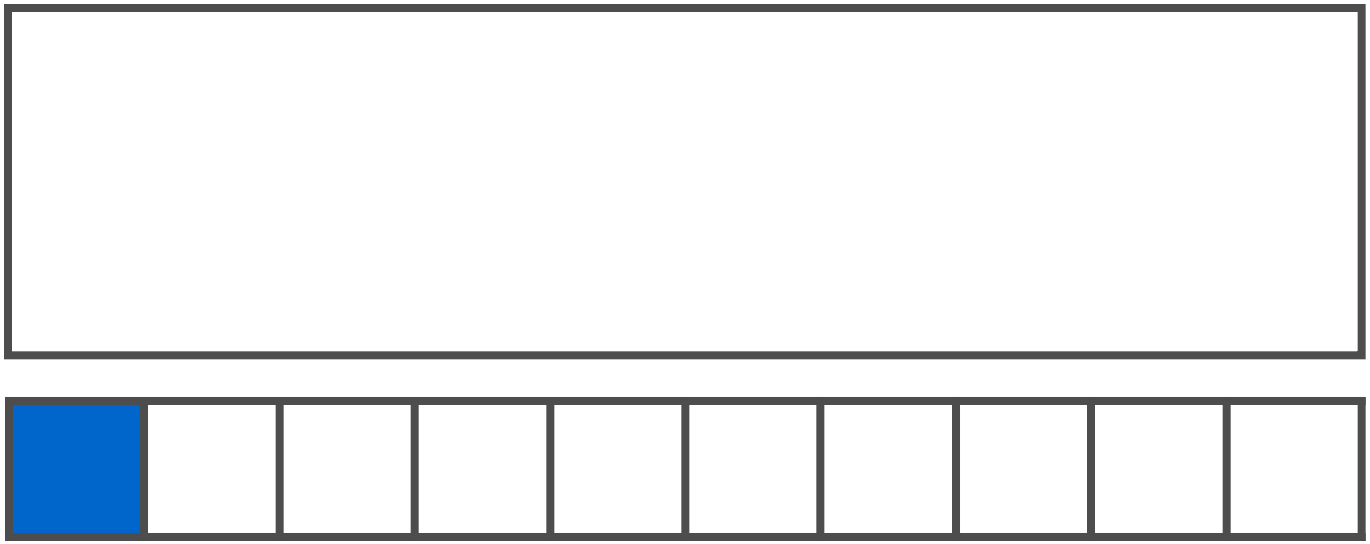

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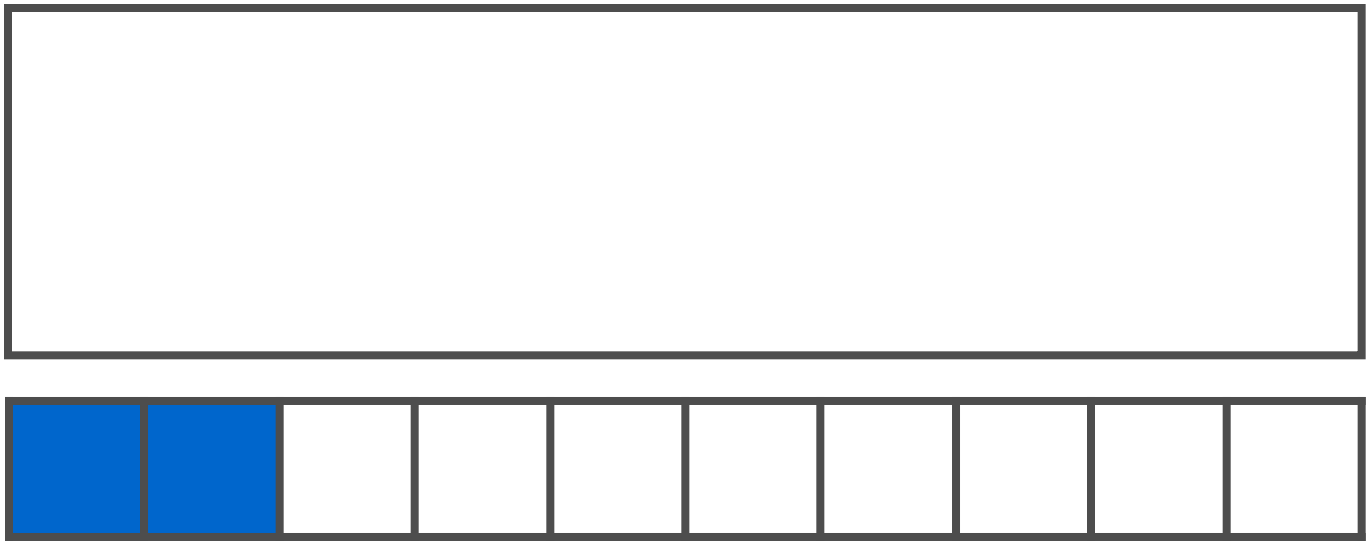

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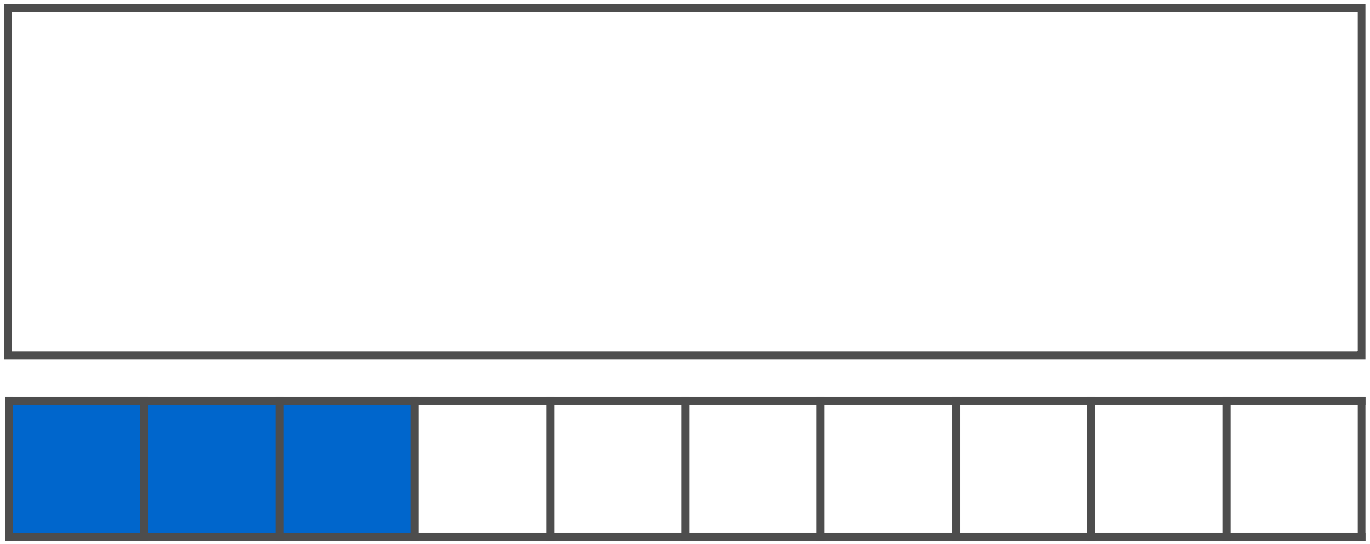

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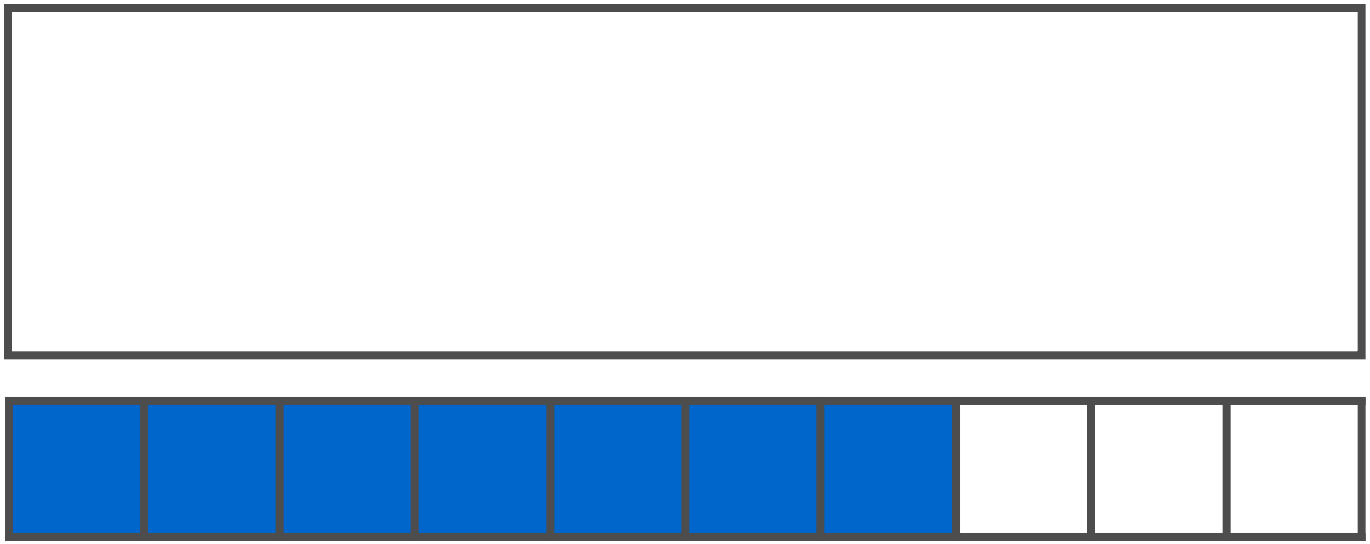

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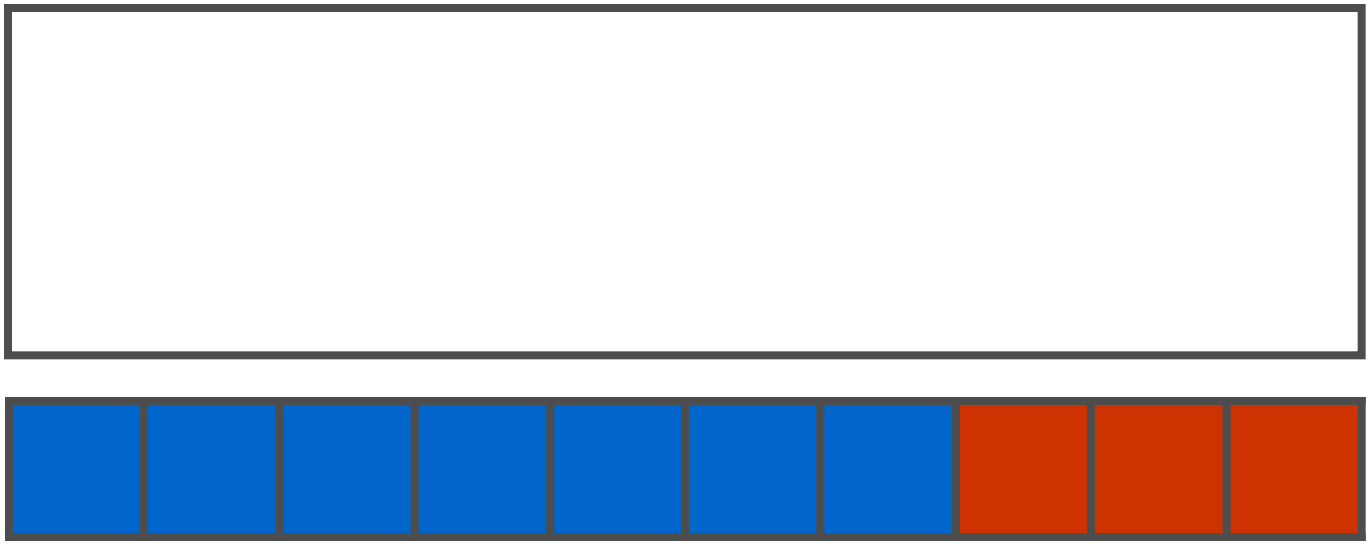

The Q + *t* mixture model: an example

$y_i \mid \blacksquare \sim f(\cdot \mid \lambda, t, Q)$

independently for $i = 1, 2, \ldots, m$

The Q + *t* mixture model: an example

$y_i \mid \blacksquare \sim f(\cdot \mid \lambda, t, Q)$

independently for $i = m+1, \ldots, n$

Analysis of *B. burgdorferi*: the 'housekeeping genes' alignment

Analysis of *B. burgdorferi*: the 'housekeeping genes' alignment

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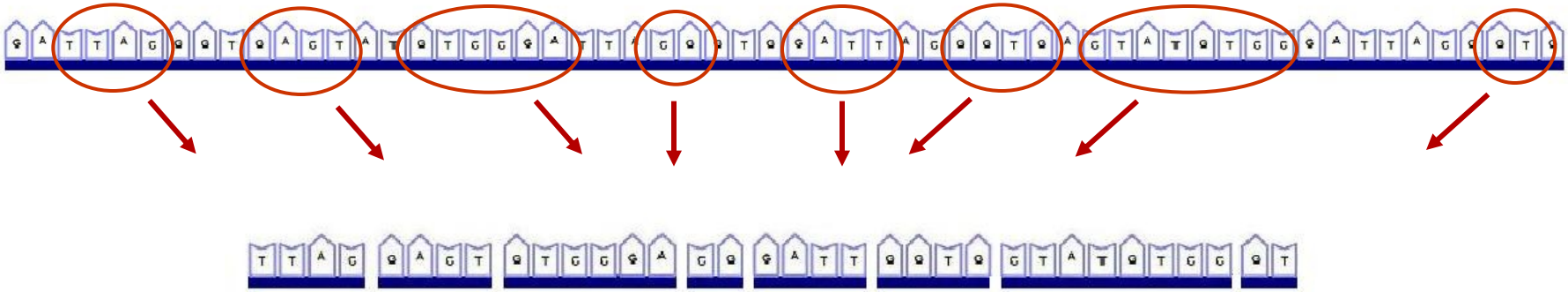

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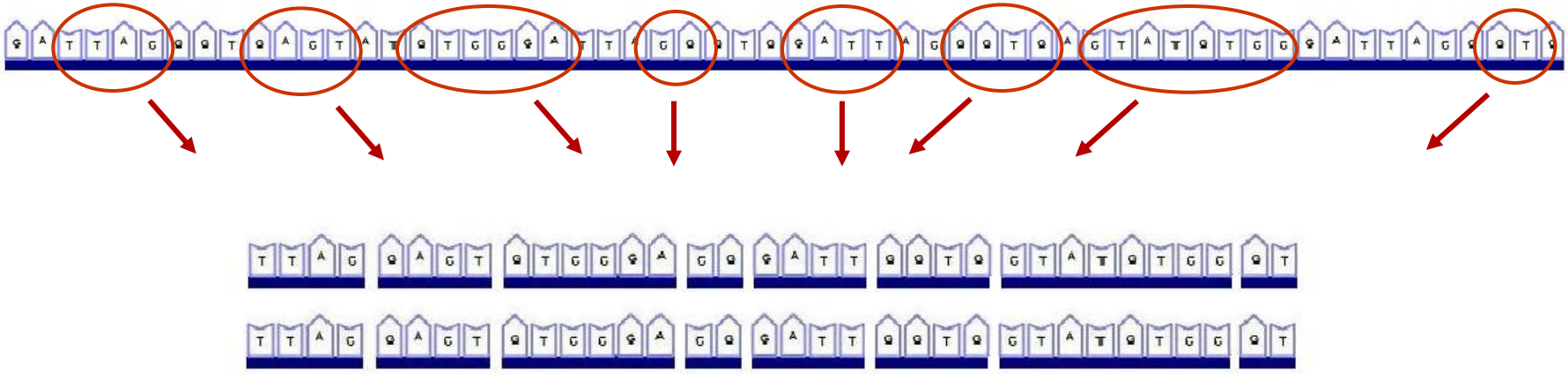

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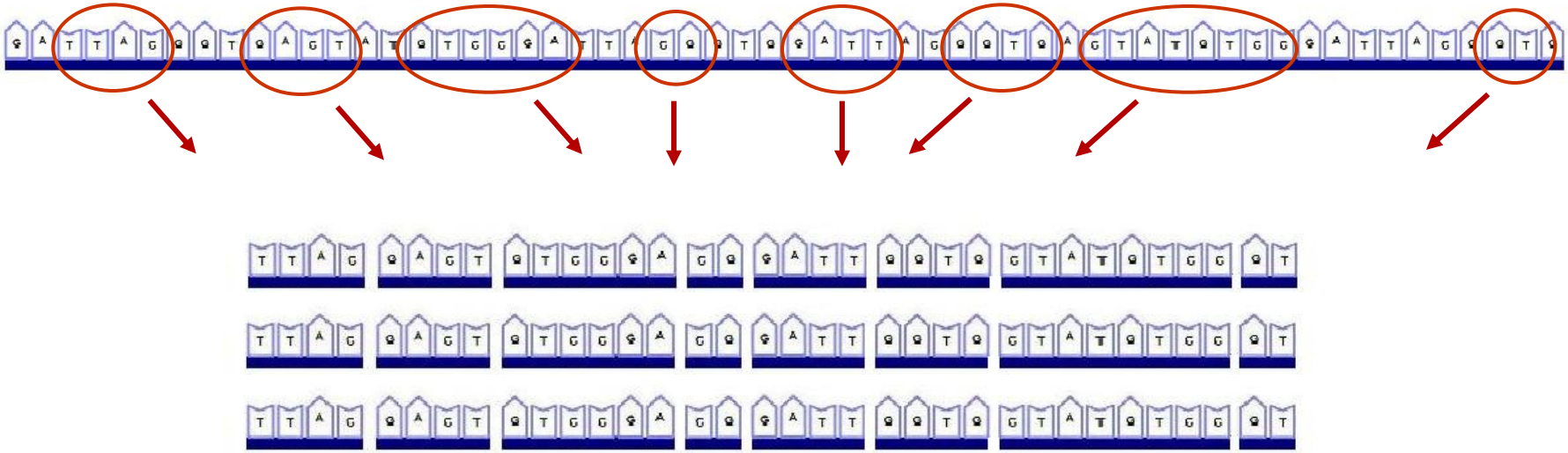

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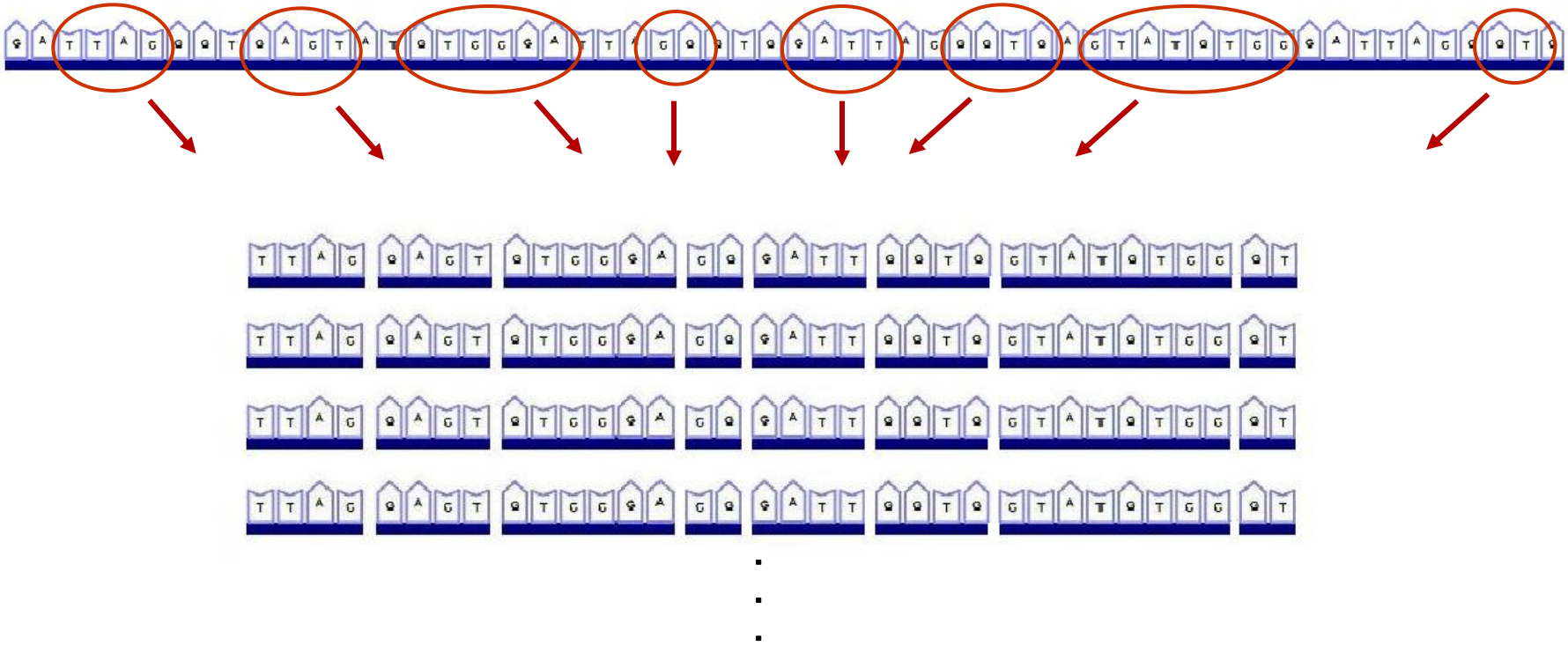

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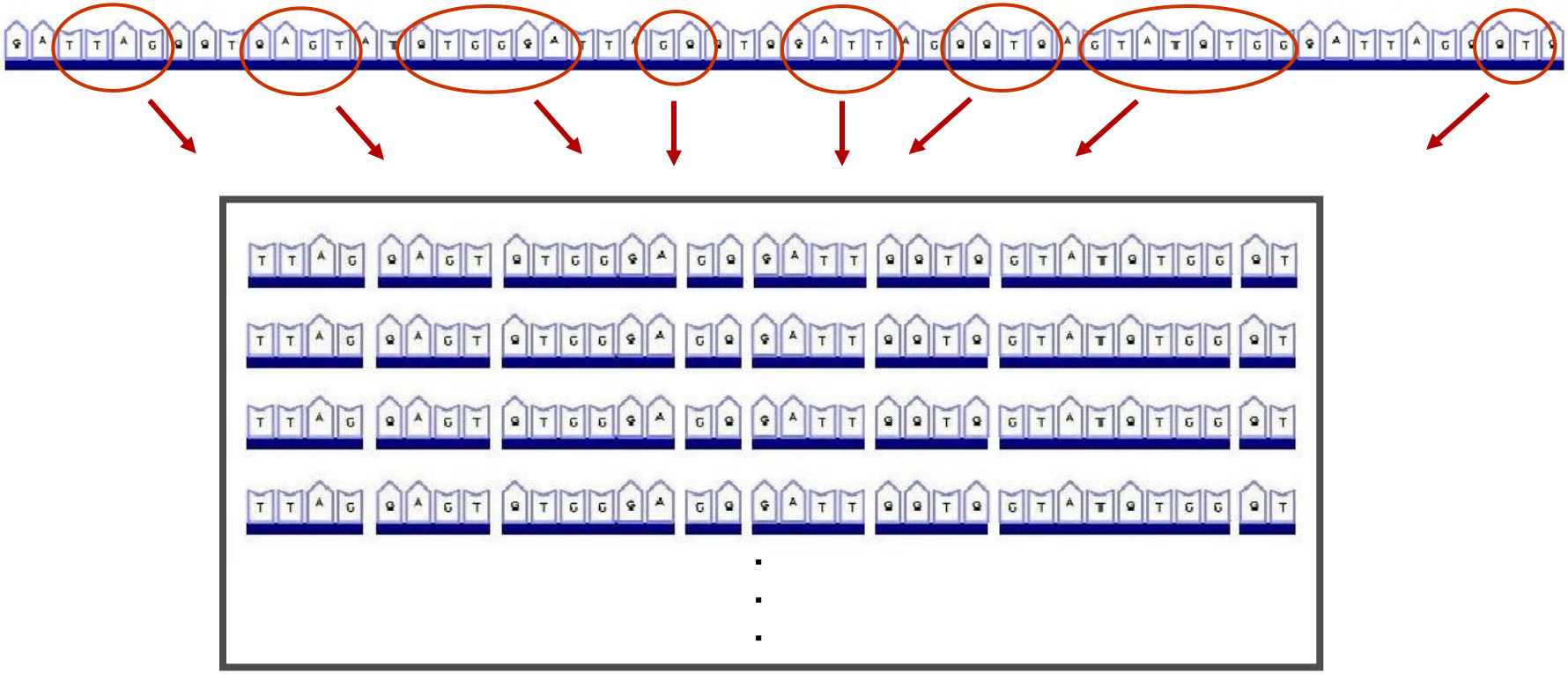

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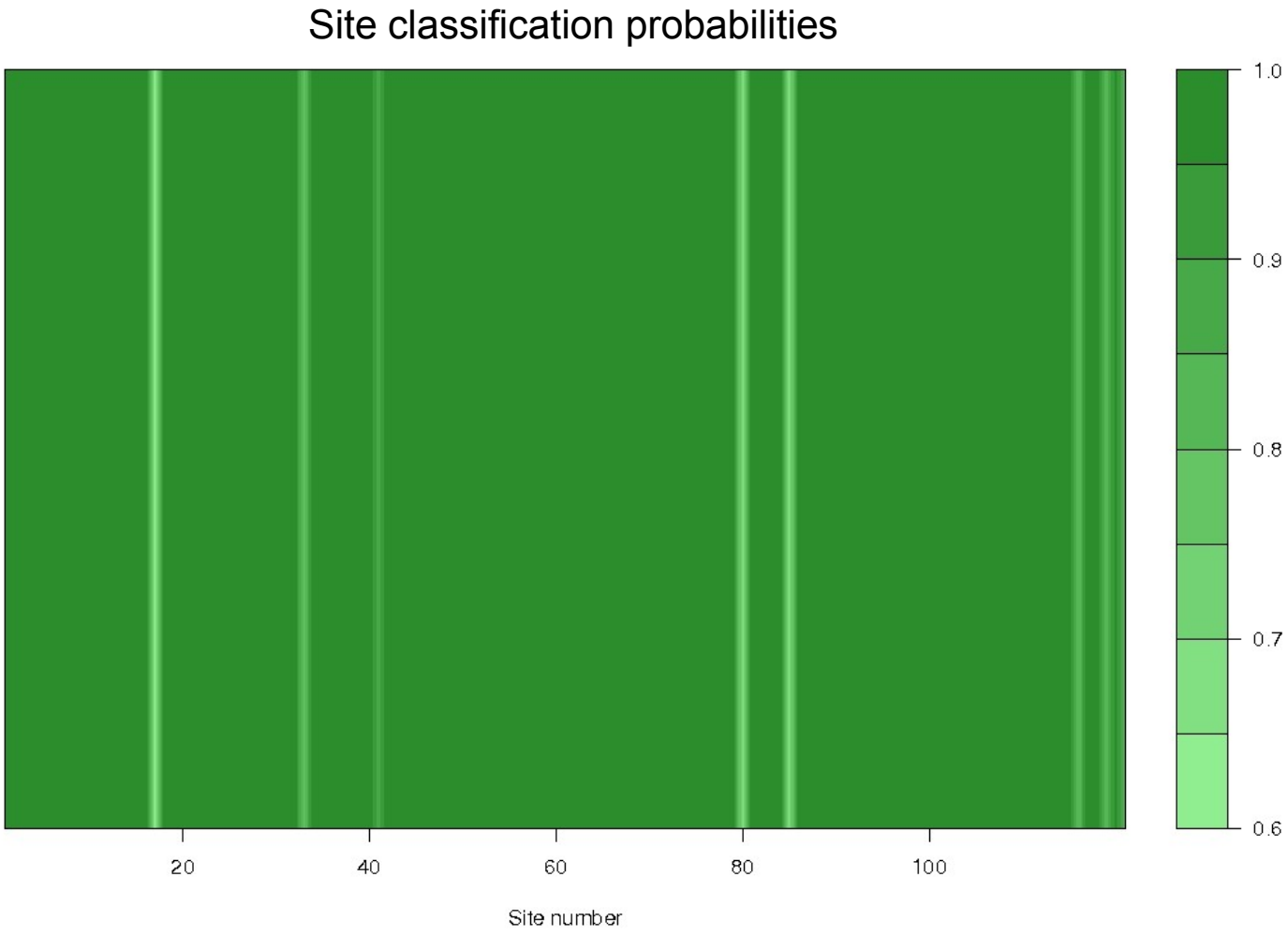
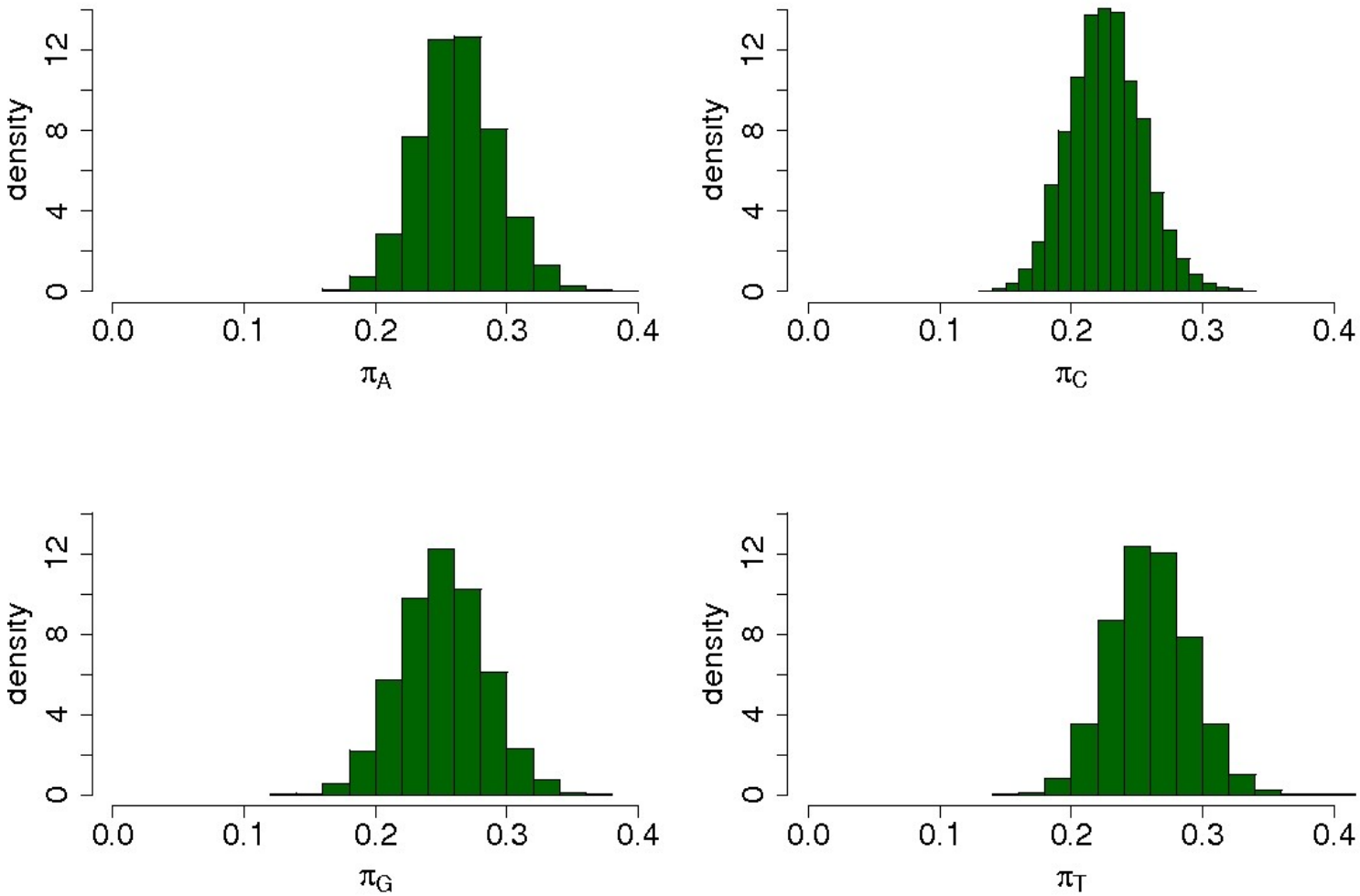


Analysis of *B. burgdorferi*: the 'housekeeping genes' alignment

Posterior densities of stationary frequencies



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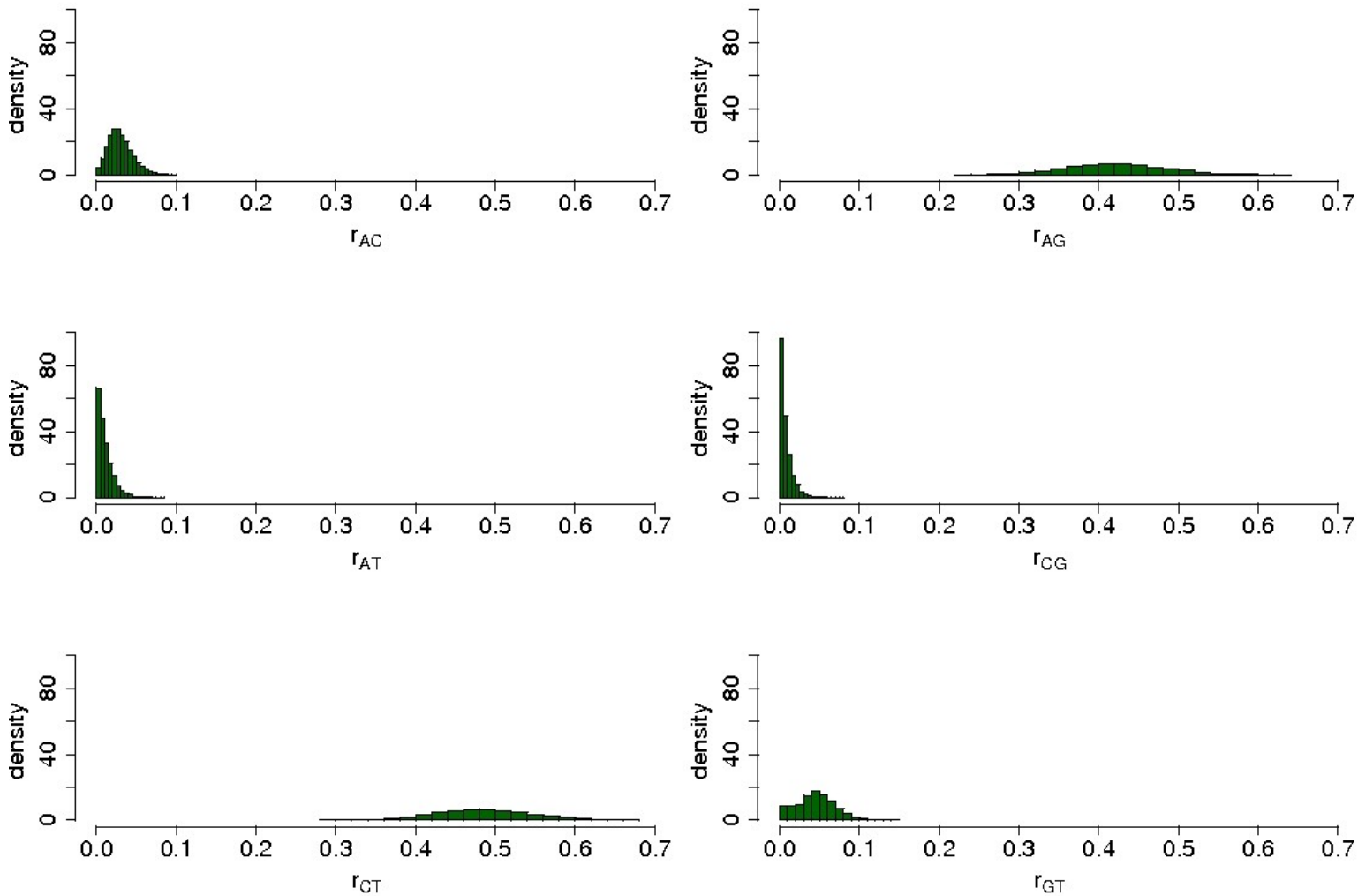
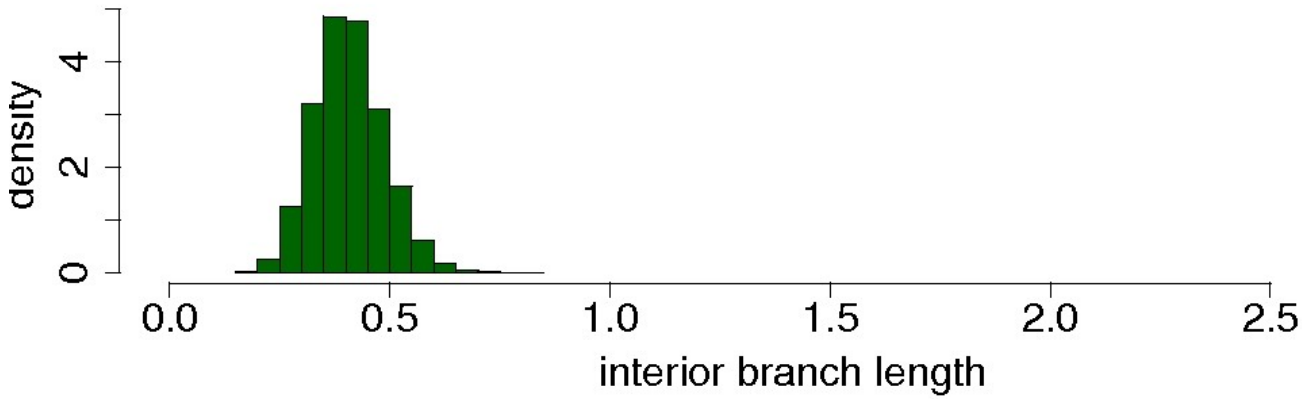
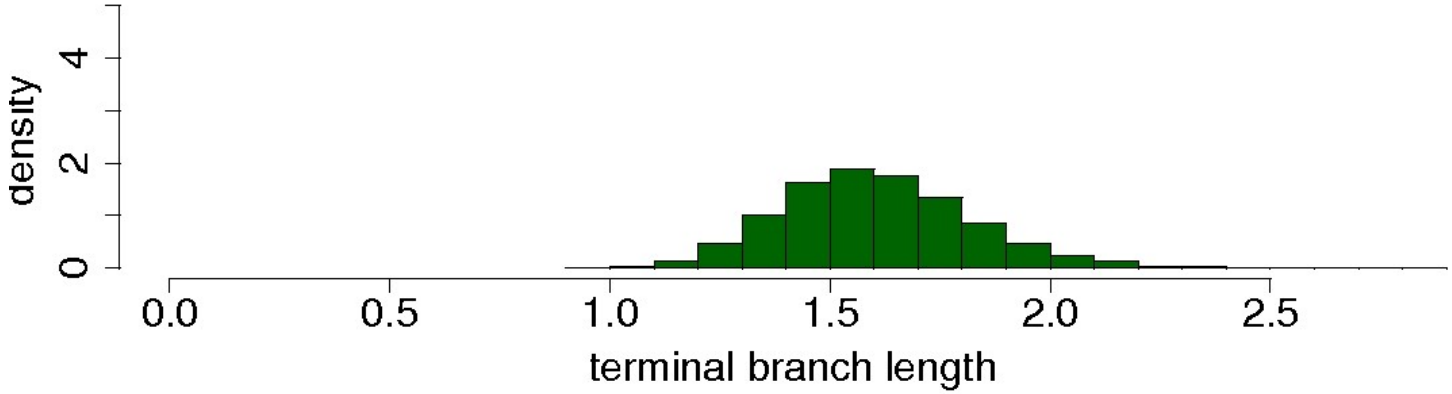
Posterior densities of substitution rates



Analysis of *B. burgdorferi*: the 'housekeeping genes' alignment

Posterior densities of branch lengths





Analysis of *B. burgdorferi*: the 'housekeeping g.|ospC' alignment

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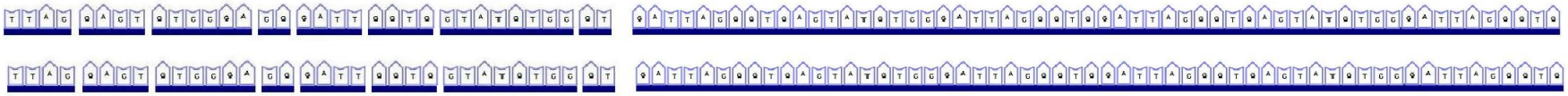

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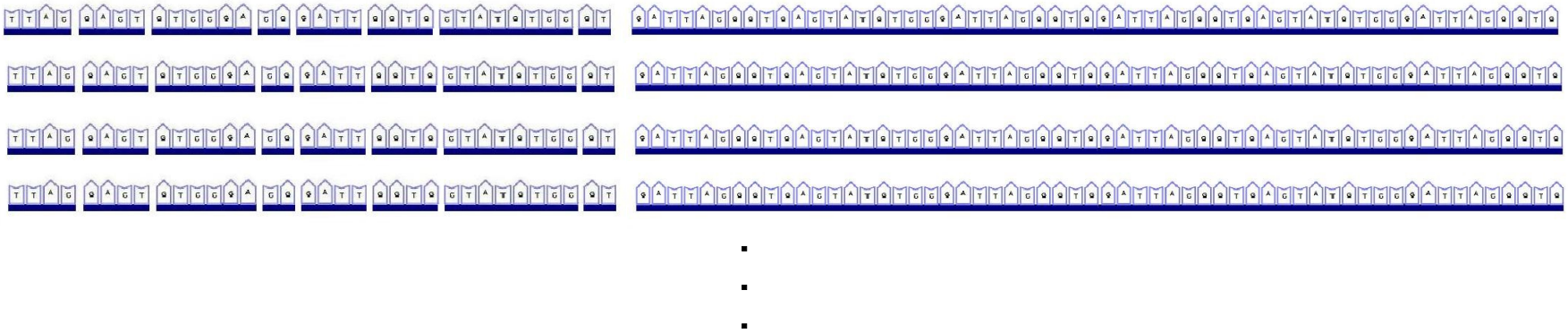

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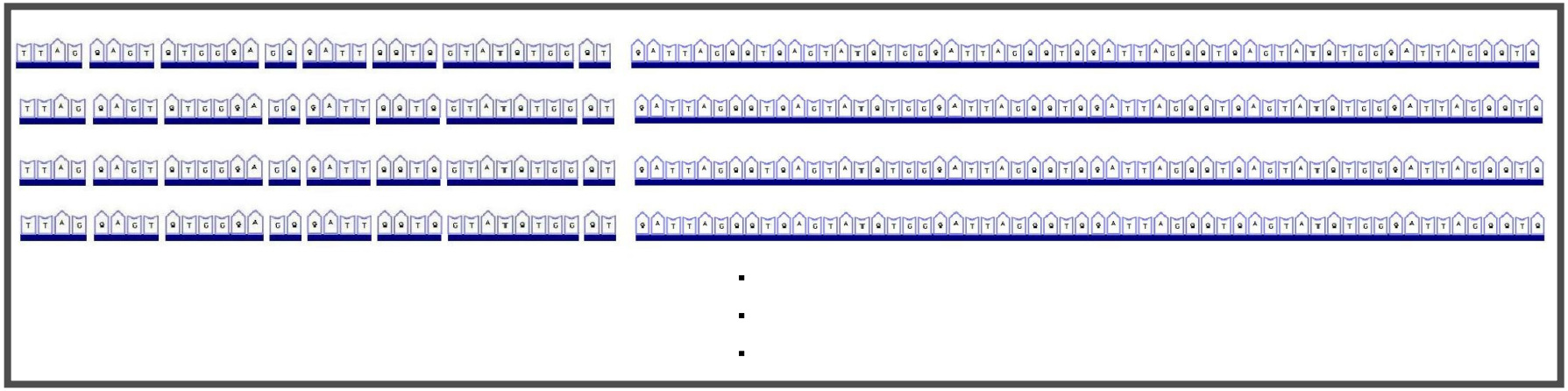

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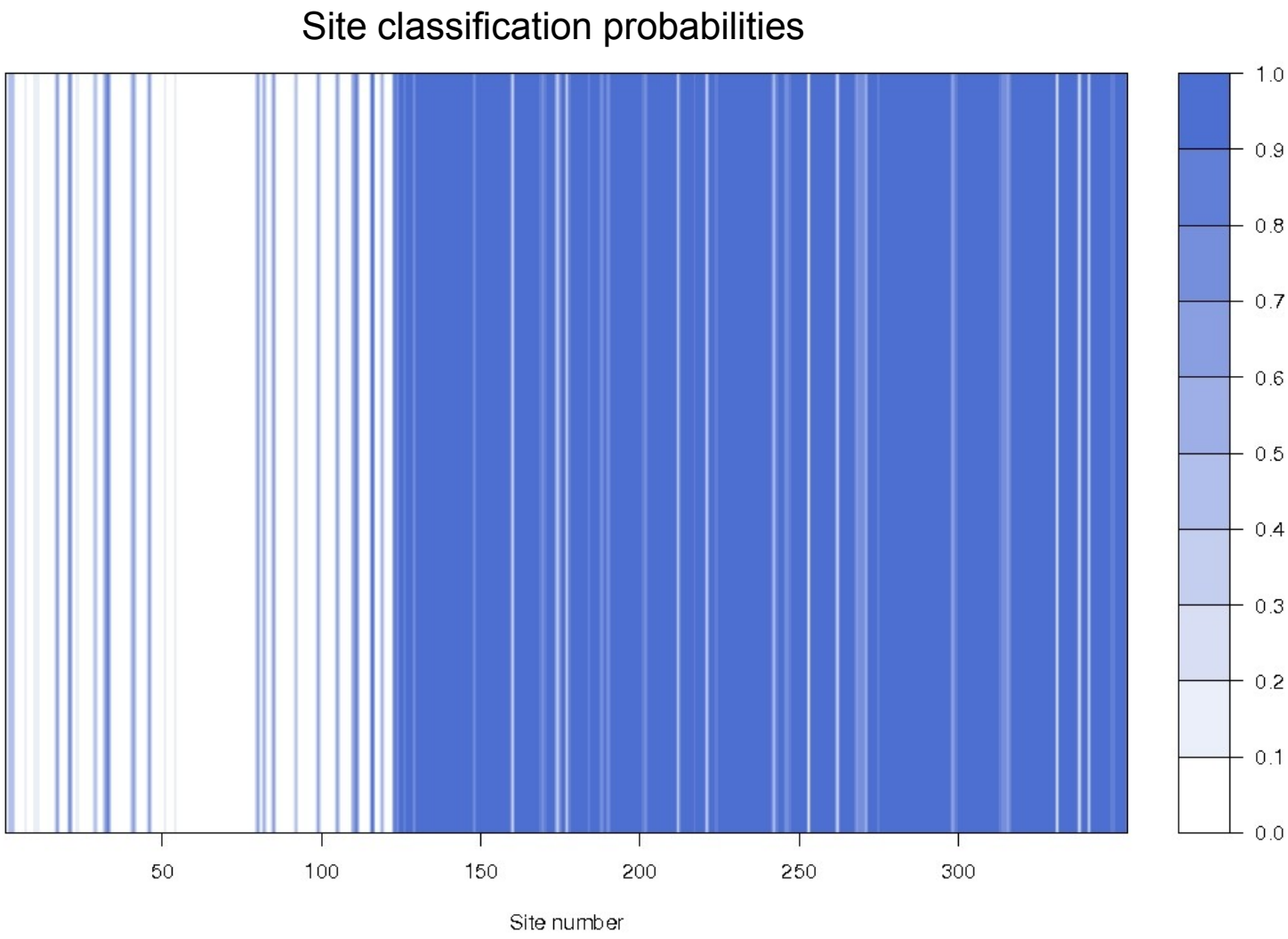
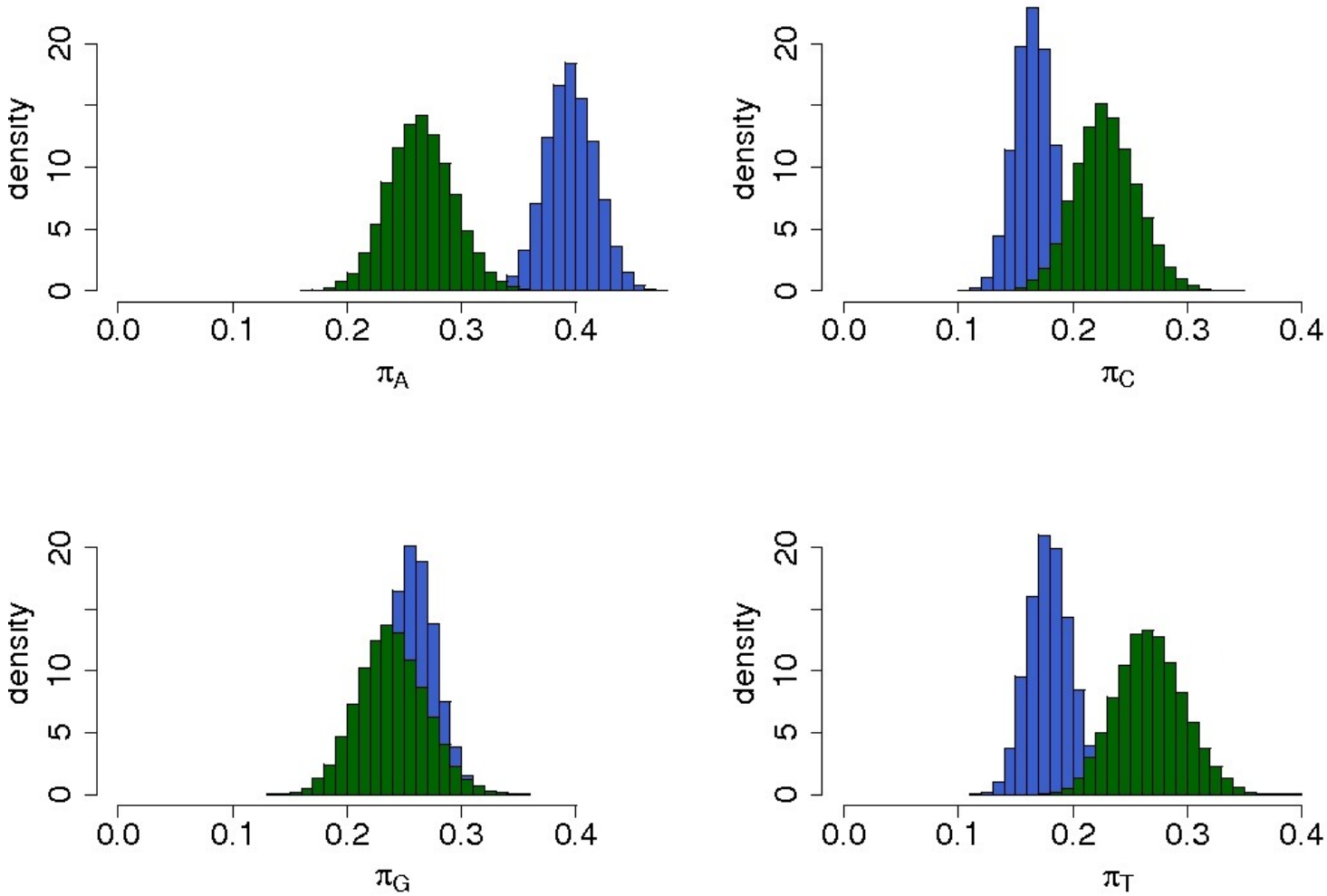


Analysis of *B. burgdorferi*: the 'housekeeping g.|ospC' alignment

Posterior densities of stationary frequencies



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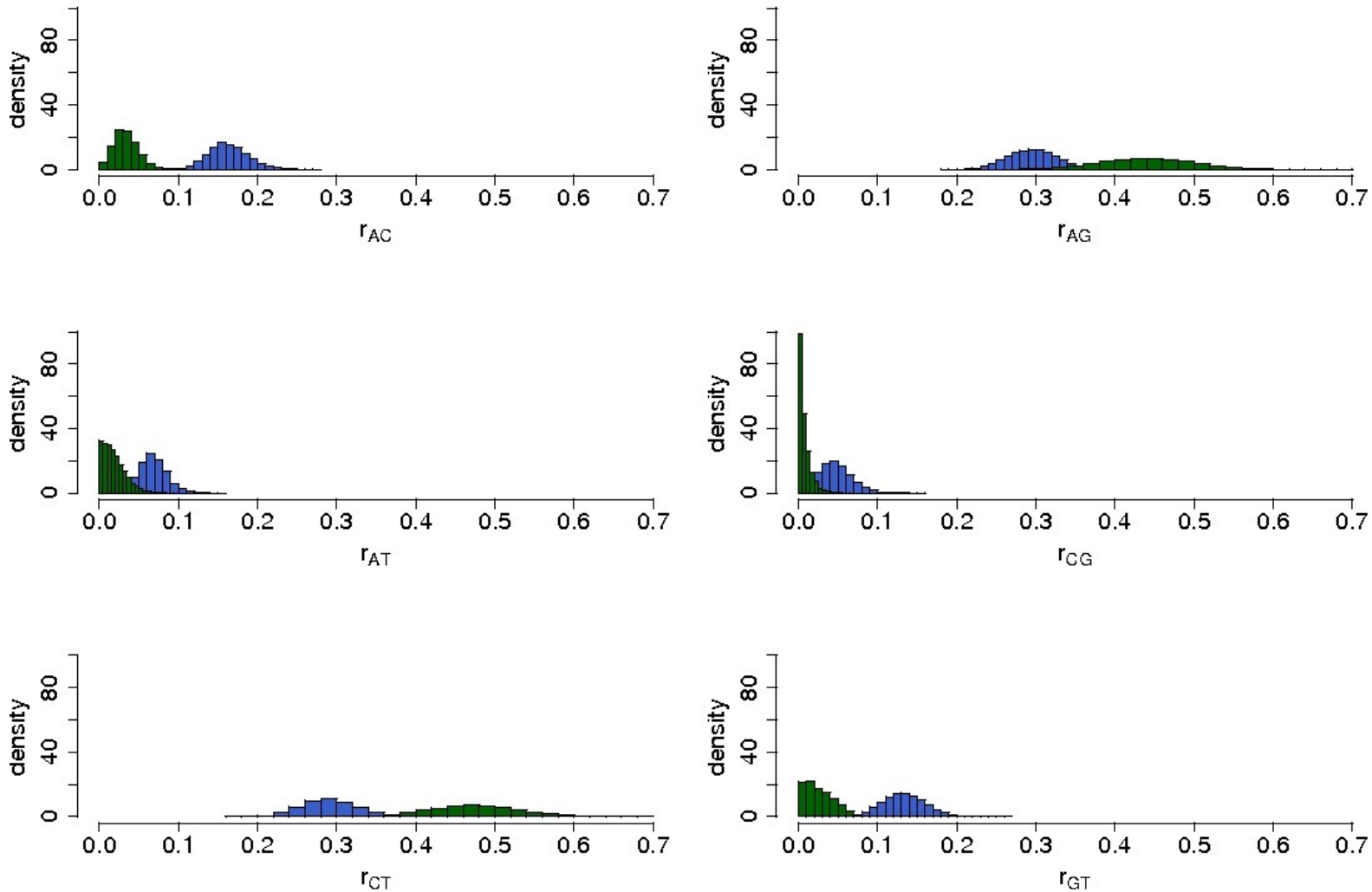
Posterior densities of substitution rates



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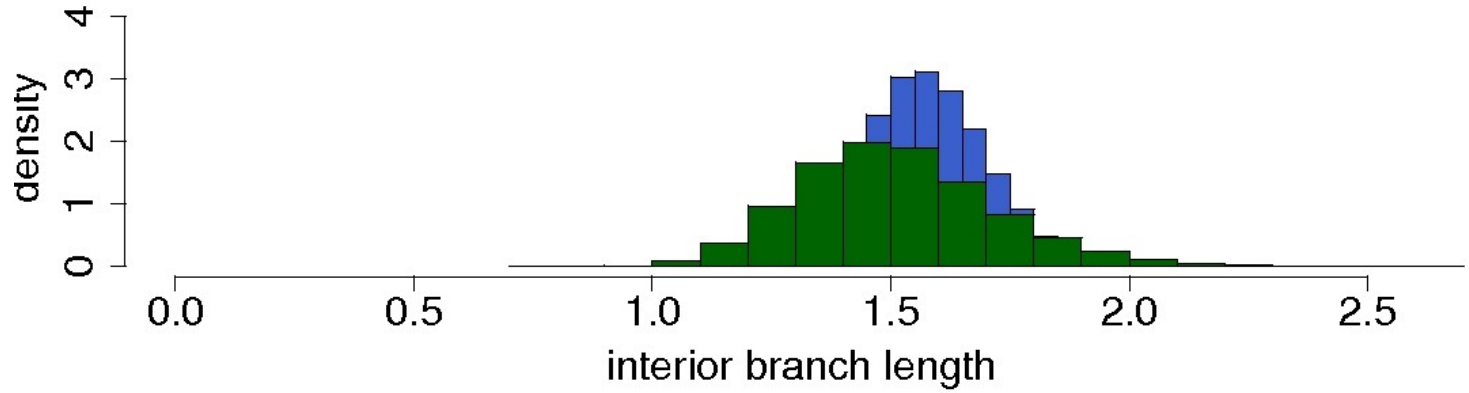
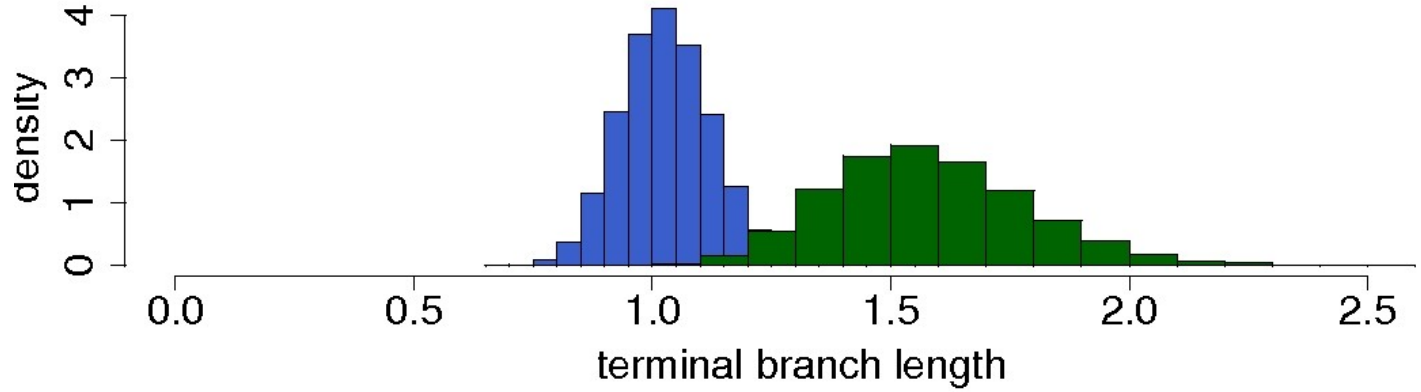
Posterior densities of branch lengths





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- *B. burgdorferi* data is just one application of many other possibilities.

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