A case study in object-oriented programming

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Searching for Evidence of Recombination in Alignments of DNA

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Husmeier, Wright (2001)
Journal of Computational Biology 8, 401-427.

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Searching for Evidence of Recombination in Alignments of DNA

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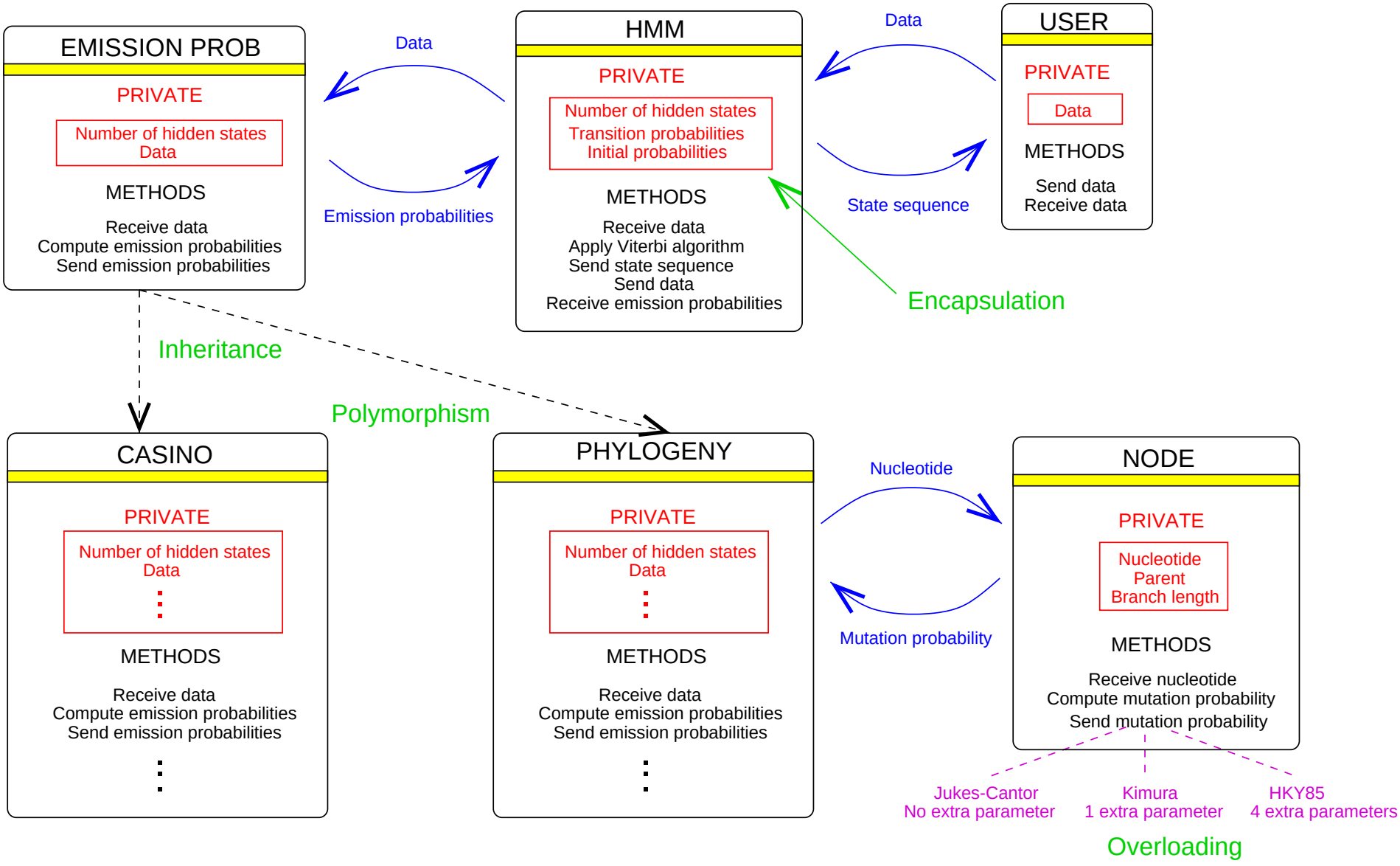
- HMMs
- Phylogenetic trees
- Recombination
- Object-oriented programming implementation


EMISSION PROB
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Number of hidden states
Data
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Receive data
Compute emission probabilities
Send emission probabilities
Data
Emission probabilities
HMM
PRIVATE
Number of hidden states
Transition probabilities
Initial probabilities
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Apply Viterbi algorithm
Send state sequence
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Data
State sequence
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PRIVATE
Data
METHODS
Send data
Receive data
Encapsulation
Inheritance
Polymorphism
CASINO
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PHYLOGENY
PRIVATE
Number of hidden states
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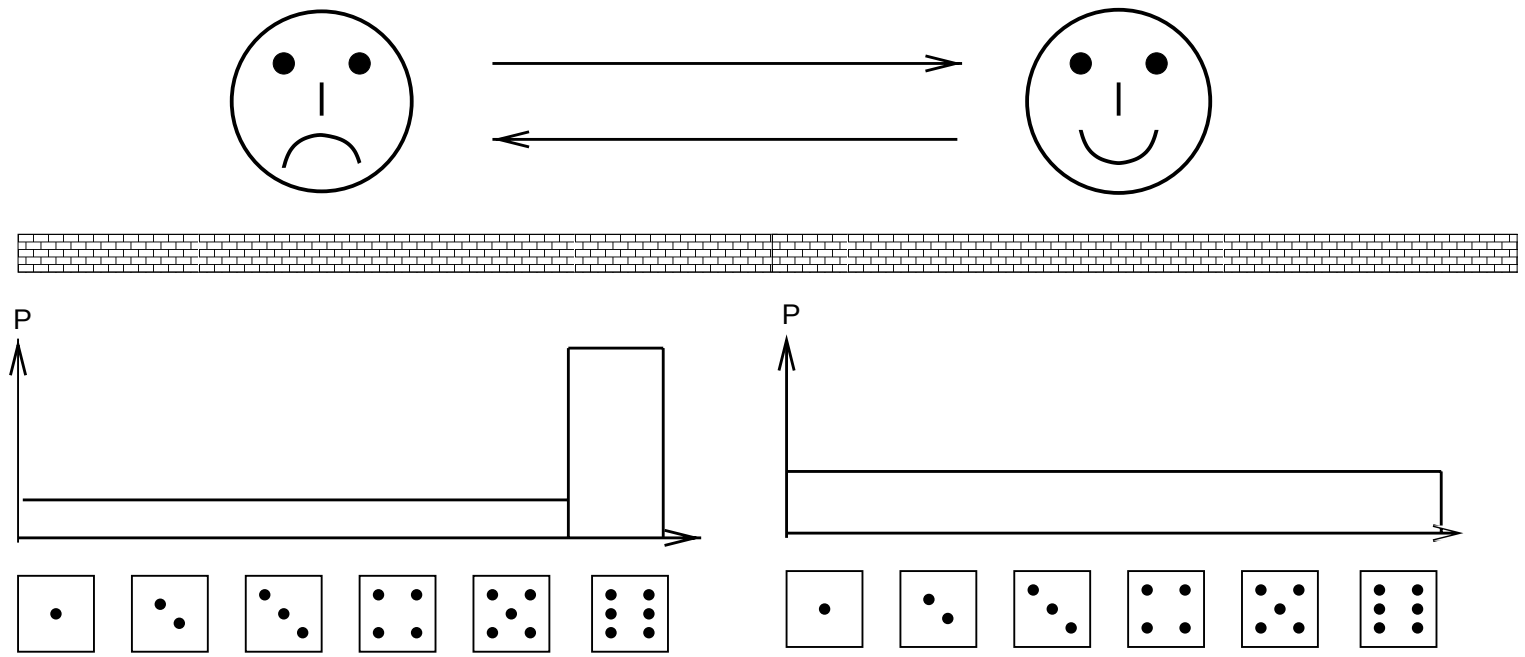
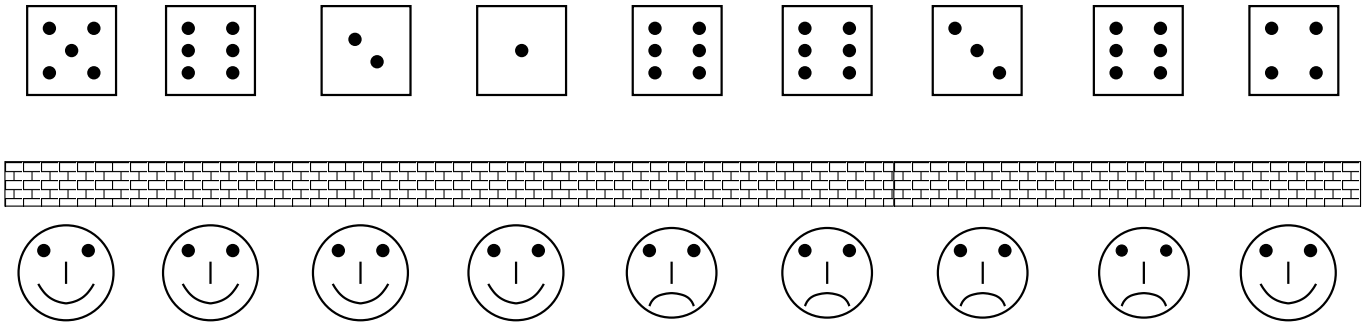
Send emission probabilities
Nucleotide
Mutation probability
NODE
PRIVATE
Nucleotide
Parent
Branch length
METHODS
Receive nucleotide
Compute mutation probability
Send mutation probability
Jukes-Cantor
No extra parameter
Kimura
1 extra parameter
HKY85
4 extra parameters
Overloading

Hidden Markov Models

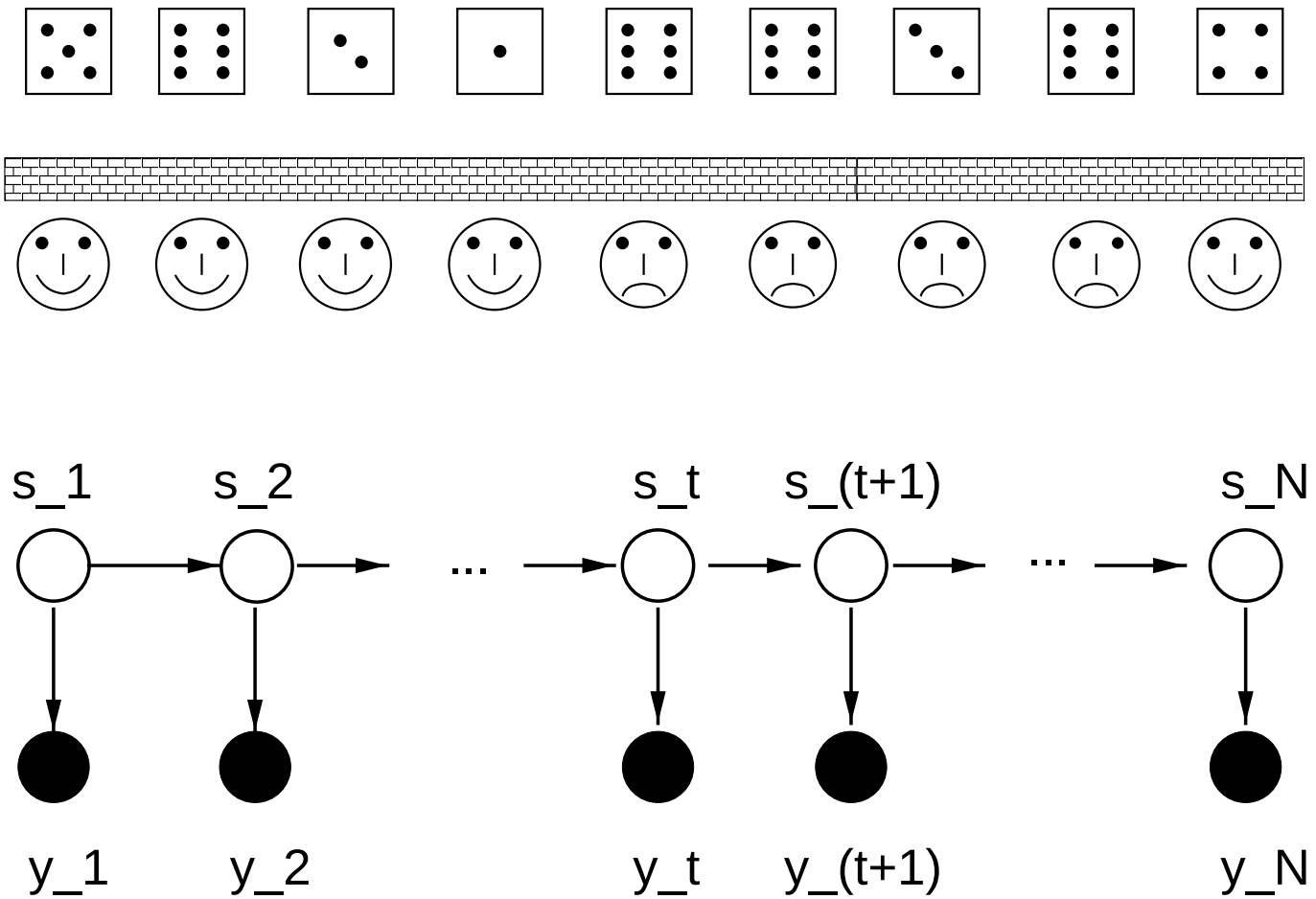
Example: The occasionally corrupt casino



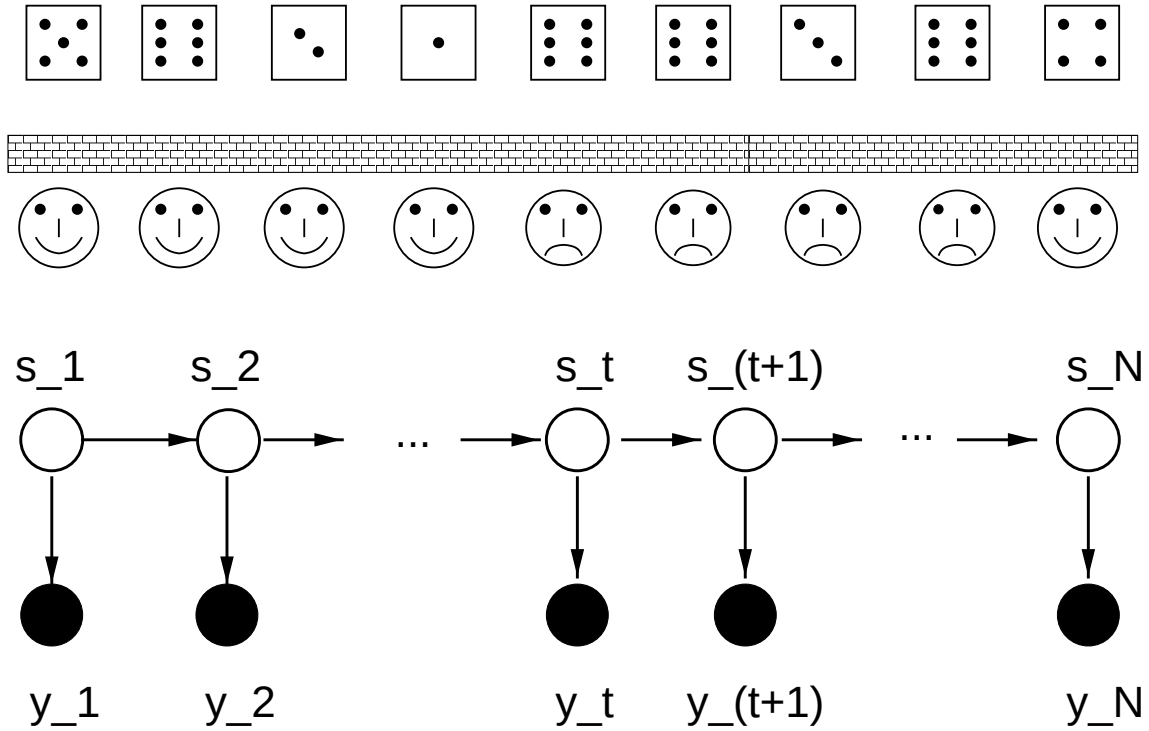
Example: HMM



Example: HMM



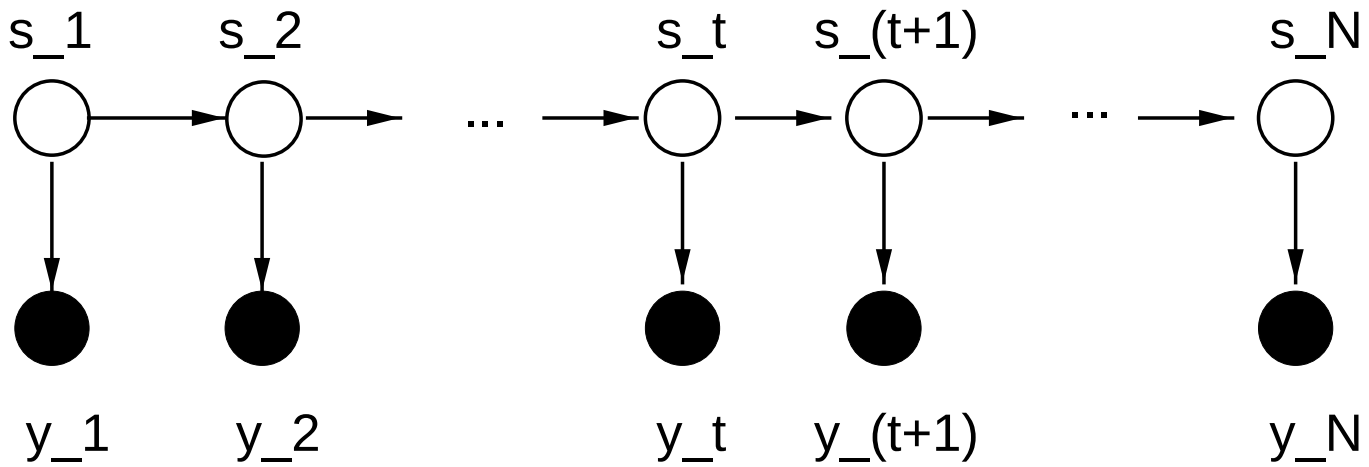
The most likely state sequence



Find the mode of $P(S_1, \ldots, S_N | y_1, \ldots, y_N)$

Problem:$(S_1, \ldots, S_N)$: 2^N different sequences.

Factorisation in HMMs

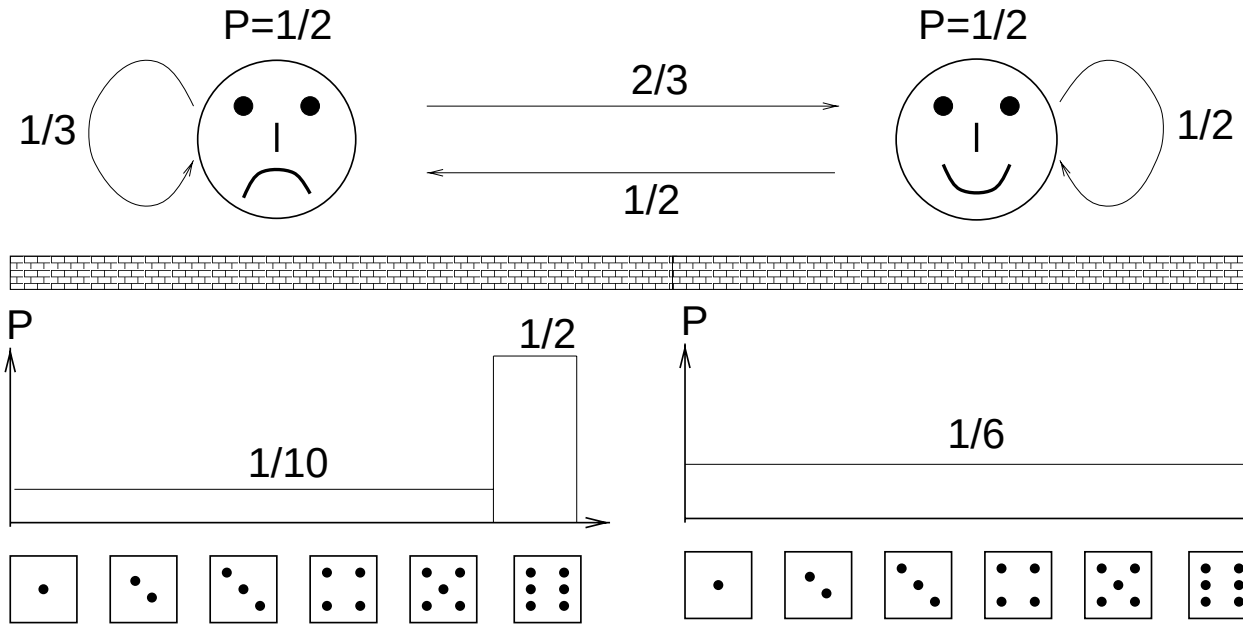


$$P(y_1, \ldots, y_N, S_1, \ldots, S_N) = \prod_{t=1}^{N} P(y_t|S_t) \prod_{t=2}^{N} P(S_t|S_{t-1}) P(S_1)$$

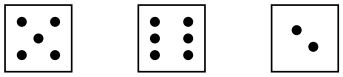
Viterbi algorithm $\longrightarrow P(S_1, \ldots, S_N|y_1, \ldots, y_N)$

Computational complexity and example

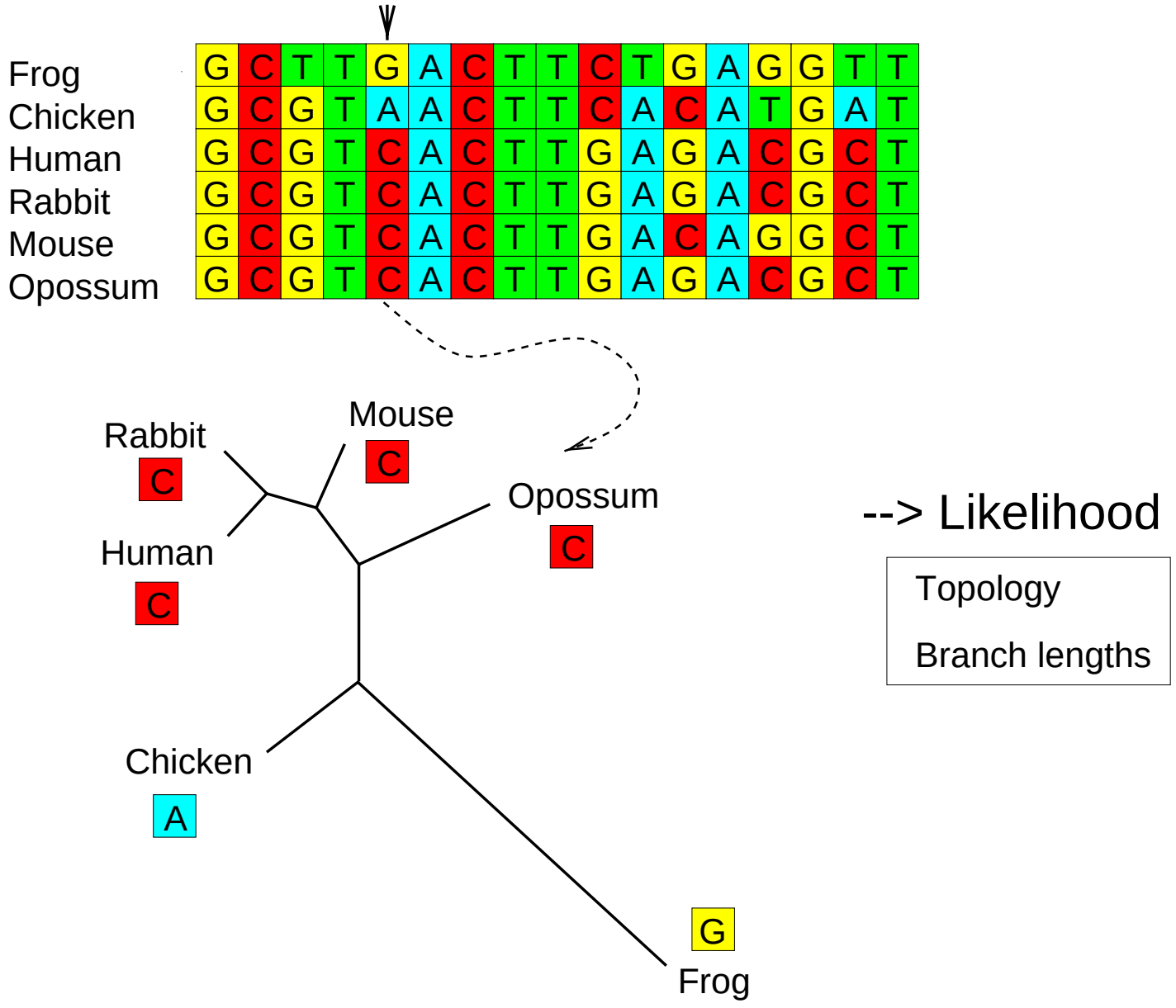
Computation complexity: $|\mathcal{H}|^N \longrightarrow N \times |\mathcal{H}|^2$



Observed sequence:

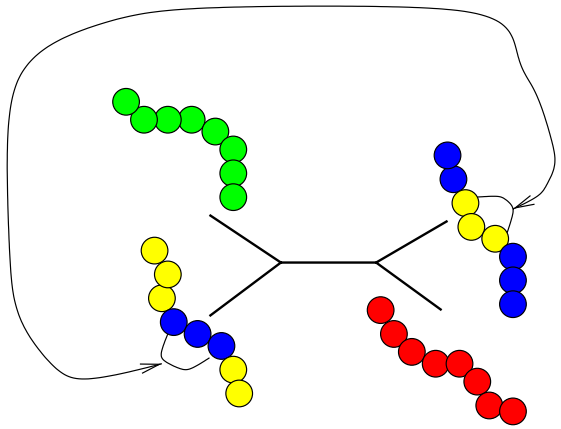


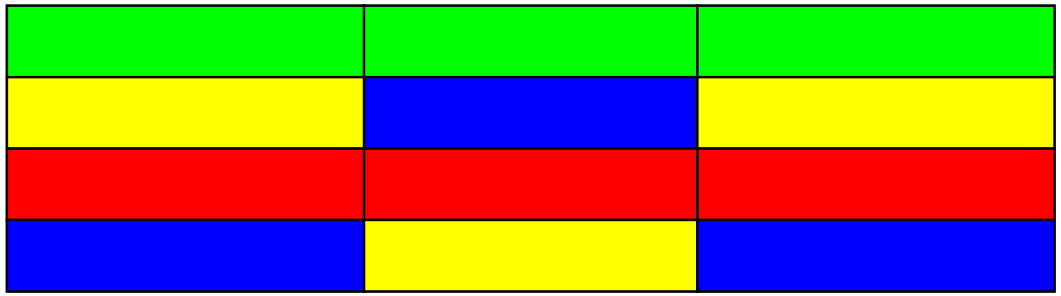
Phylogenetic trees

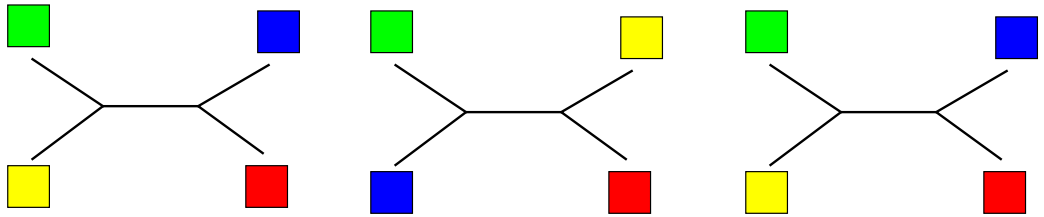

Frog
Chicken
Human
Rabbit
Mouse
Opossum
G C T T G A C T T C T G A G G T T
G C G T A A C T T C A C A T G A T
G C G T C A C T T G A G A C G C T
G C G T C A C T T G A G A C G C T
G C G T C A C T T G A C A G G C T
G C G T C A C T T G A G A C G C T
Rabbit
C
Mouse
C
Opossum
C
Human
C
Chicken
A
G
Frog
--> Likelihood
Topology
Branch lengths

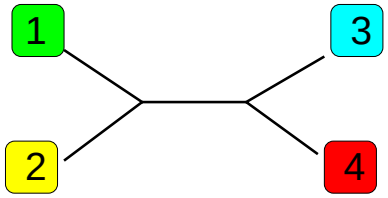
Recombination

Recombination

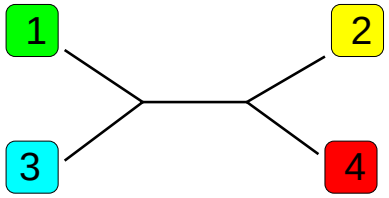




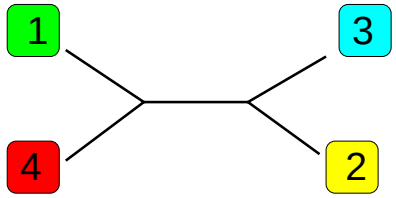




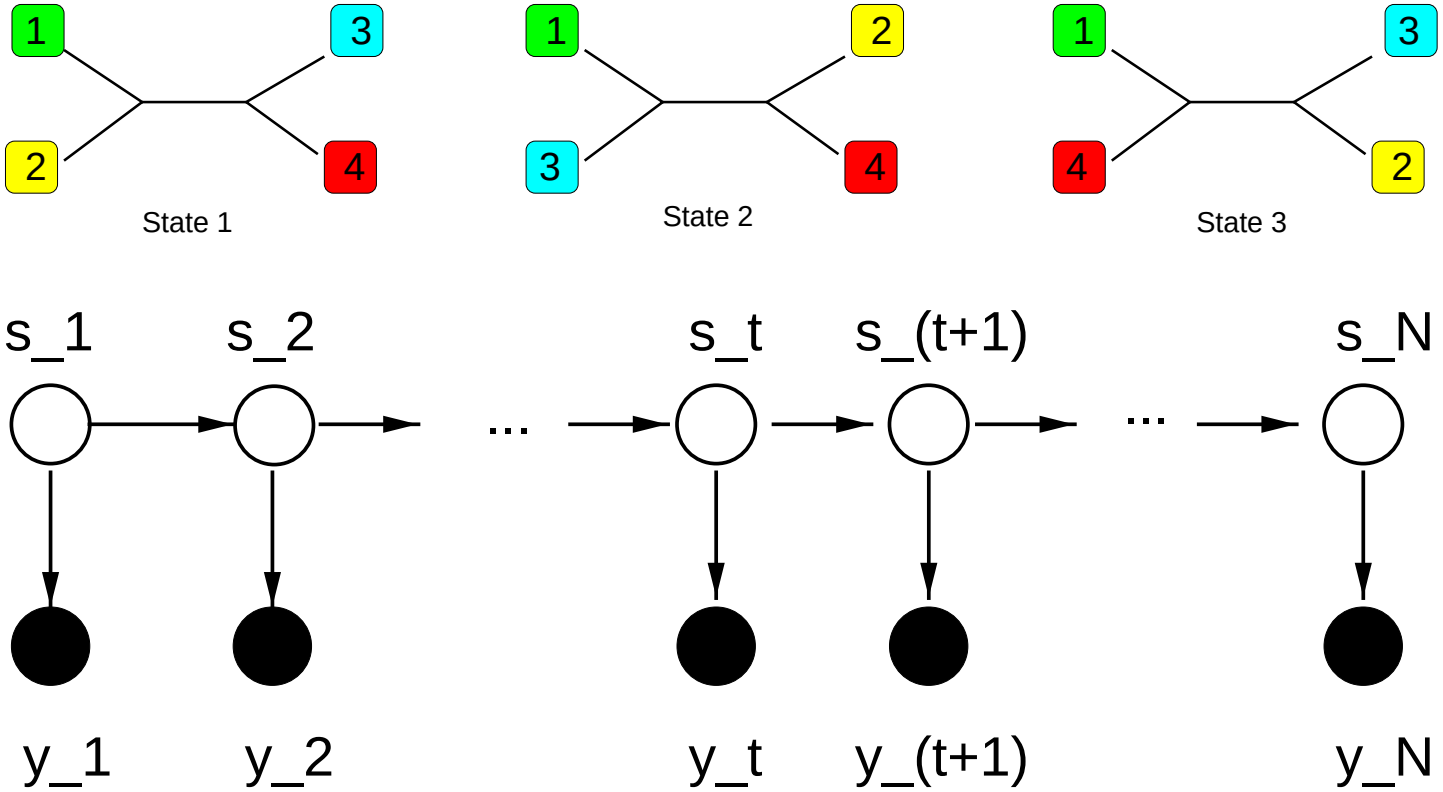
State 1



State 2



State 3



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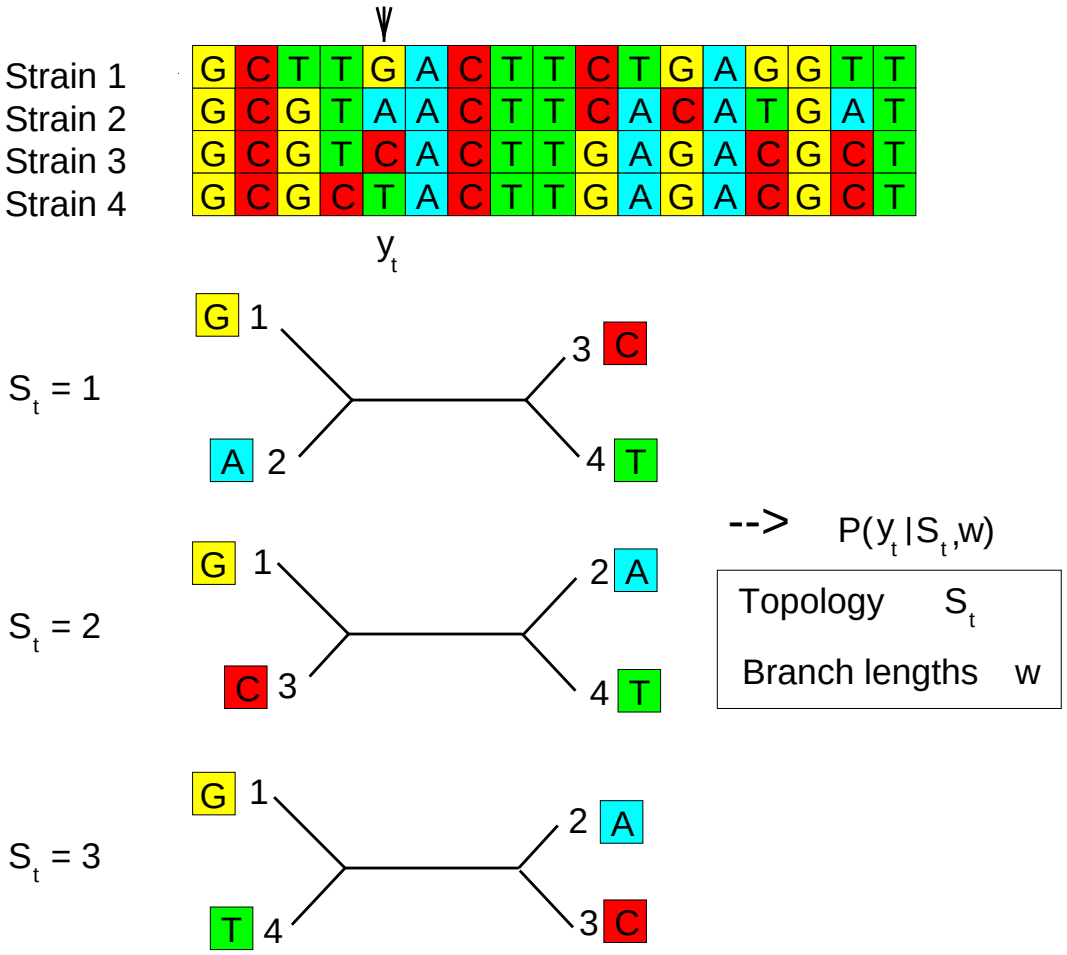
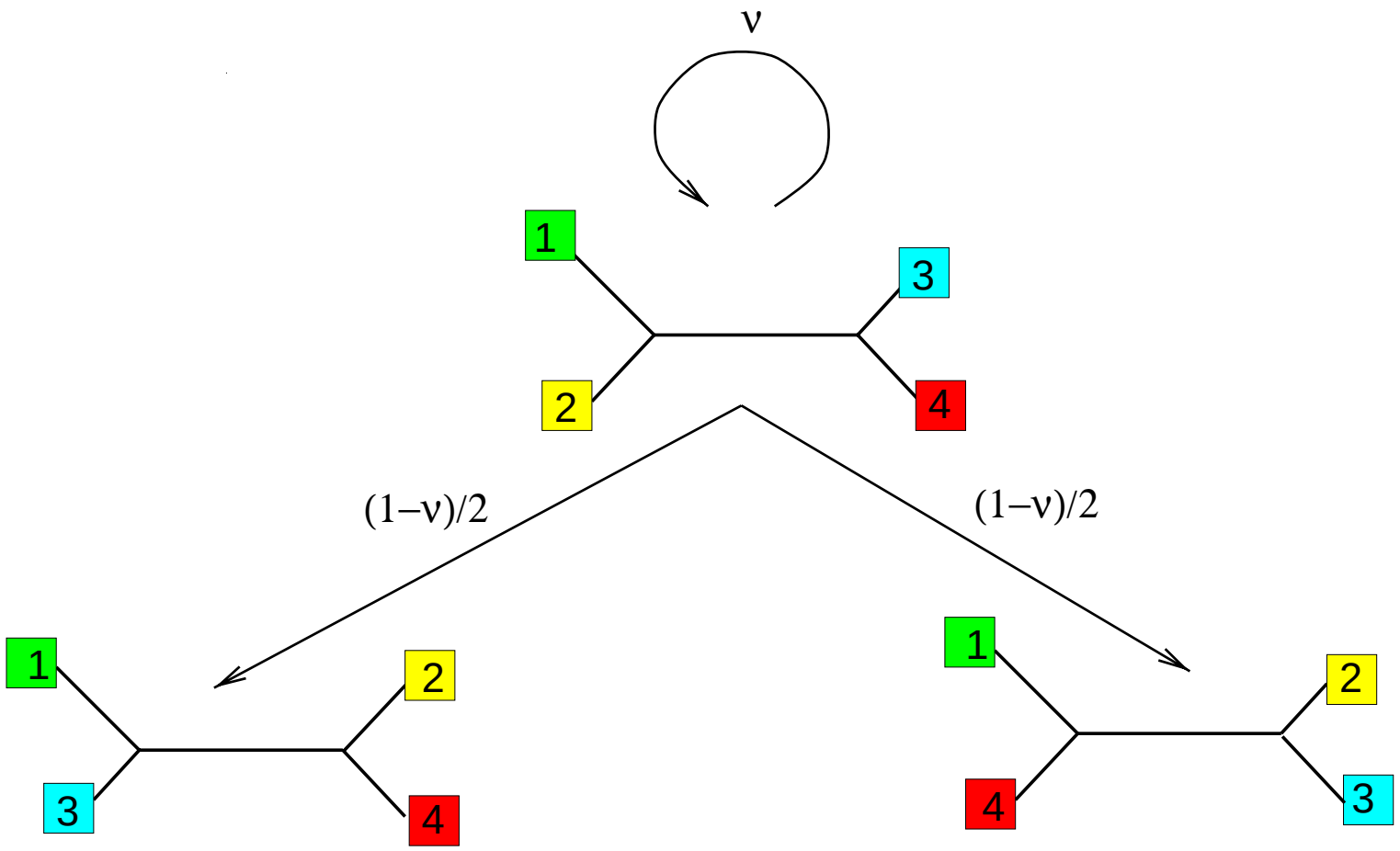
TGTGTCGCTCAAGATTGCCATCGCGCG
TGTCGTGGTCTAGATTGCCATCGCGCG
TGTATCGCTCTAGTTTGCCAGCTCCCG

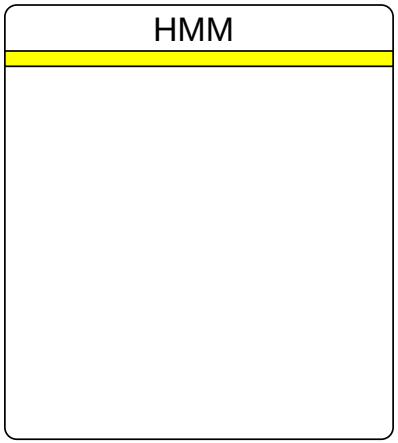
Emission probabilities

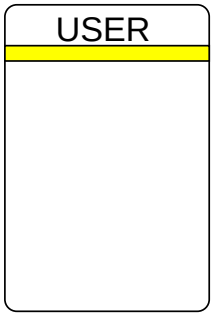


Transition probabilities



Object-oriented programming


HMM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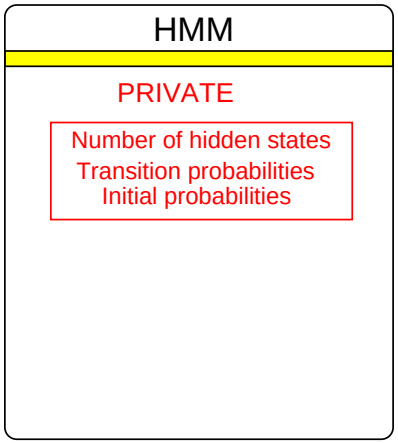
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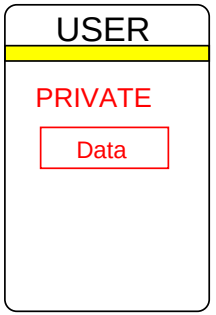
Number of hidden states
Transition probabilities
Initial probabilities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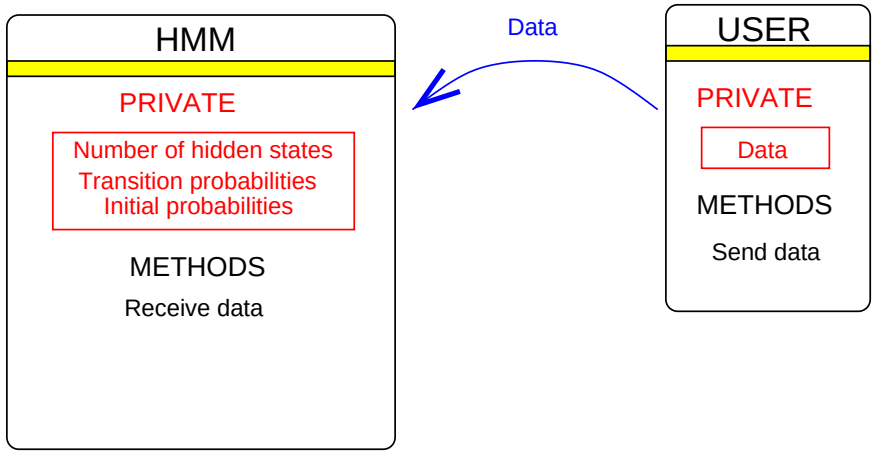
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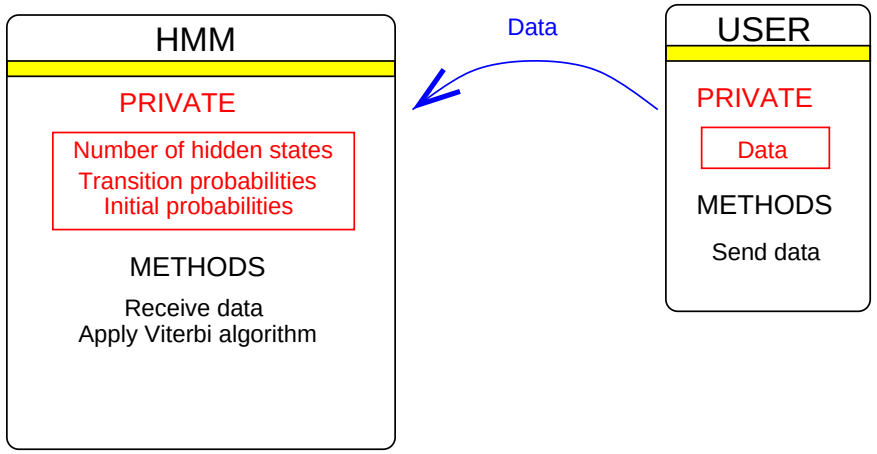
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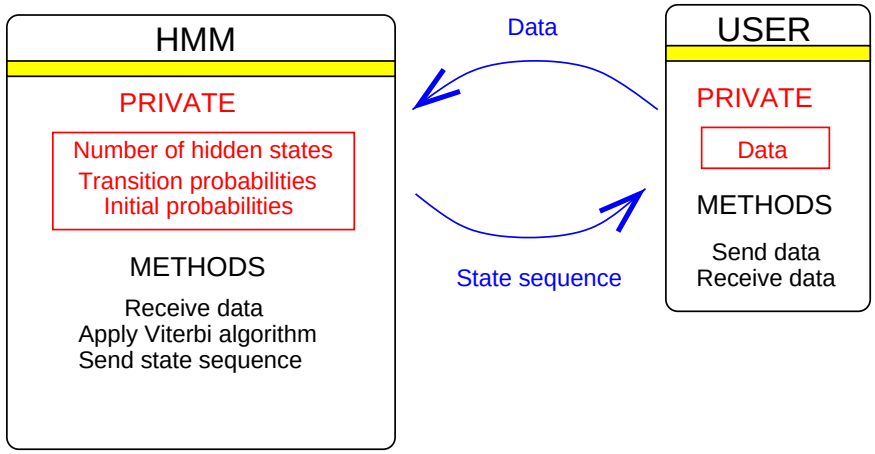
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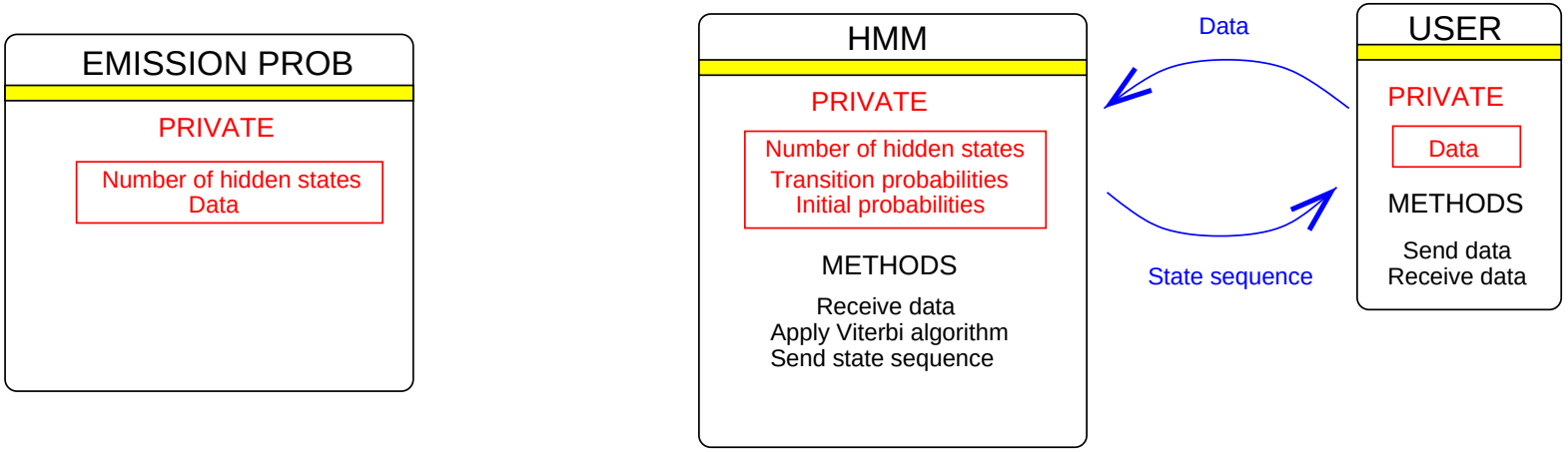
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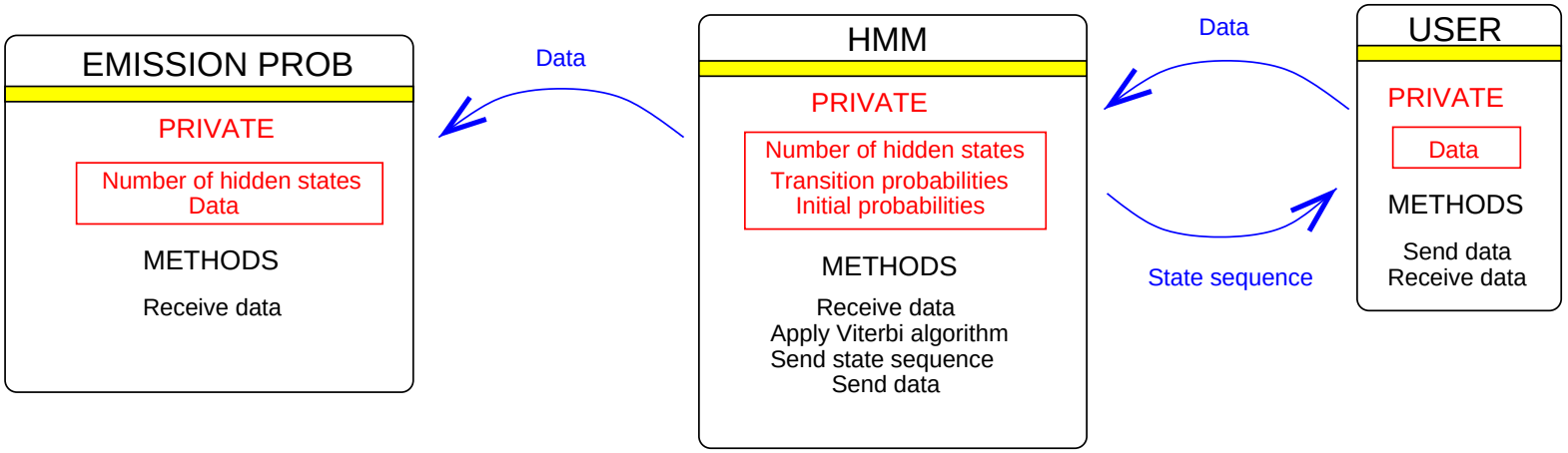
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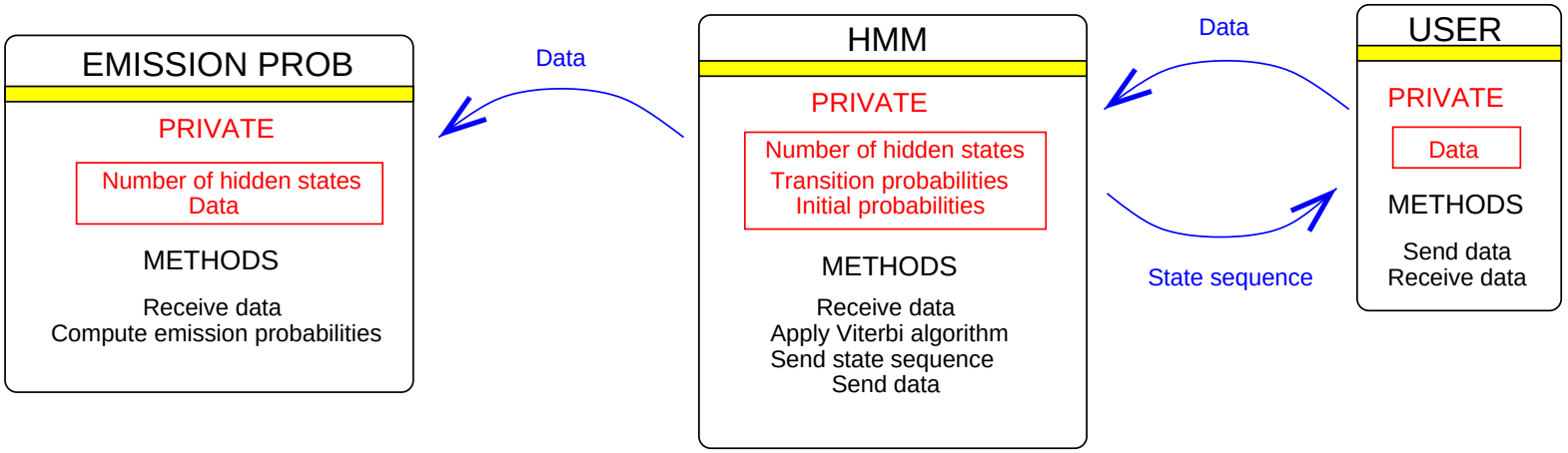
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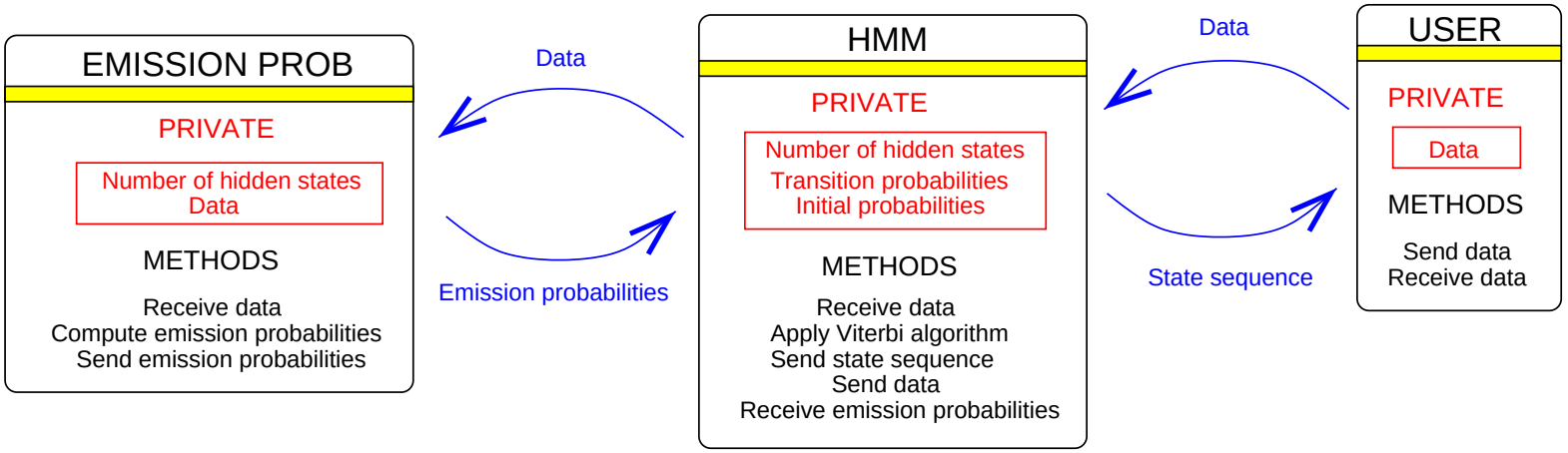
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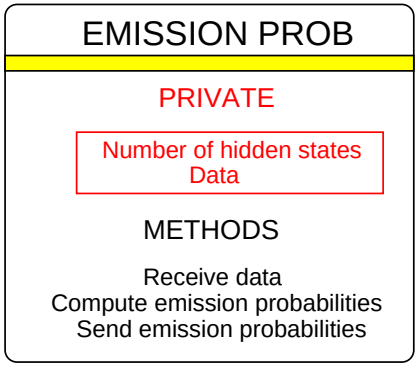
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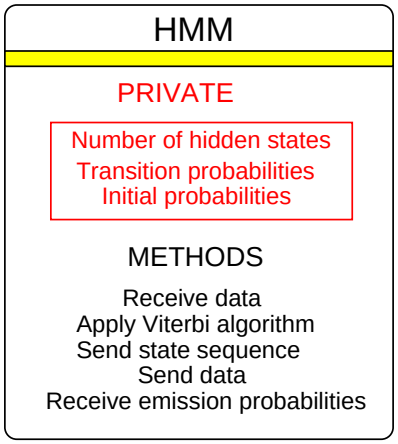
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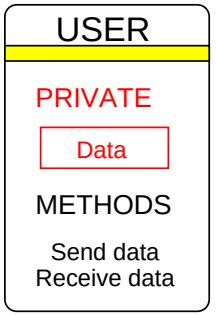
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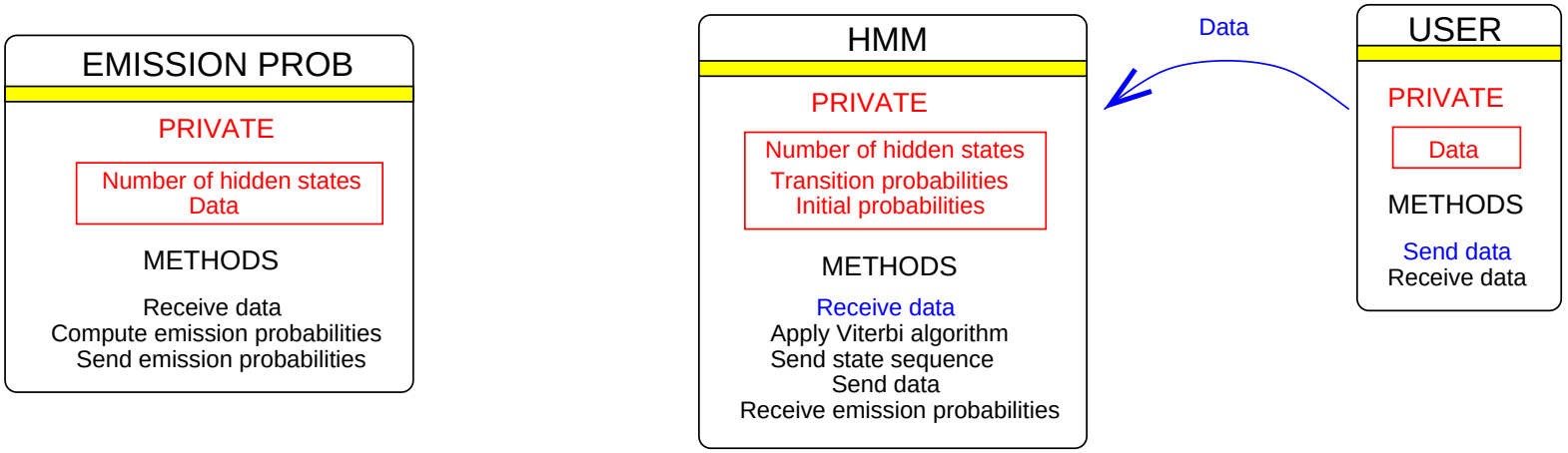
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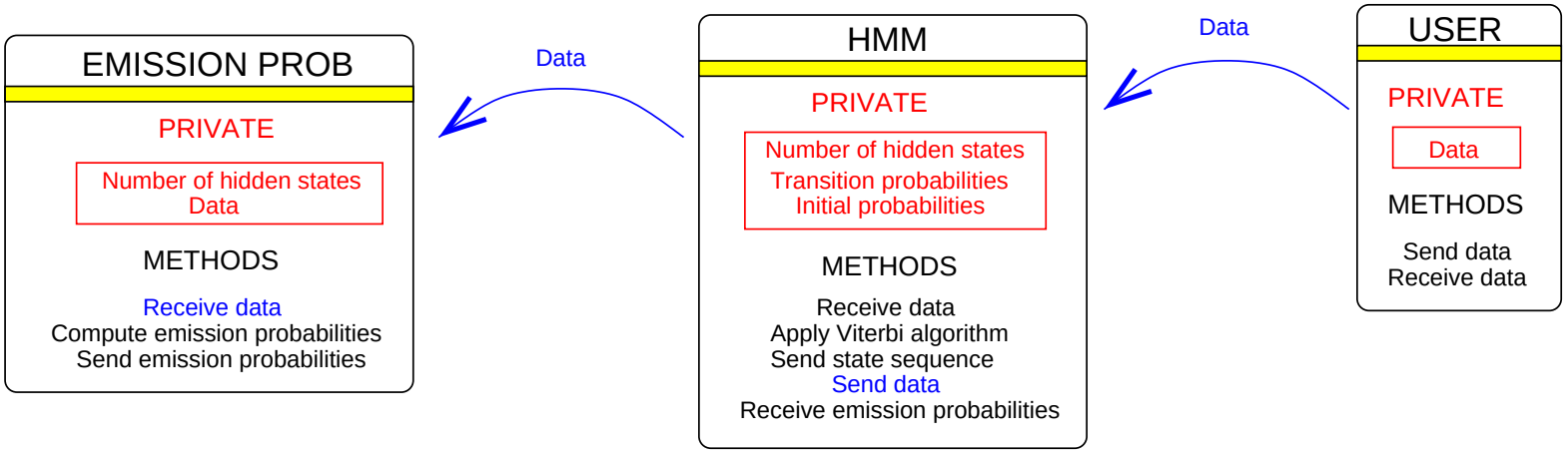
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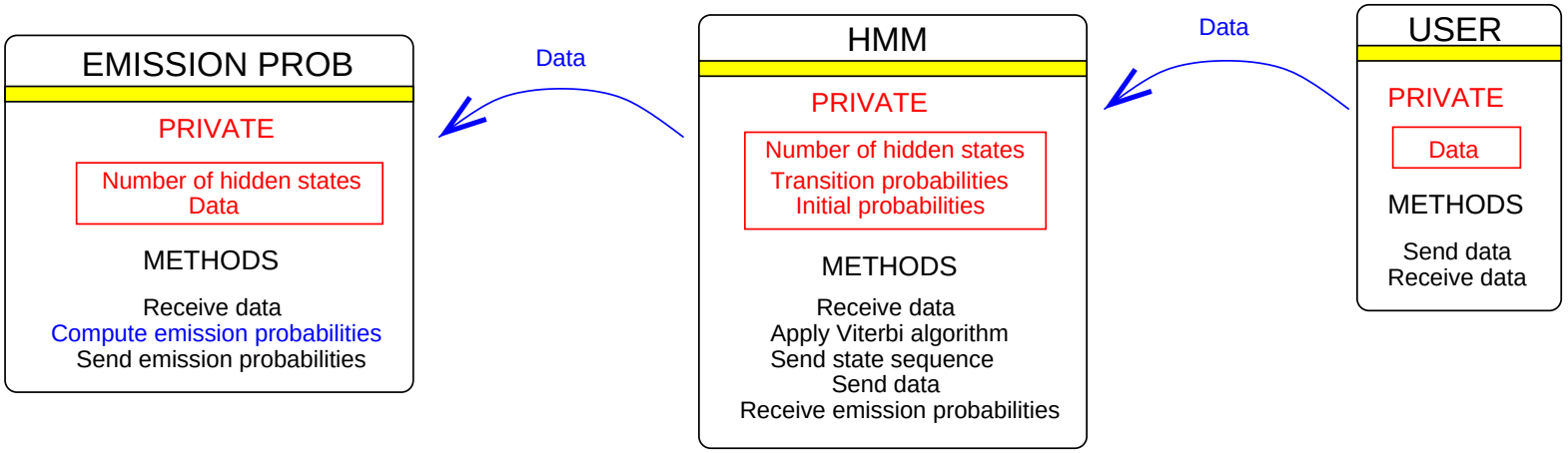
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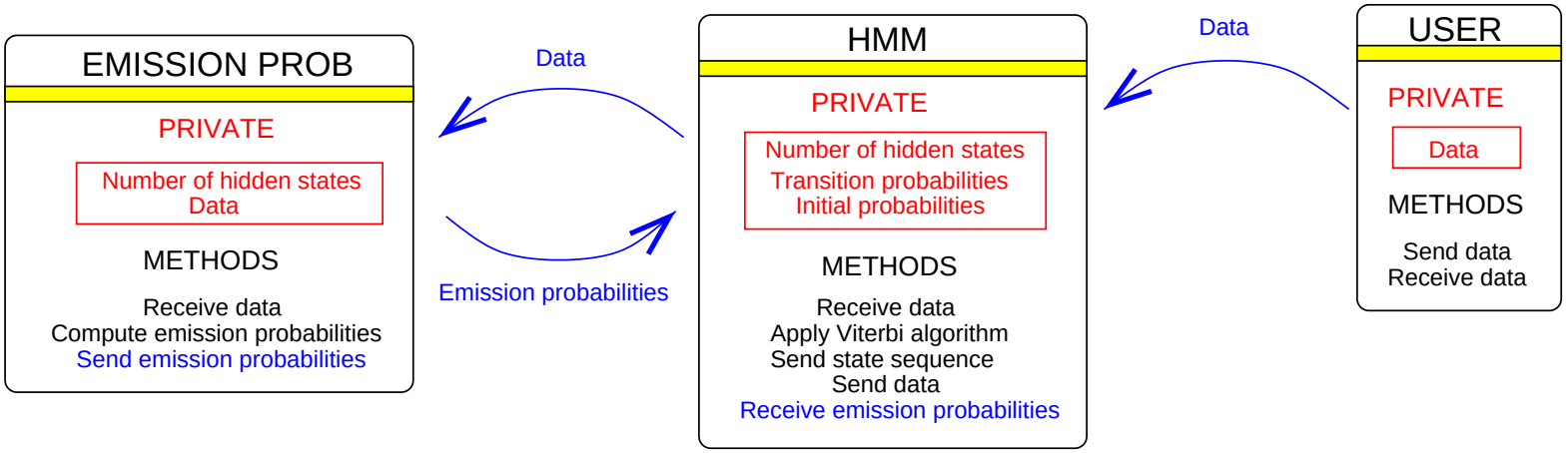
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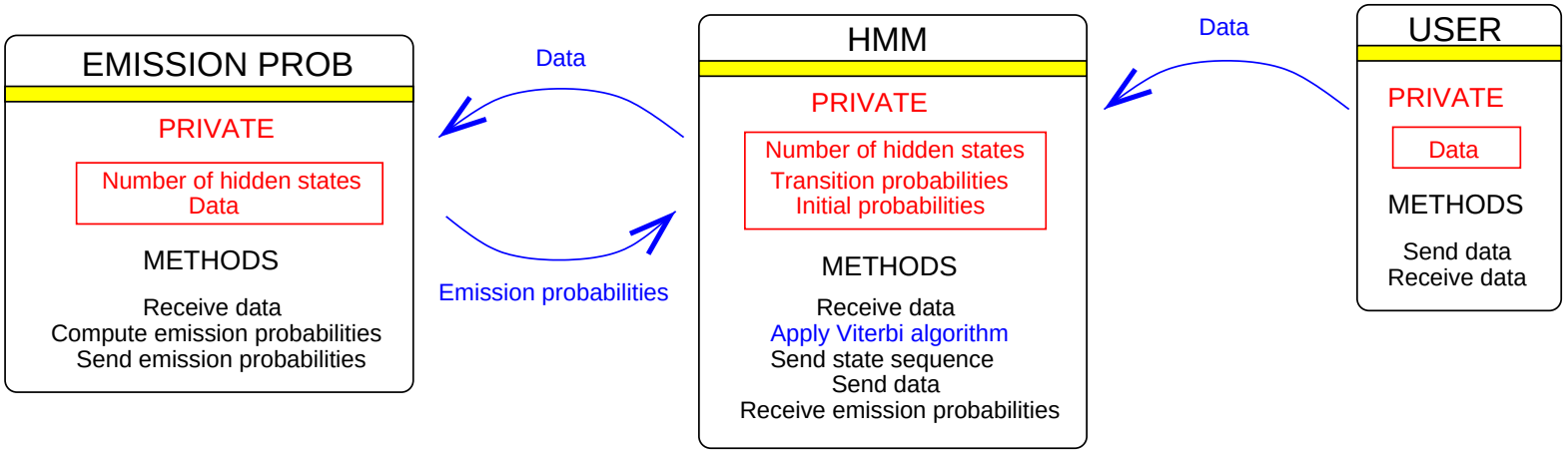
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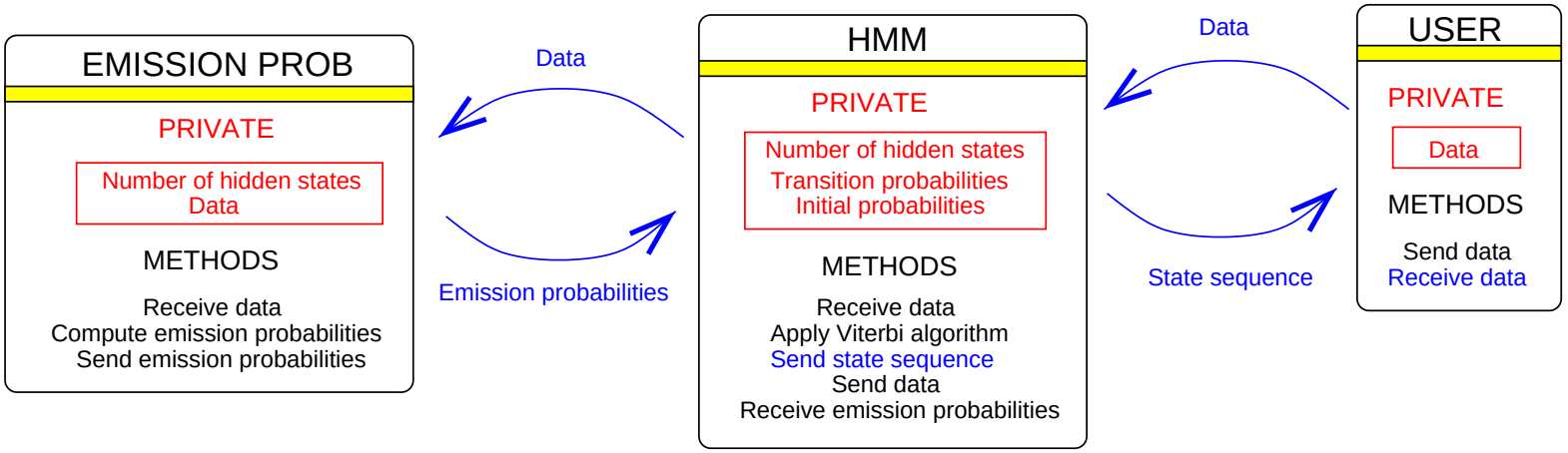
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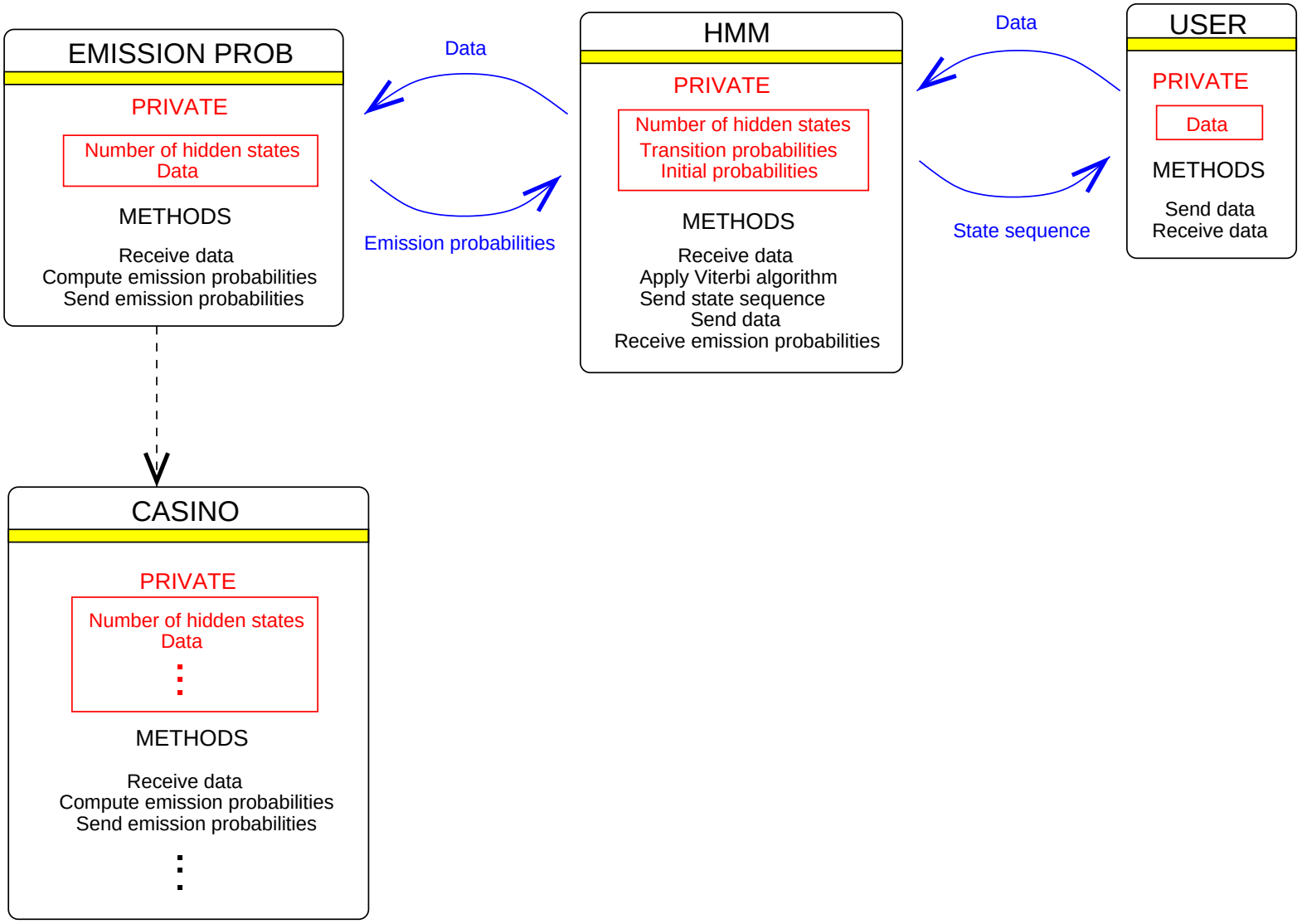
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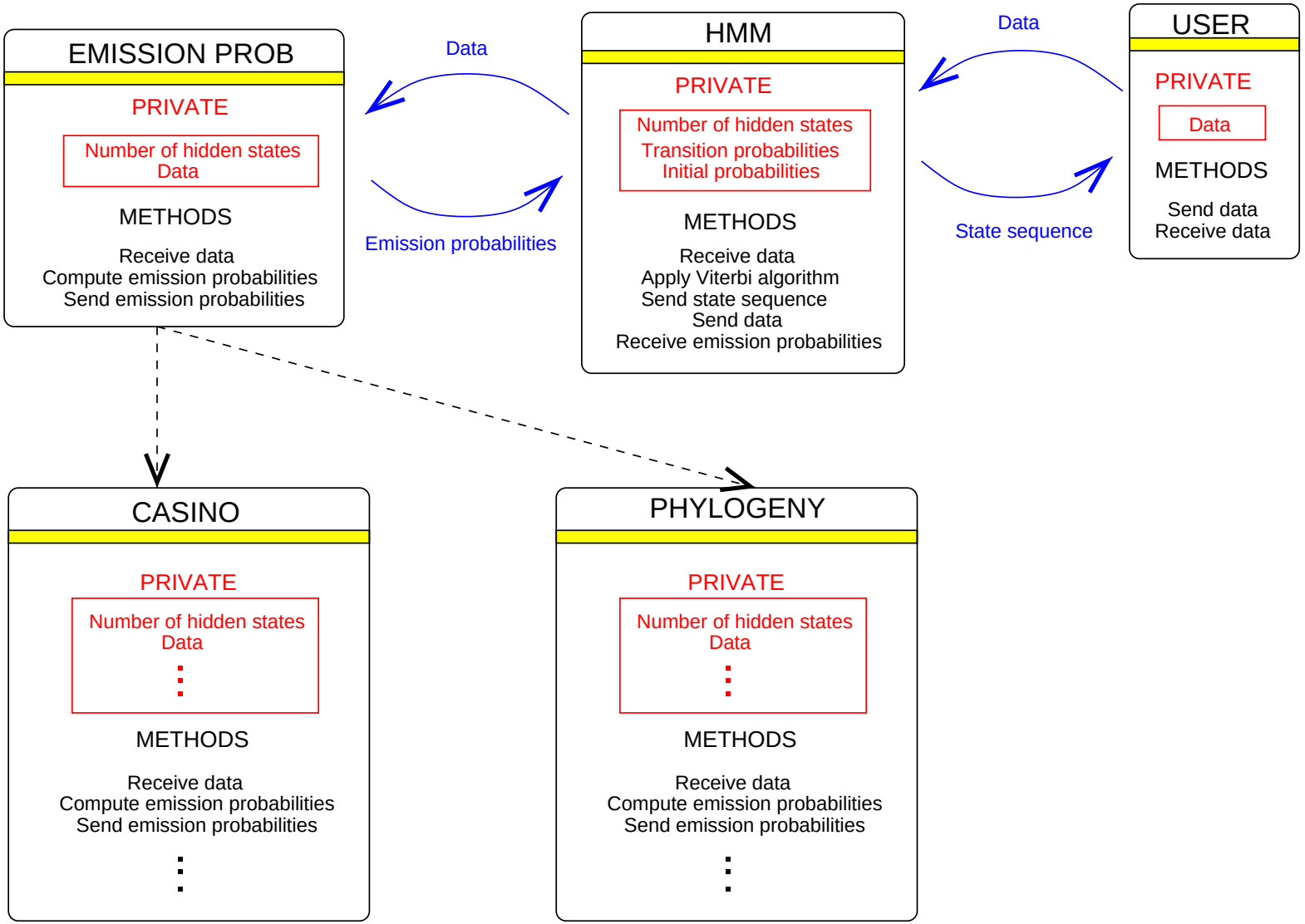
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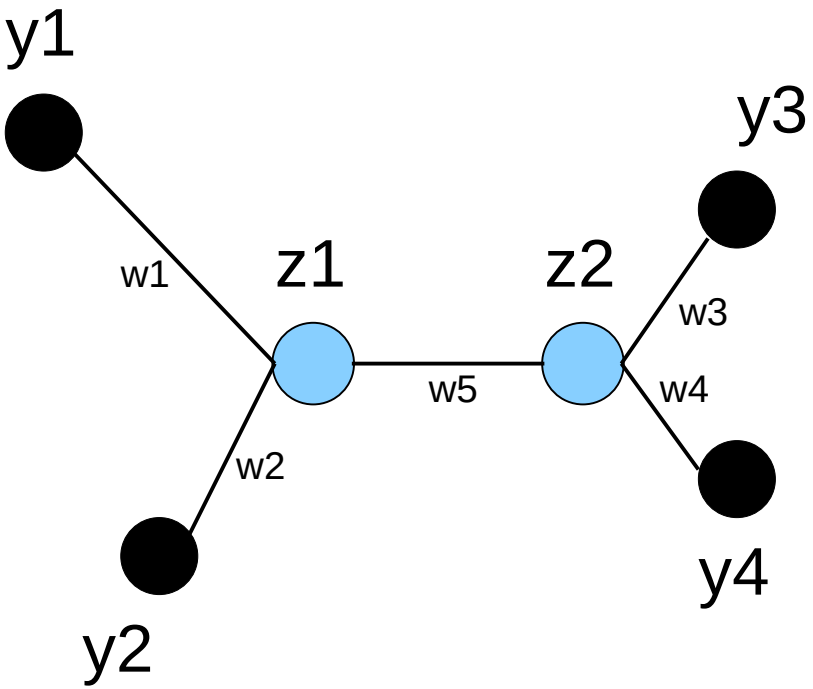
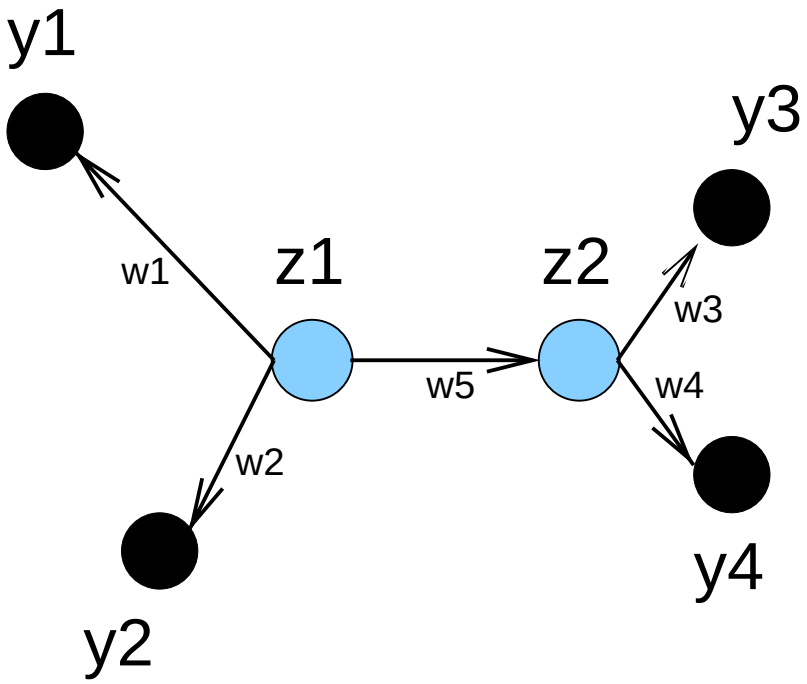
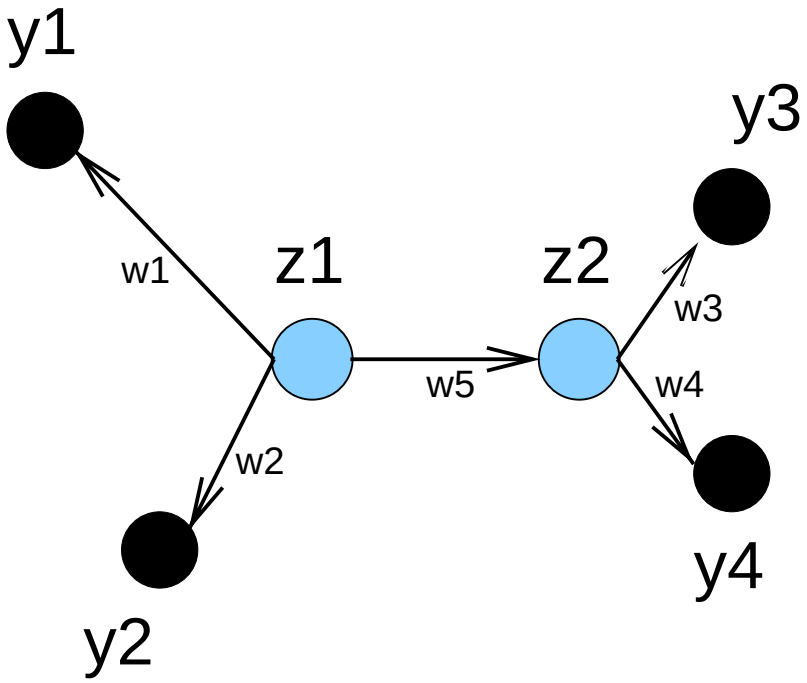


$$P(y_1, y_2, y_3, y_4, z_1, z_2 | \mathbf{w})$$

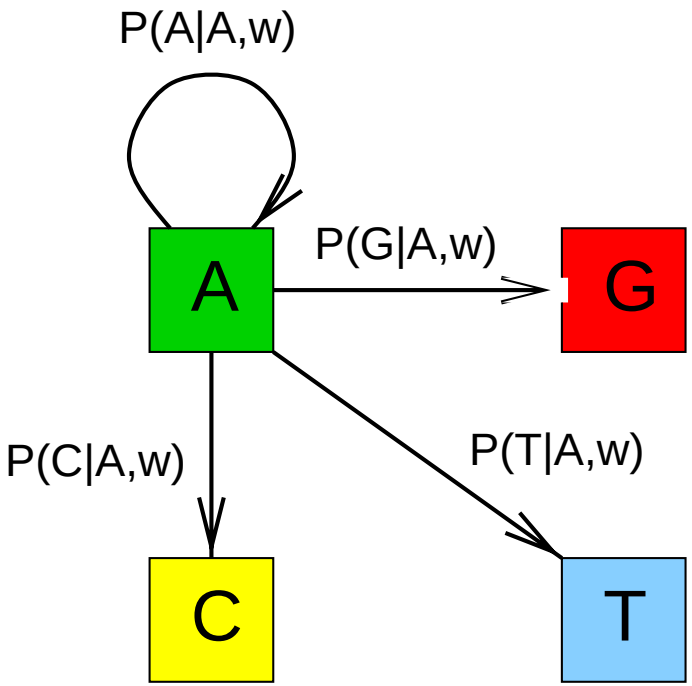


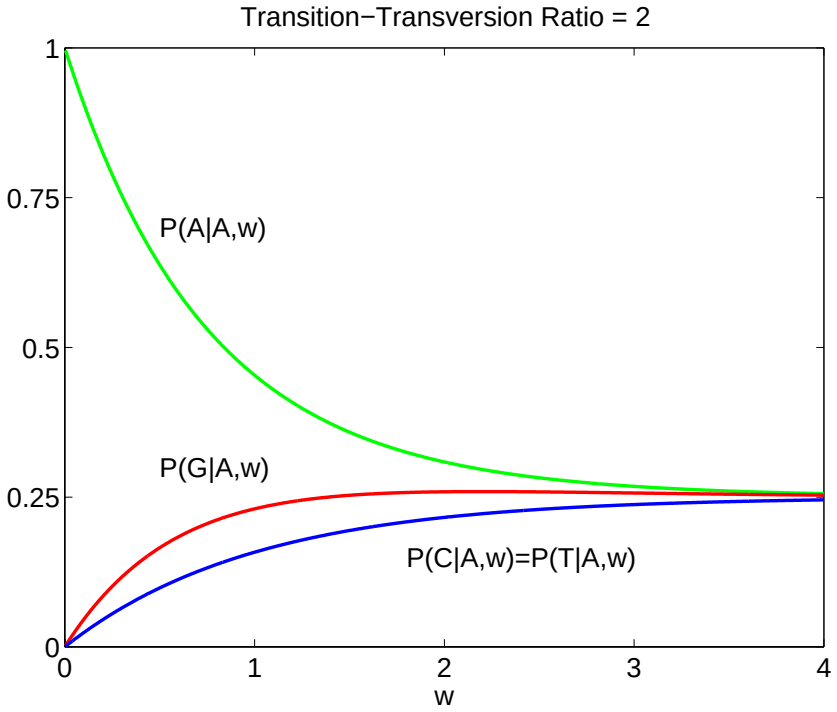
$$P(y_1, y_2, y_3, y_4, z_1, z_2 | \mathbf{w})$$

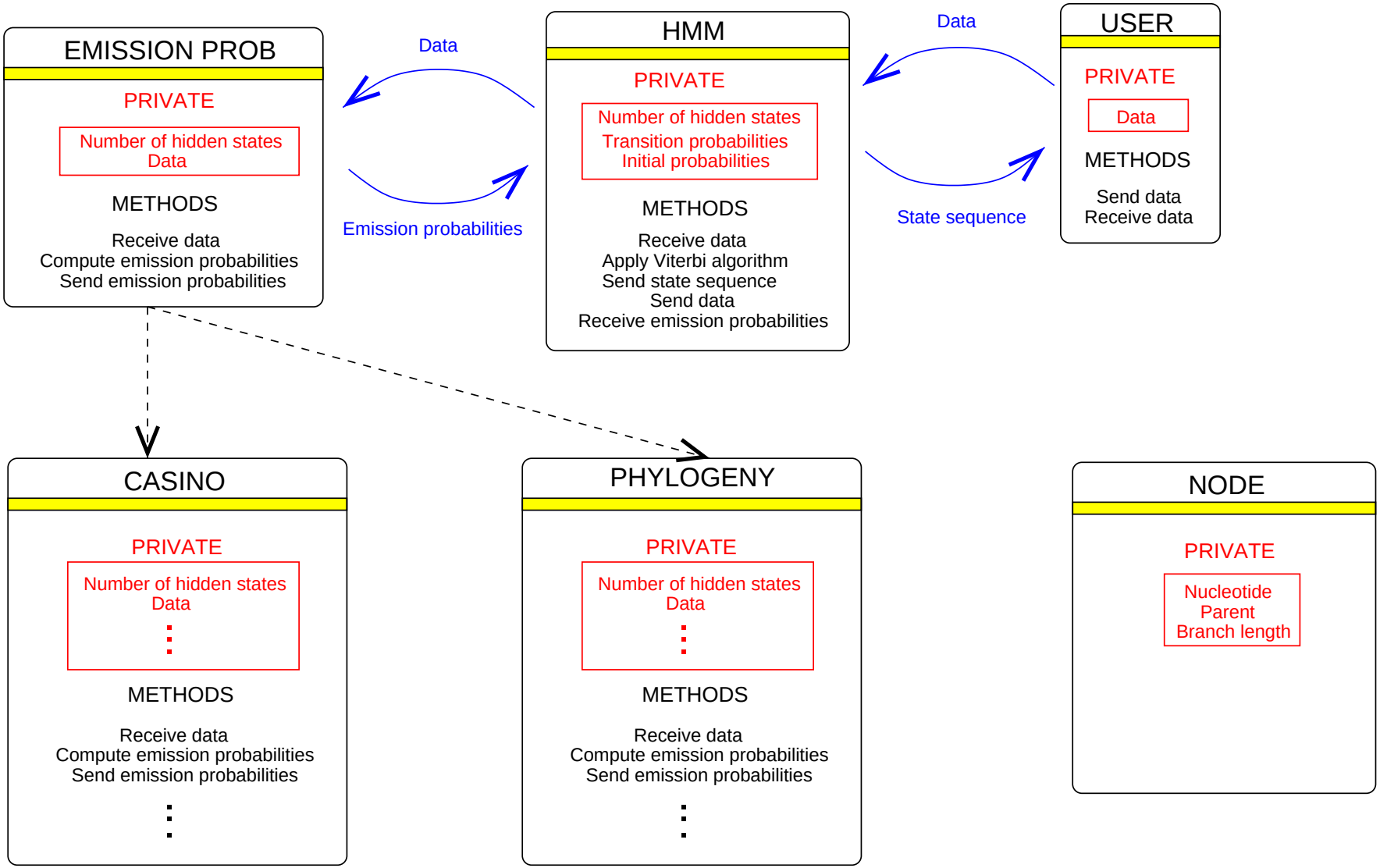


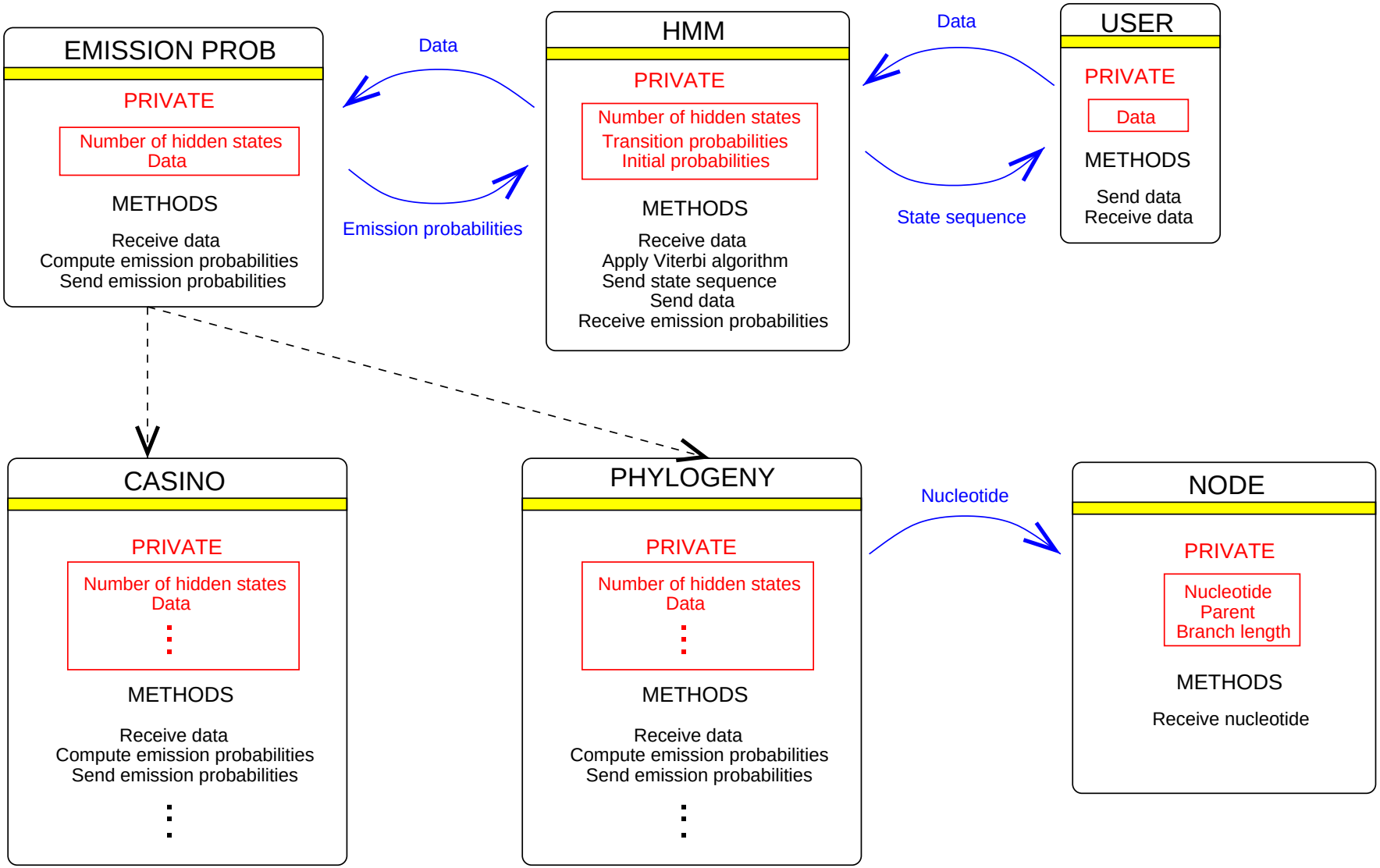
$$P(y_1, y_2, y_3, y_4, z_1, z_2 | \mathbf{w})$$

$$= P(y_1|z_1, w_1)P(y_2|z_1, w_2)P(z_2|z_1, w_5)P(y_3|z_2, w_3)P(y_4|z_2, w_4)P(z_1)$$


P(A|A,w)
A
P(G|A,w)
G
P(C|A,w)
P(T|A,w)
C
T


Transition−Transversion Ratio = 2
1
0.75
0.5
0.25
0
P(A|A,w)
P(G|A,w)
P(C|A,w)=P(T|A,w)
0
1
2
3
4
w


EMISSION PROB
PRIVATE
Number of hidden states
Data
METHODS
Receive data
Compute emission probabilities
Send emission probabilities
Data
Emission probabilities
HMM
PRIVATE
Number of hidden states
Transition probabilities
Initial probabilities
METHODS
Receive data
Apply Viterbi algorithm
Send state sequence
Send data
Receive emission probabilities
Data
State sequence
USER
PRIVATE
Data
METHODS
Send data
Receive data
CASINO
PRIVATE
Number of hidden states
Data
METHODS
Receive data
Compute emission probabilities
Send emission probabilities
PHYLOGENY
PRIVATE
Number of hidden states
Data
METHODS
Receive data
Compute emission probabilities
Send emission probabilities
NODE
PRIVATE
Nucleotide
Parent
Branch length


EMISSION PROB
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METHODS
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CASINO
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Nucleotide
NODE
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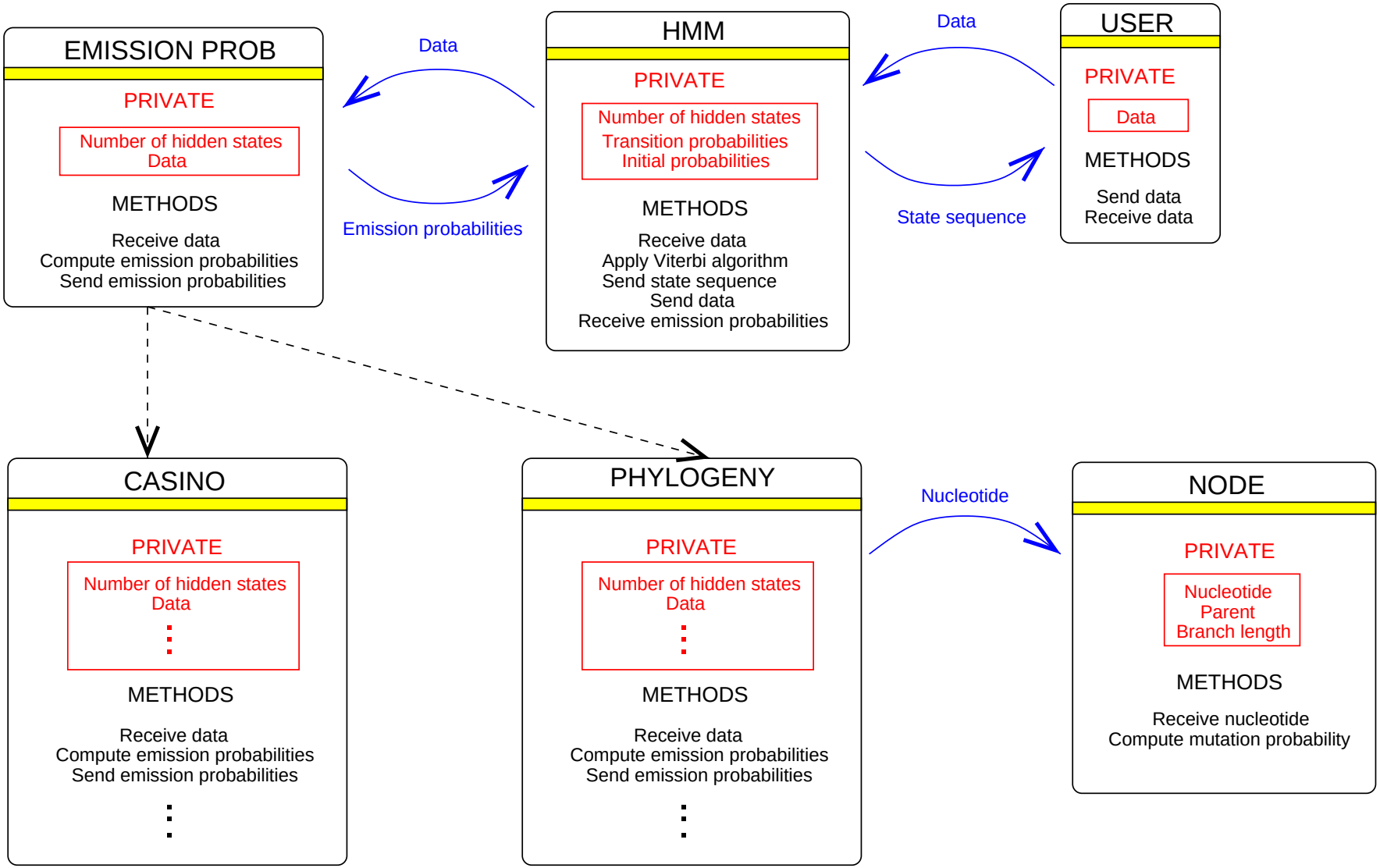
Nucleotide
Parent
Branch length
METHODS
Receive nucleotide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Compute emission probabilities
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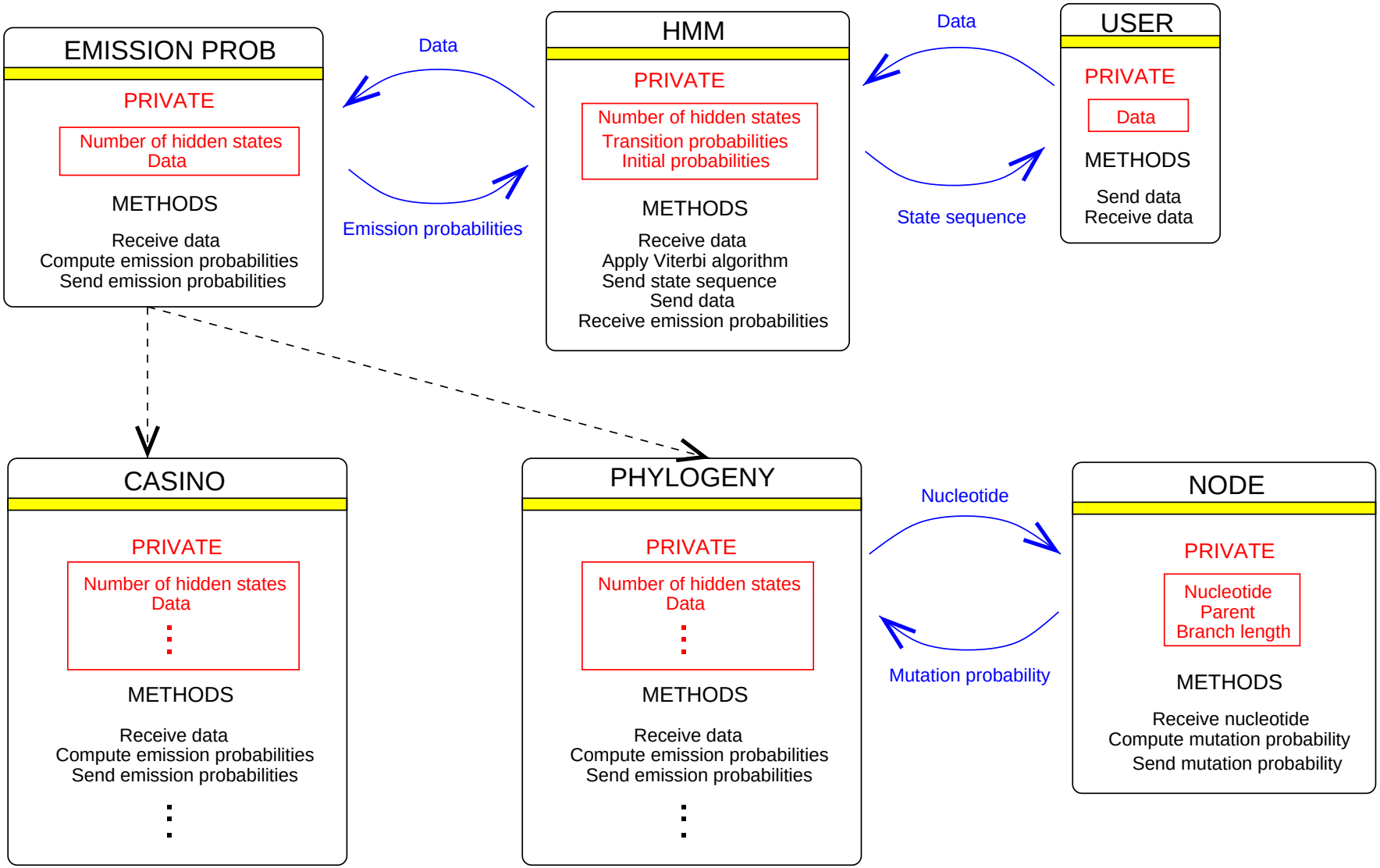
NODE
PRIVATE
Nucleotide
Parent
Branch length
METHODS
Receive nucleotide
Compute mutation probability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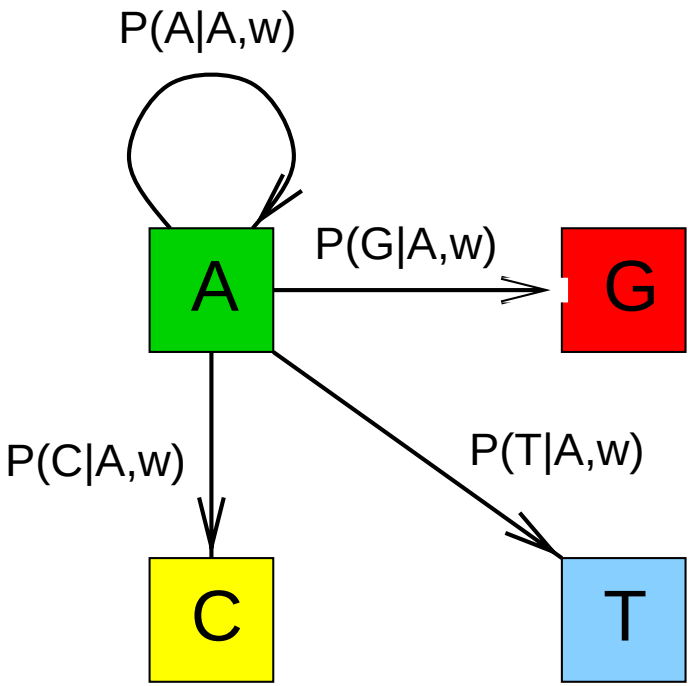
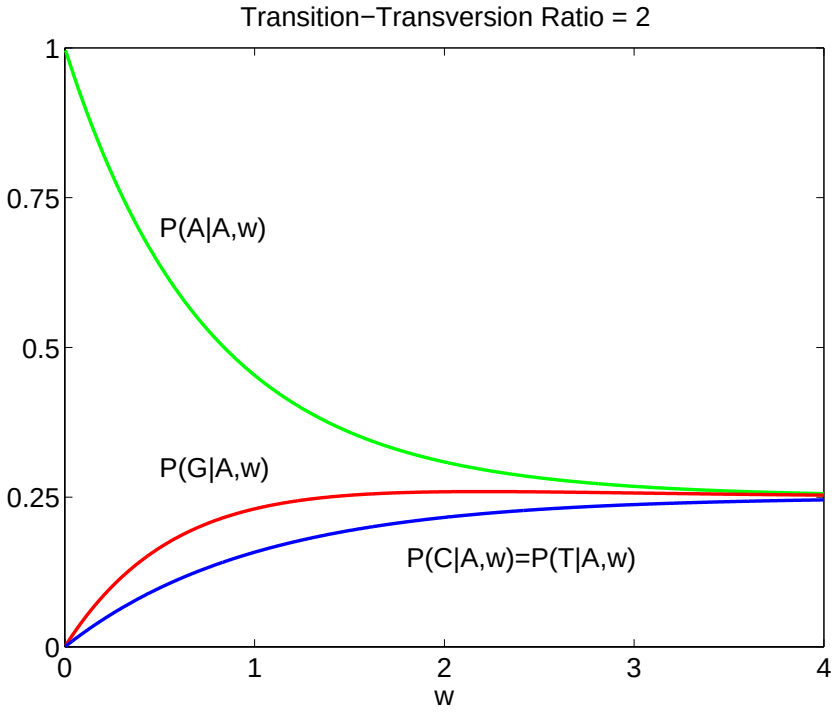
Data
METHODS
Receive data
Compute emission probabilities
Send emission probabilities
Nucleotide
Mutation probability
NODE
PRIVATE
Nucleotide
Parent
Branch length
METHODS
Receive nucleotide
Compute mutation probability
Send mutation probability


P(A|A,w)
A
P(G|A,w)
G
P(C|A,w)
P(T|A,w)
C
T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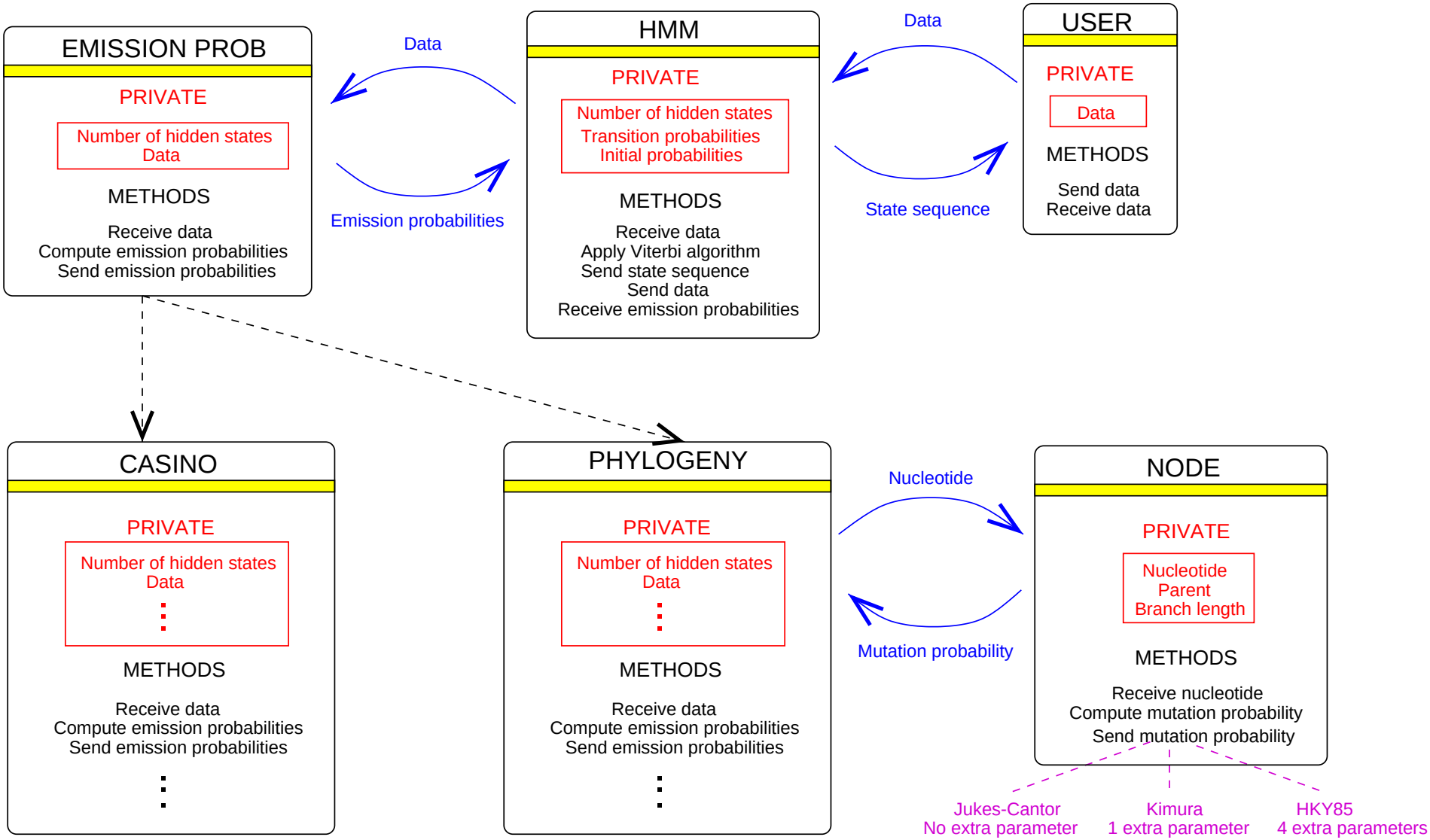
3
4
w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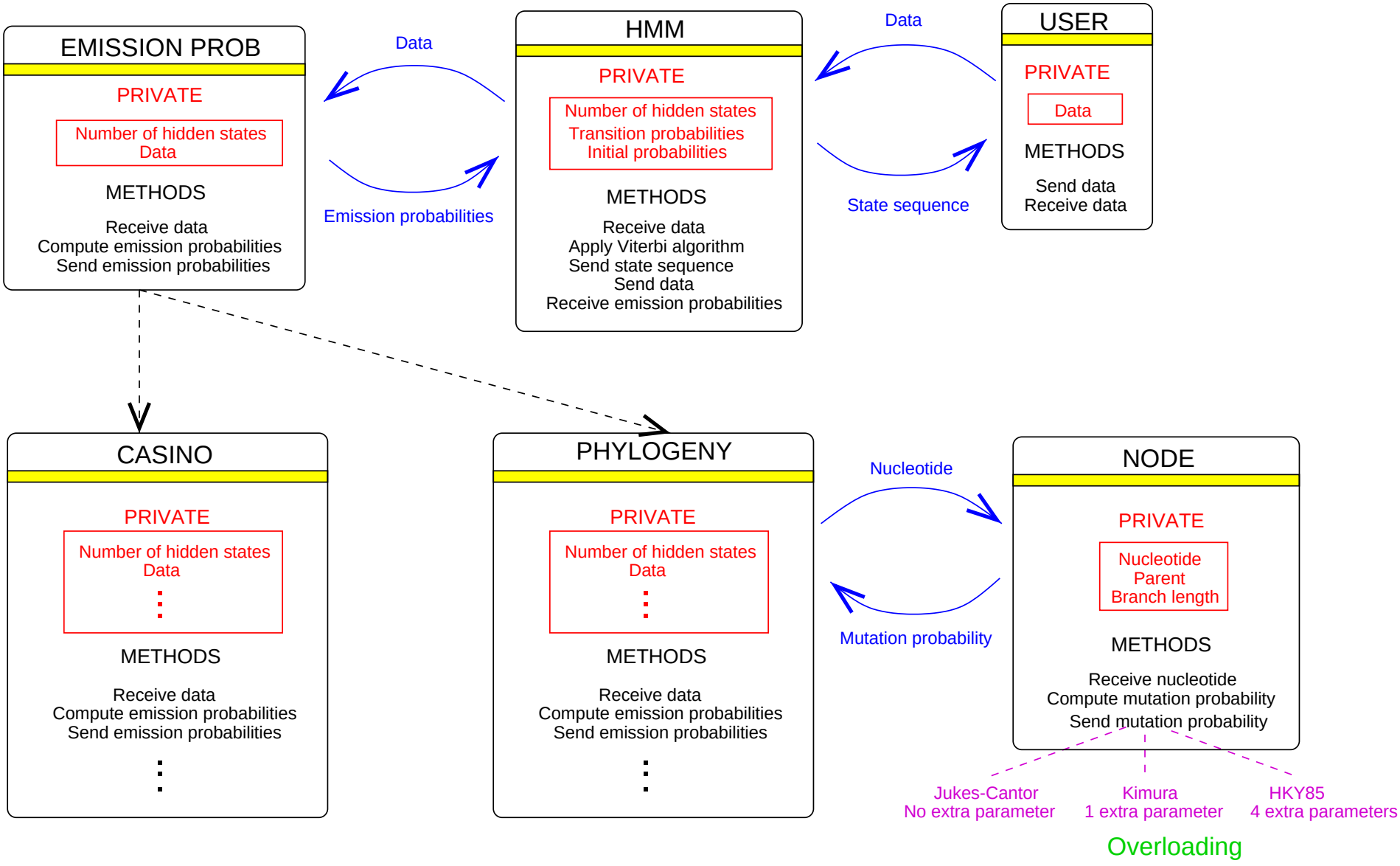
Data
METHODS
Receive data
Compute emission probabilities
Send emission probabilities
Nucleotide
Mutation probability
NODE
PRIVATE
Nucleotide
Parent
Branch length
METHODS
Receive nucleotide
Compute mutation probability
Send mutation probability
Jukes-Cantor
No extra parameter
Kimura
1 extra parameter
HKY85
4 extra parameters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Kimura
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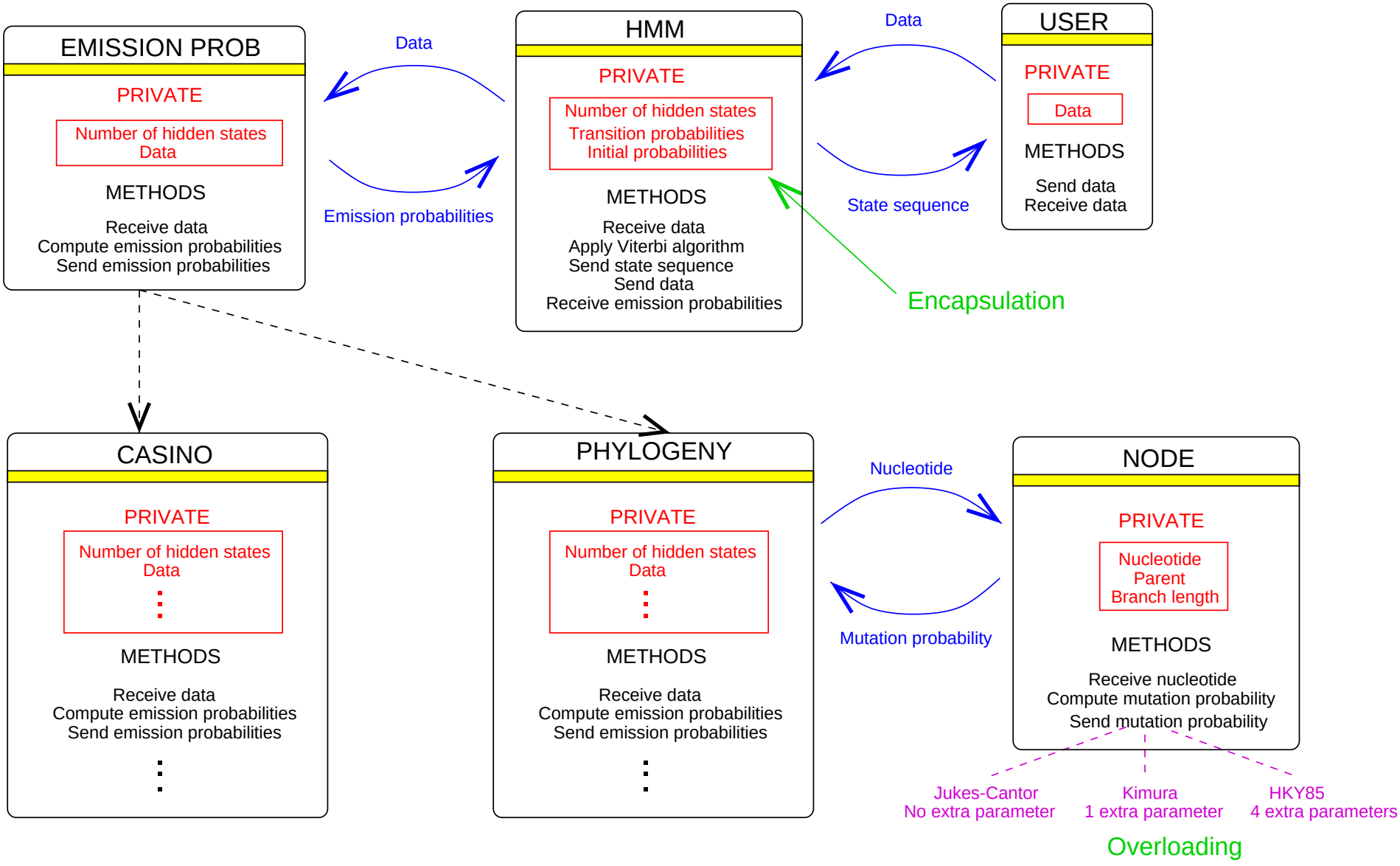
HKY85
4 extra parameters
Overloading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USER
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Encapsulation
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PRIVATE
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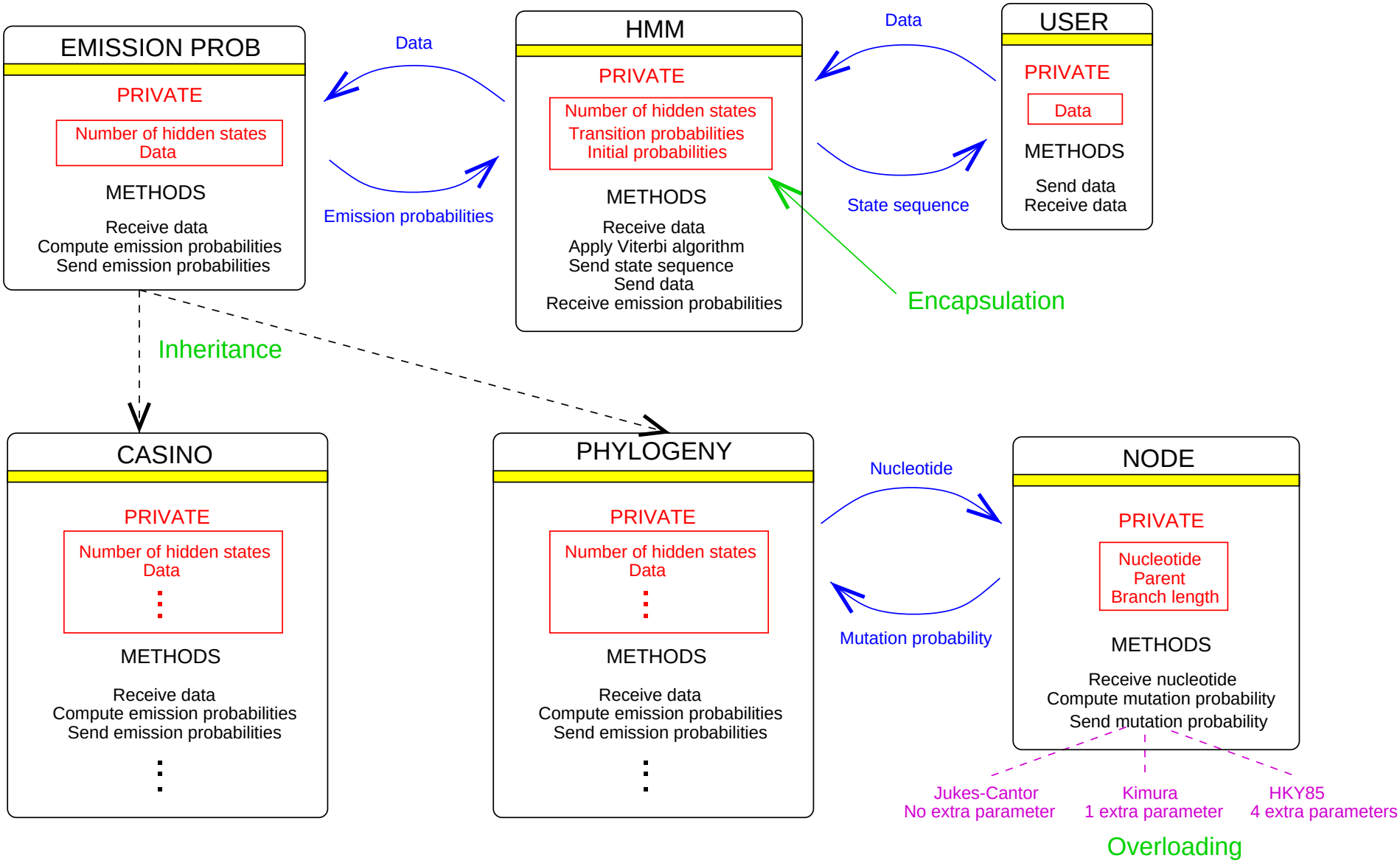
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Initial probabilities
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Receive data
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State sequence
USER
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METHODS
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Encapsulation
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Number of hidden states
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Send emission probabilities
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Number of hidden states
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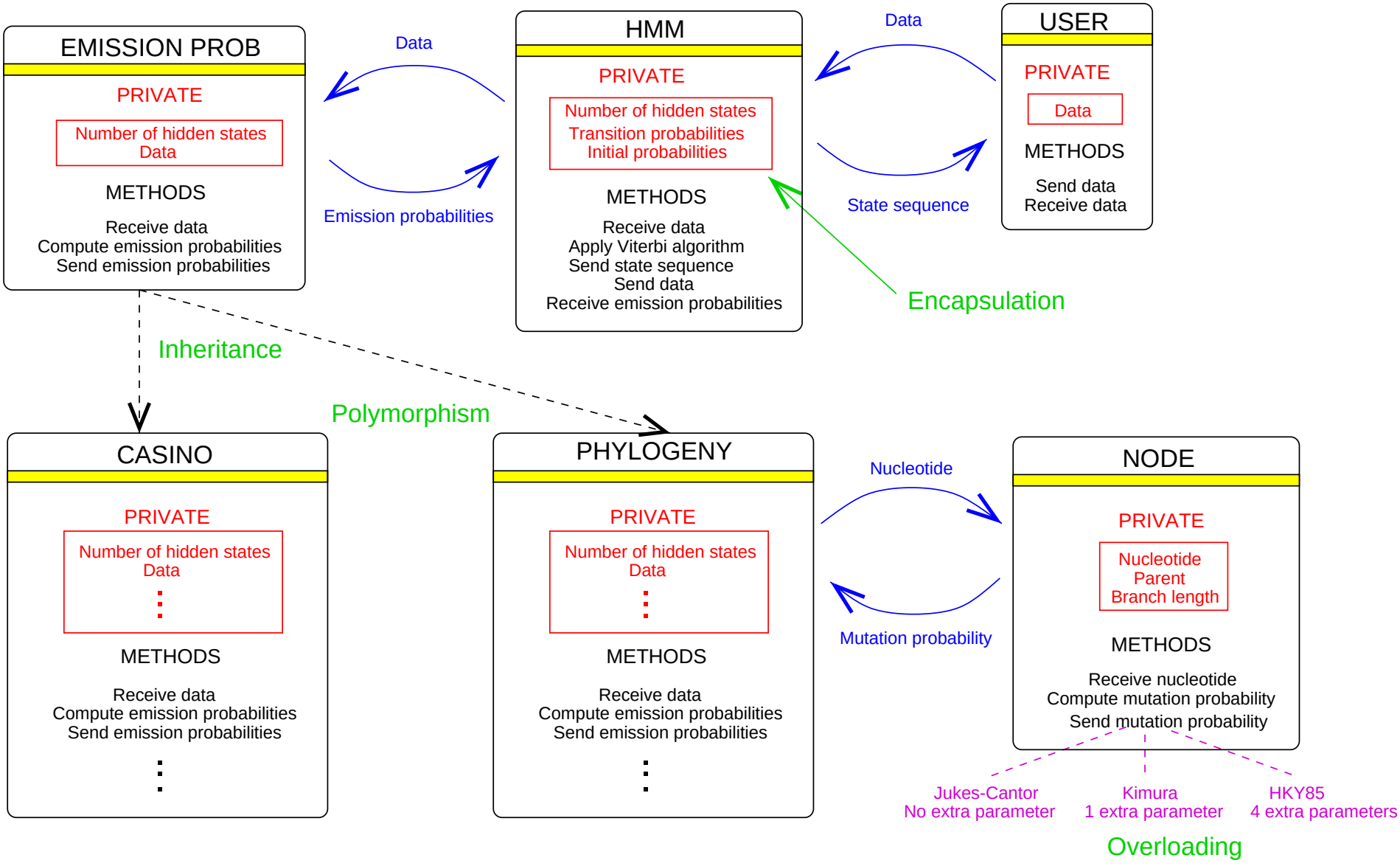
Overloading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Receive emission probabilities
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State sequence
USER
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METHODS
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