Hidden Markov Models

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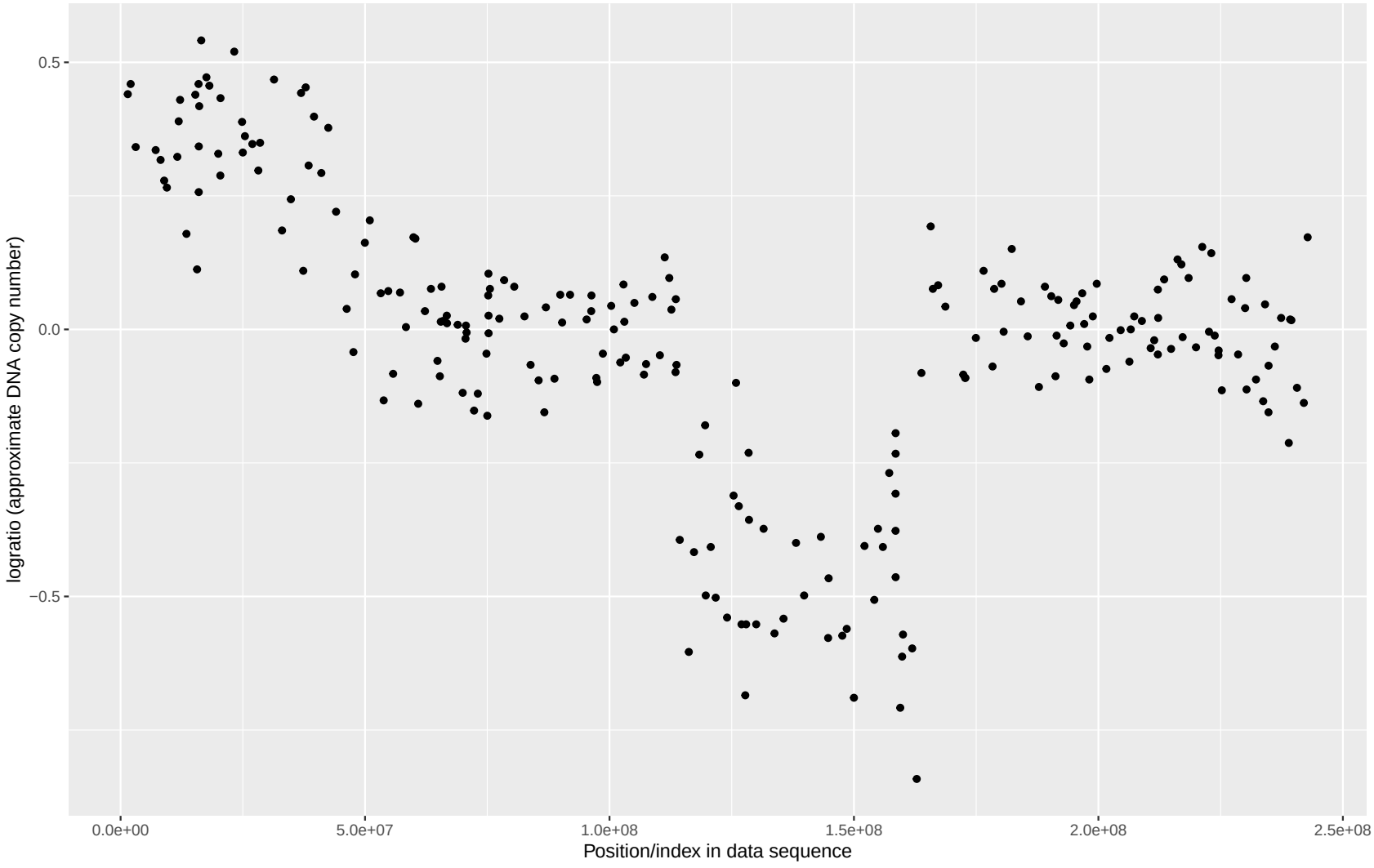
Background: detecting abrupt changes is important

Example from cancer diagnosis: breakpoints are associated with aggressive disease in neuroblastoma.

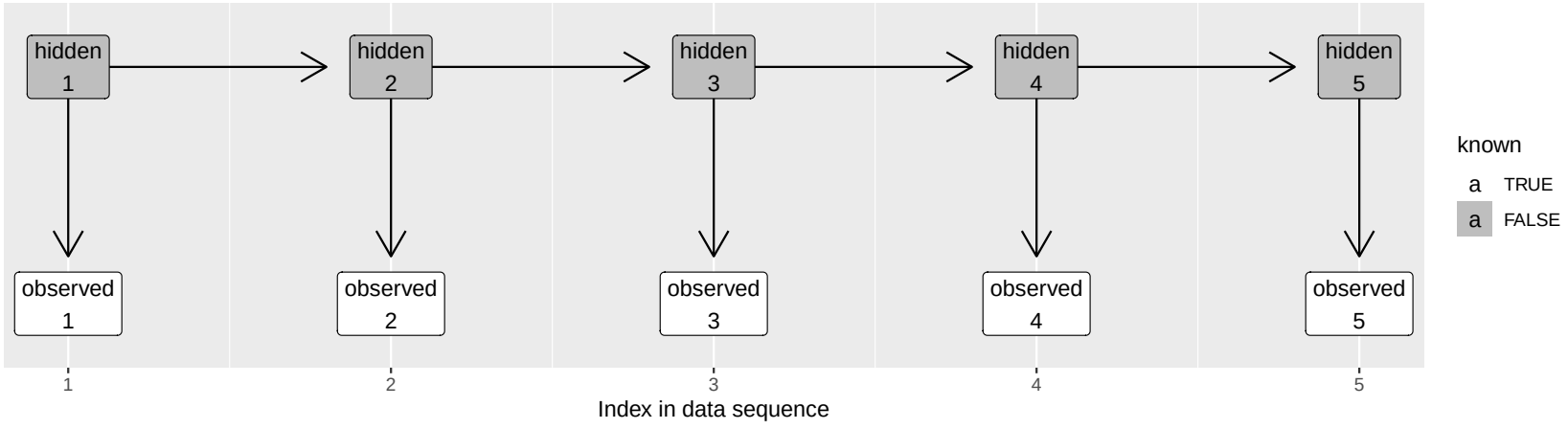


Motivation for Hidden Markov Models (HMMs)

- Sometimes we have an interpretation / expectation of what the segments/clusters mean.
- For example in DNA copy number data the logratio=0 means normal copy number (two copies – one from each parent), whereas higher logratio values indicate gain/amplification and lower values indicate loss/deletion.

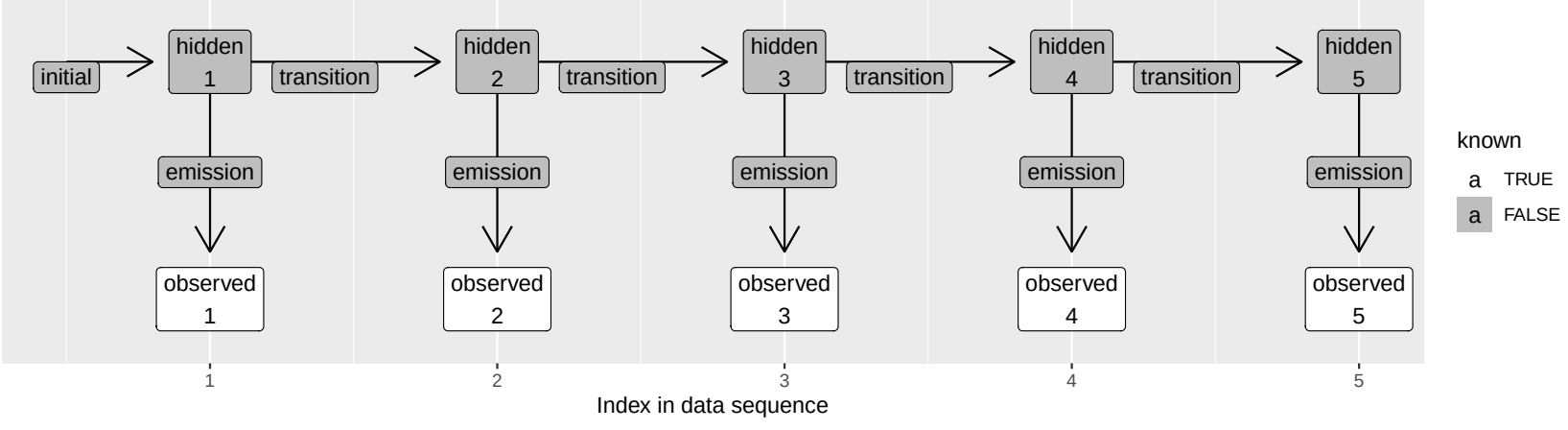
HMM ideas

- Each observed data variable in the sequence has a corresponding un-observed (hidden) state variable.
- There are typically a finite number of possible values for each hidden state variable, $k \in \{1, \ldots, K\}$.
- Markov assumption: first-order dependency (each hidden variable only depends on the previous hidden variable in the sequence).



Parameters of HMM

- transition matrix: $A \in [0,1]^{K \times K}$ for K clusters. Each entry a_{ij} is the probability of transitioning from state i to state j.
- initial state distribution: $\pi \in [0,1]^K$ (prior weights).
- emission: likelihood of observing data y in state k, $b_k(y) = \text{NormalDensity}(y, \mu_k, \sigma^2) \in \mathbb{R}$, parameterized by mean μ_k, variance σ^2 (or standard deviation $= \text{sd} = \sigma$).
- These parameters are unknown in advance and must be learned from the data.
- Comparison with Gaussian Mixture Models: HMM has all of GMM parameters, plus transition matrix.

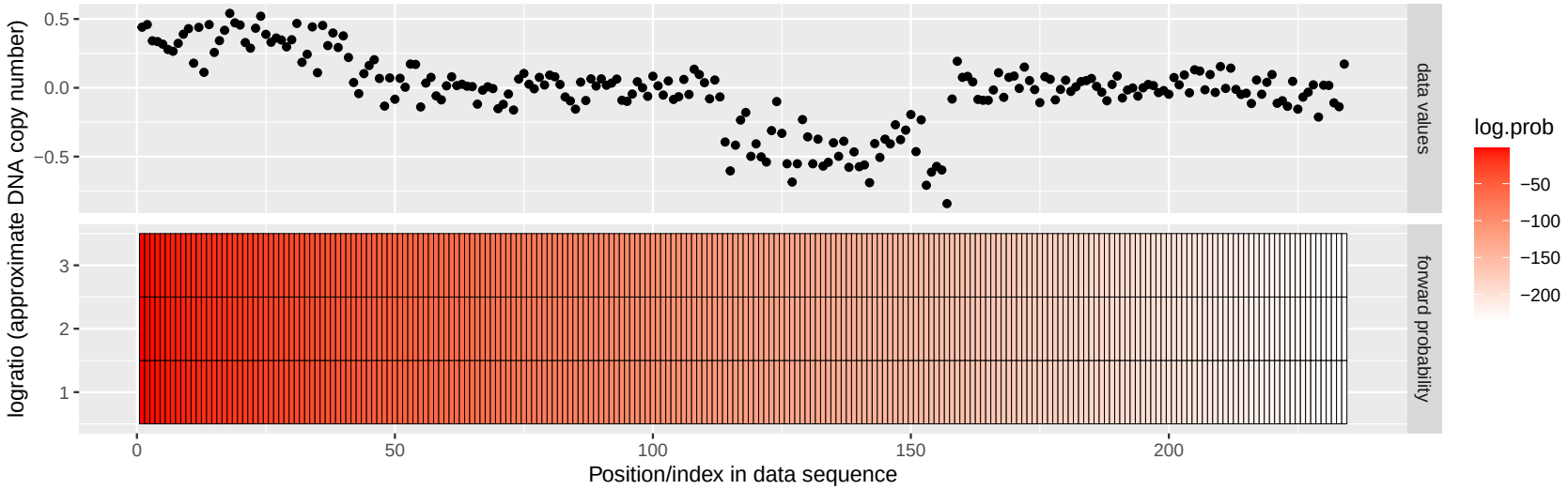


Three problems and algorithms

- Evaluation of likelihood of a given data sequence and model parameters $=>$ forward algorithm.
- Decoding most likely sequence of hidden states given observed data and model parameters $=>$ Viterbi algorithm.
- Learning model parameters that maximize likelihood of a given data set $=>$ Baum-Welch algorithm.

Forward algorithm

- Assume each state $k \in \{1, \ldots, K\}$ has an emission probability function $b_k(o_t)$ for observed data o_t at time t.
- Let a_{kj} be a transition parameter (probability of going from state k to state j).
- Initialization: for all states $j \in \{1, \ldots, K\}$, $\alpha_1(j) = \pi_j b_j(o_1)$.
- Then we can recursively compute the forward path probability, $\alpha_t(j) = \sum_{k=1}^{K} \alpha_{t-1}(k) a_{kj} b_j(o_t)$.
- Total log likelihood is summed over all states at the last data point in the sequence.



The numerical underflow problem

- Probability p_t at each time t is in [0,1] so $\prod_{t=1}^{N} p_t \to 0$.
- For large enough N (several hundred) double precision arithmetic underflows (probability $= 0$ on computer although it is non-zero mathematically).

```
N.data <- seq(321, 325)
prob <- 0.1^N.data
data.table(N.data, prob, log.prob=log10(prob))
```

```
##    N.data          prob  log.prob
## 1:    321 9.980126e-322 -321.0009
## 2:    322 9.881313e-323 -322.0052
## 3:    323 9.881313e-324 -323.0052
## 4:    324  0.000000e+00      -Inf
## 5:    325  0.000000e+00      -Inf
```

Implementation details to avoid numerical underflow

- Use a double precision number to store log(probability) value instead of probability value.
- Instead of multiplying probability values, sum log(probability) values.

```
N.data <- seq(321, 325)
log.prob <- N.data*log10(0.1)
data.table(N.data, log.prob, prob=10^log.prob)
```

```
##    N.data log.prob          prob
## 1:    321     -321 9.980126e-322
## 2:    322     -322 9.881313e-323
## 3:    323     -323 9.881313e-324
## 4:    324     -324  0.000000e+00
## 5:    325     -325  0.000000e+00
```

Implementation details to avoid numerical underflow

Instead of summing probability values, use log-sum-exp trick (subtract away $m = \max\{\log p, \log q\}$ in exponent), $p + q = e^{\log p} + e^{\log q}$.

$$\log(p+q) = \log(e^{\log p} + e^{\log q}) = m + \log(e^{\log p - m} - e^{\log q - m})$$

```
data.table(log.p=-324, log.q=seq(-320, -326)
)[,          m := ifelse(log.p < log.q, log.q, log.p)][,
  log.sum.exp := m + log10(10^(log.p-m)+10^(log.q-m))][,
    naive.sum := log10(10^log.p+10^log.q)][]
```

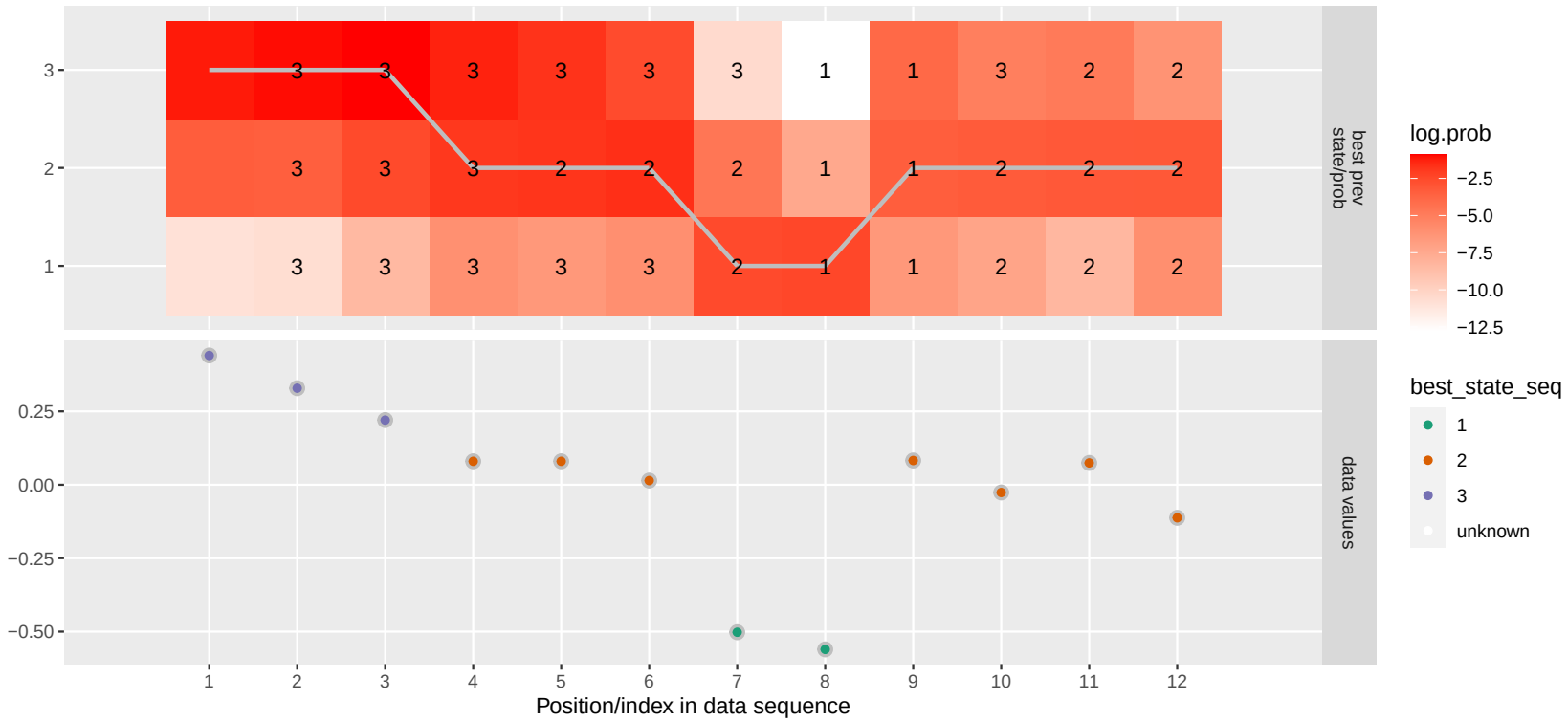
```
##    log.p log.q    m log.sum.exp naive.sum
## 1:  -324  -320 -320   -320.0000 -320.0000
## 2:  -324  -321 -321   -320.9996 -321.0009
## 3:  -324  -322 -322   -321.9957 -322.0052
## 4:  -324  -323 -323   -322.9586 -323.0052
## 5:  -324  -324 -324   -323.6990      -Inf
## 6:  -324  -325 -324   -323.9586      -Inf
## 7:  -324  -326 -324   -323.9957      -Inf
```

Viterbi algorithm

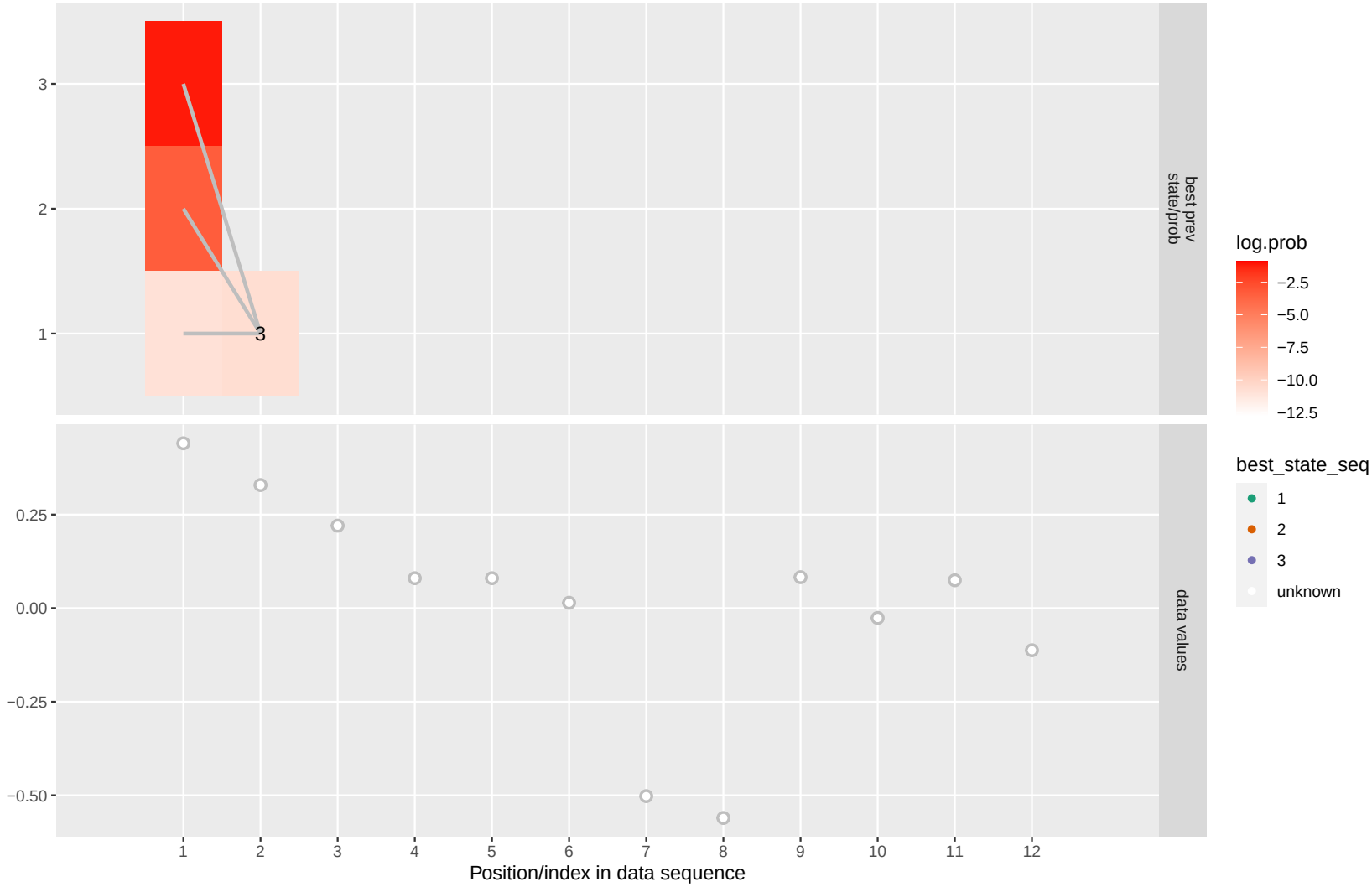
- Assume each state $k \in \{1, \ldots, K\}$ has an emission probability function $b_k(o_t)$ for observed data o_t at time t.
- Let a_{kj} be a transition parameter (probability of going from state k to state j).
- Initialization: for all states $j \in \{1, \ldots, K\}$, $v_1(j) = \pi_j b_j(o_1)$.
- Then we can recursively compute the probability of the best sequence of hidden variables that ends at data point t in state j, $v_t(j) = \max_{k \in \{1,\ldots,K\}} v_{t-1}(k) a_{kj} b_j(o_t)$.
- Also need to store a matrix of best k values which achieved the max for every t, j.
- To compute best state sequence, first find k with max $v_N(k)$ then repeatedly examine previously stored best k values.

Viterbi algorithm example for $K = 3$ states

```
## List of 4
##  $ mean      : num [1:3] -0.5 0 0.3
##  $ sd        : num 0.2
##  $ transition: num [1:3, 1:3] 0.6 0.2 0.2 0.2 0.6 0.2 0.
##  $ initial   : num [1:3] 0.6 0.2 0.2
```



Viterbi forward pass



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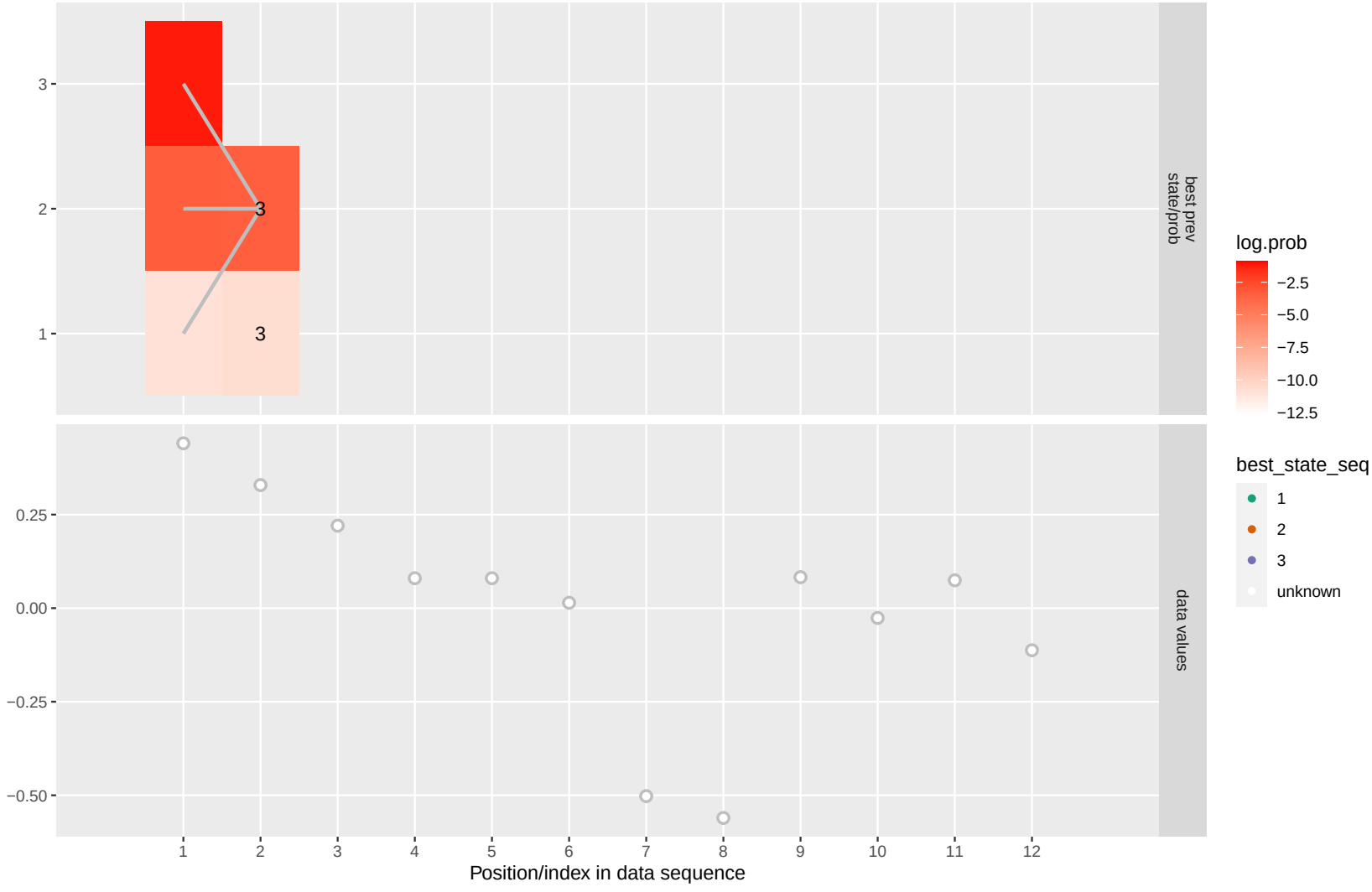

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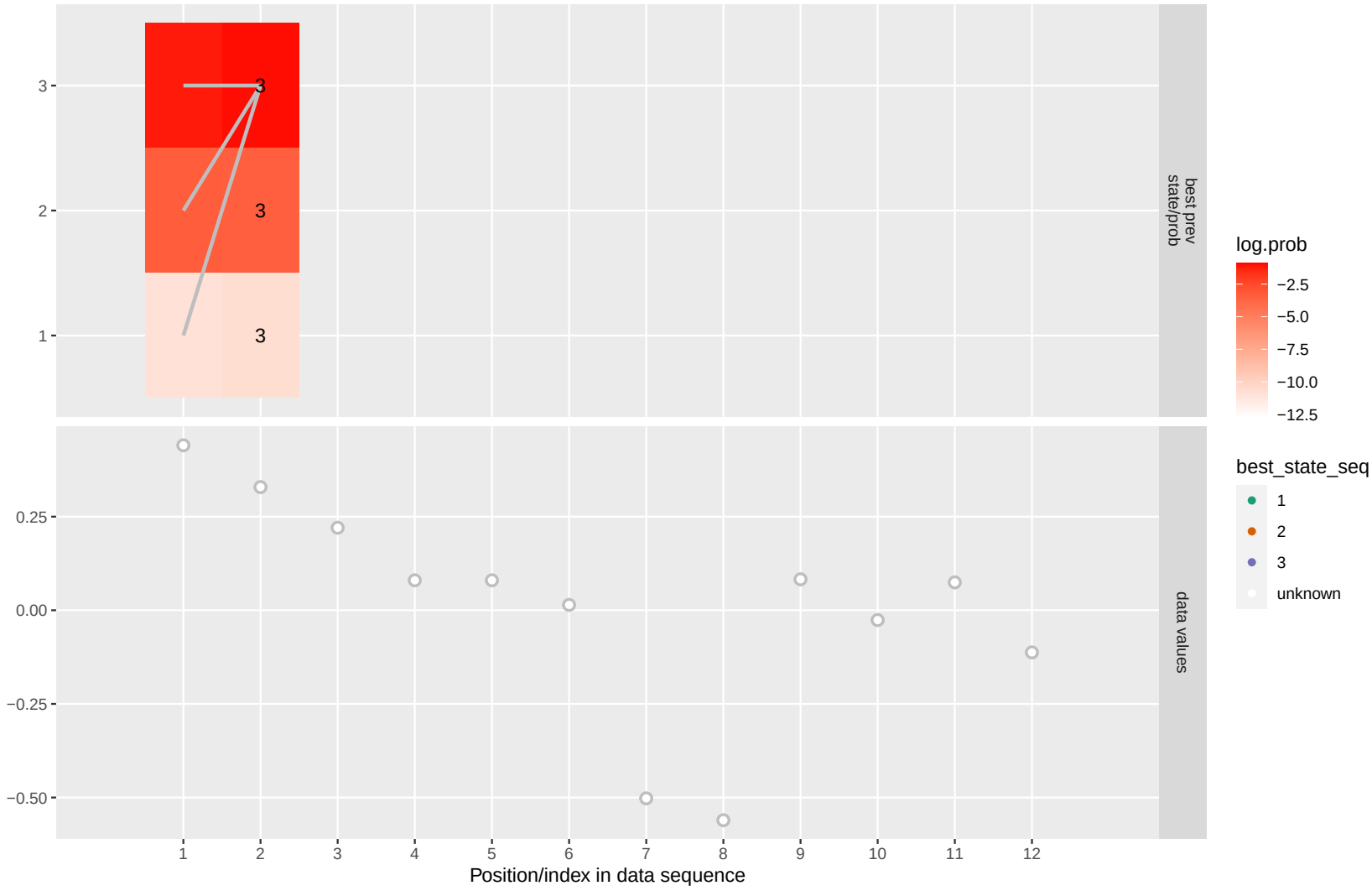

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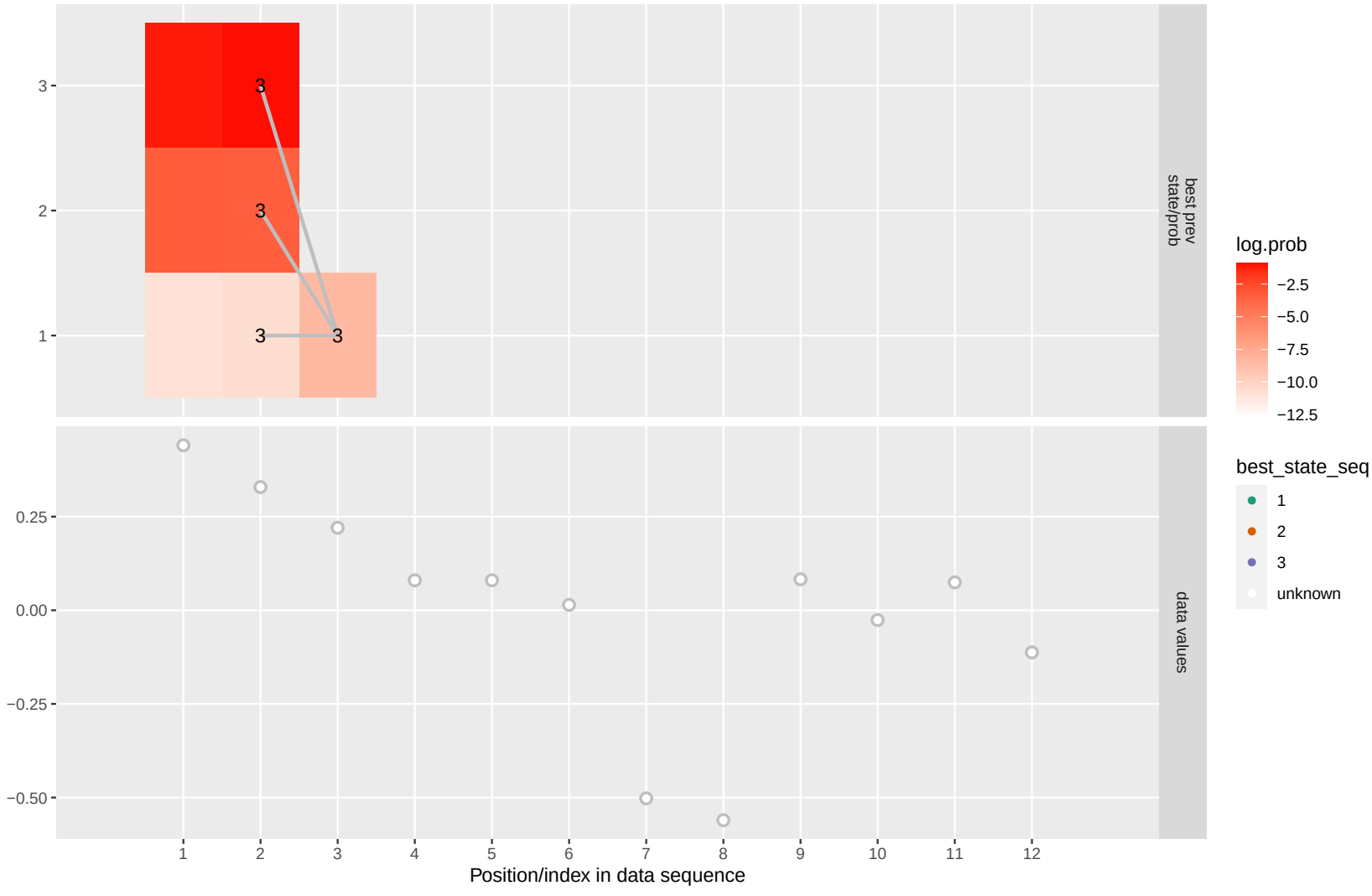

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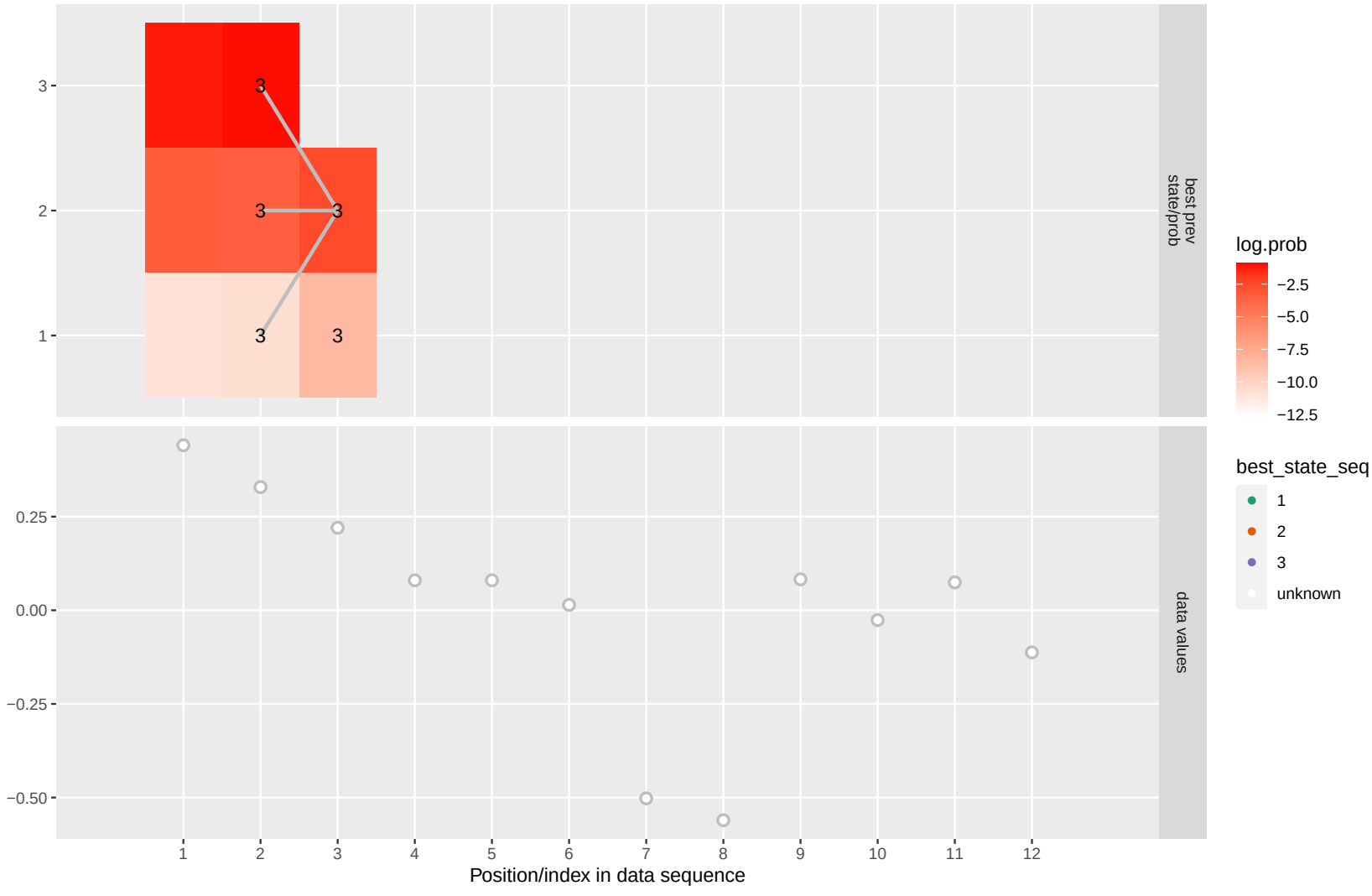

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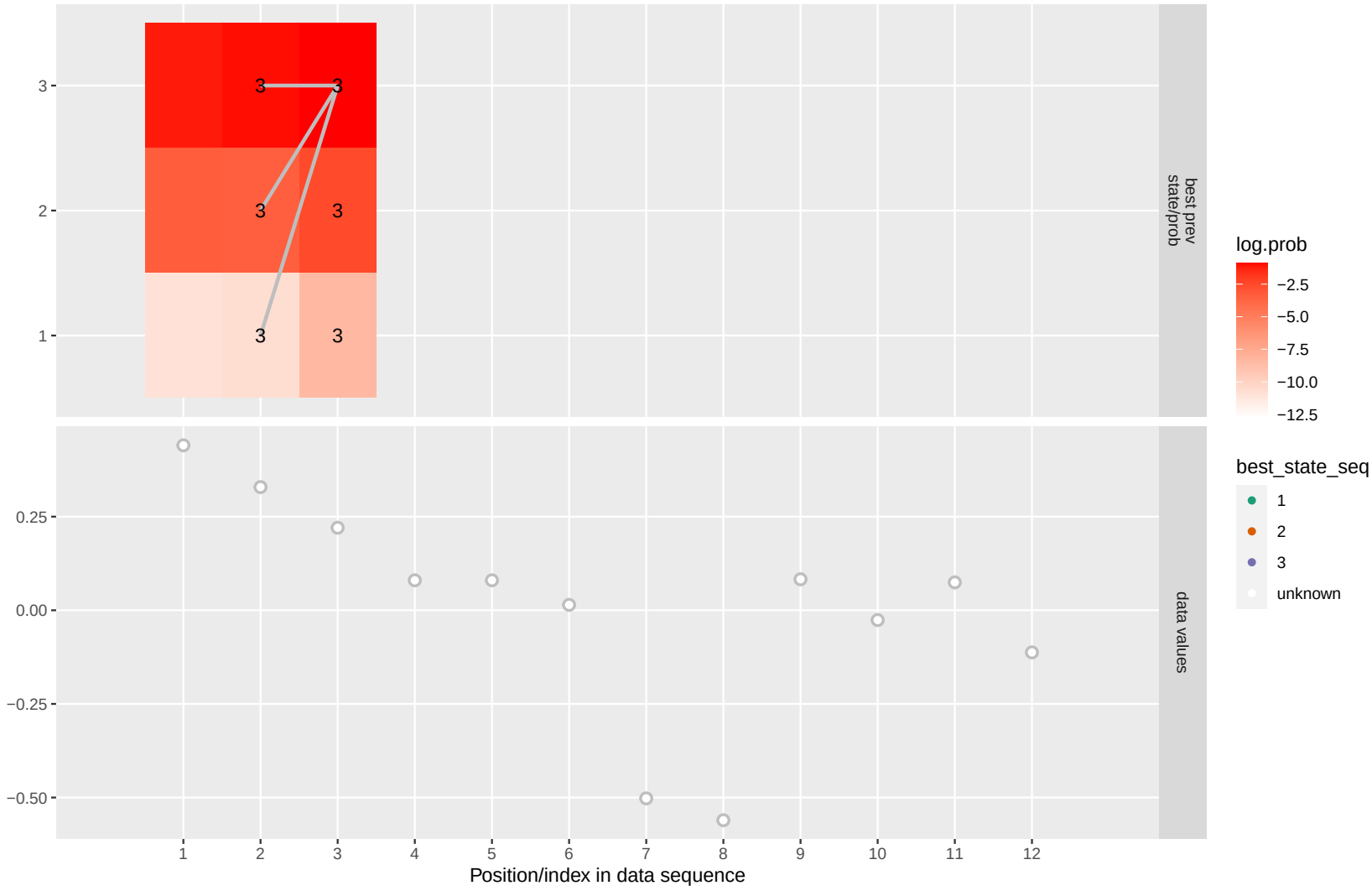

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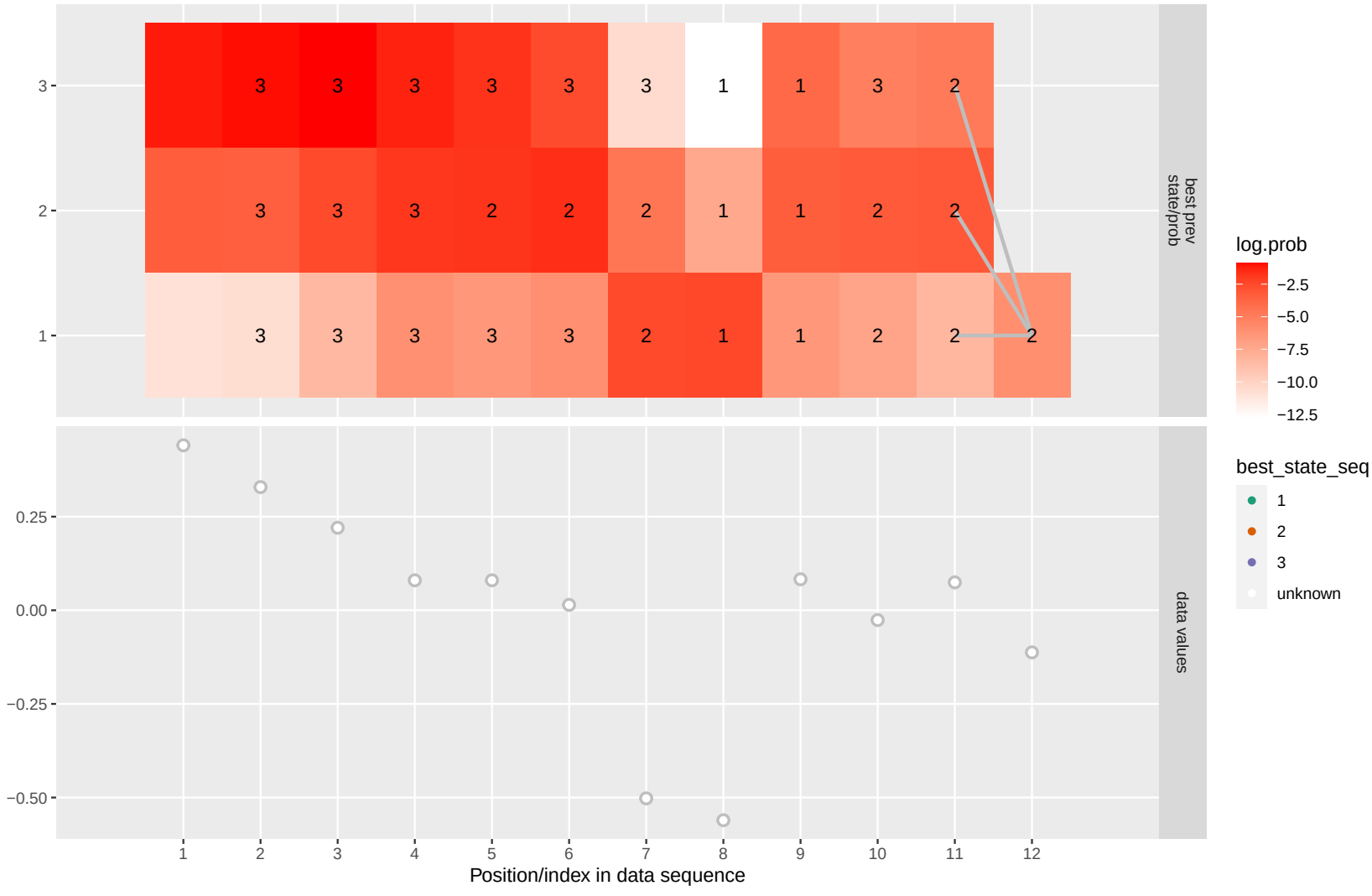

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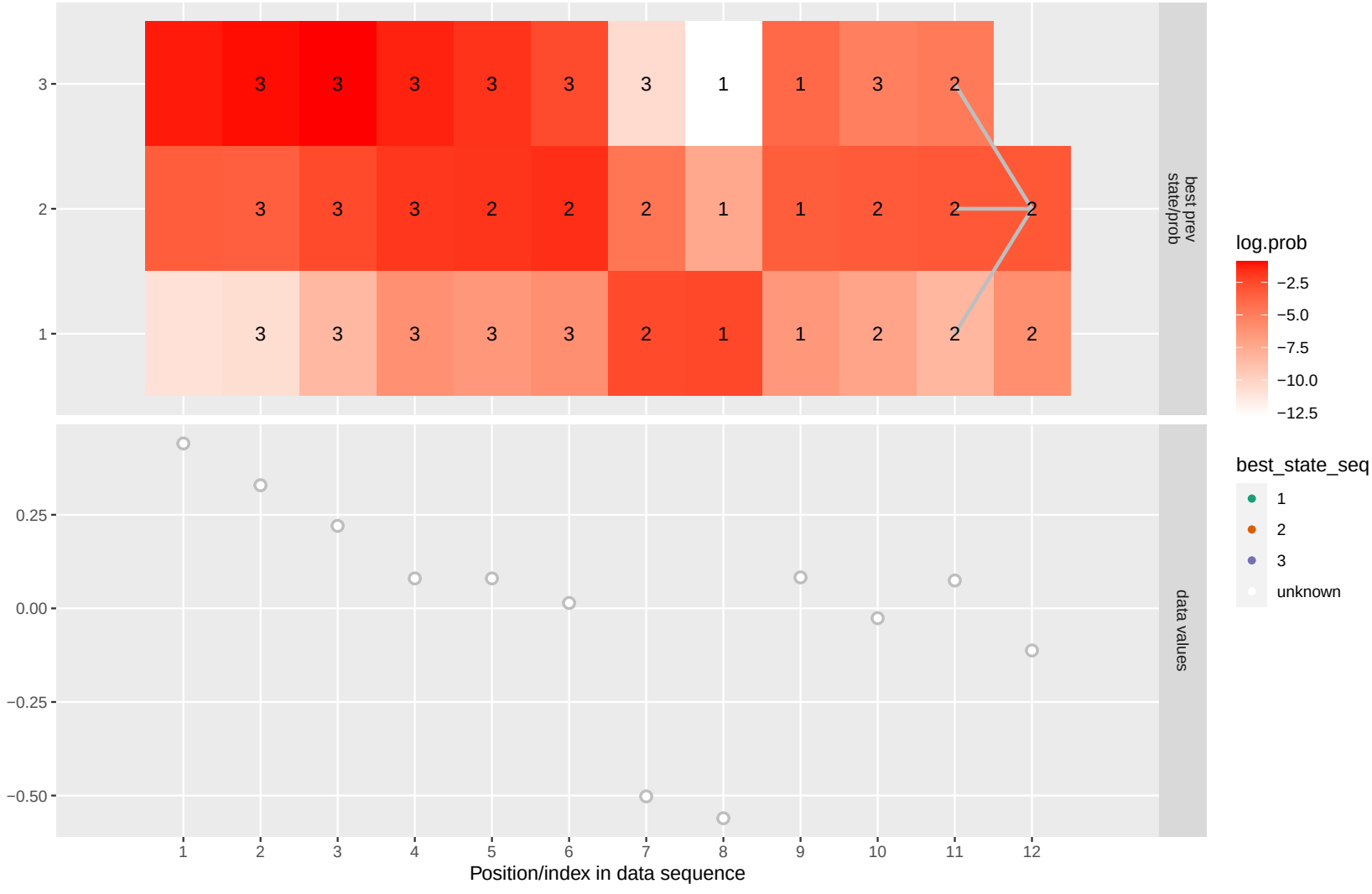

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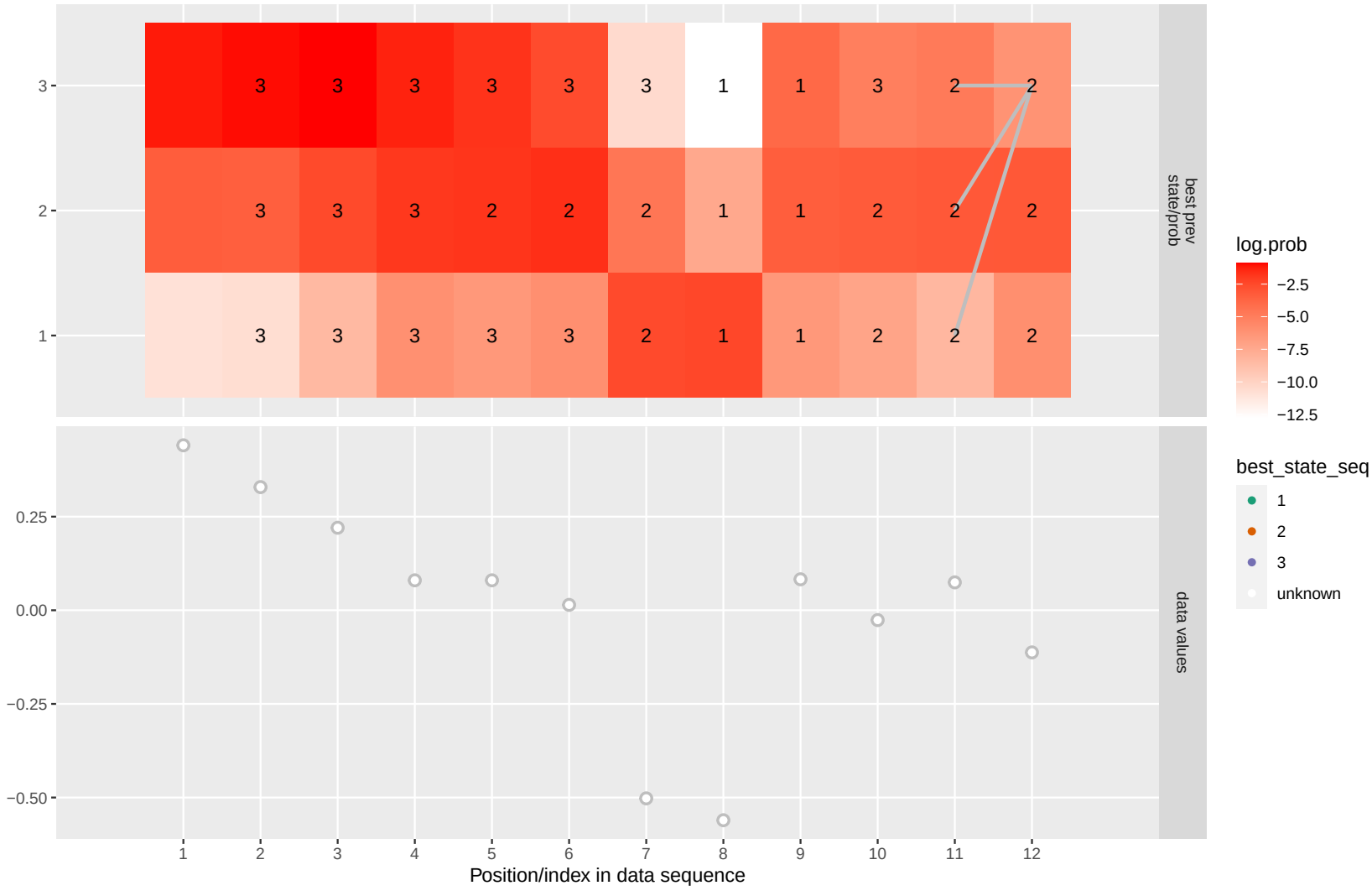
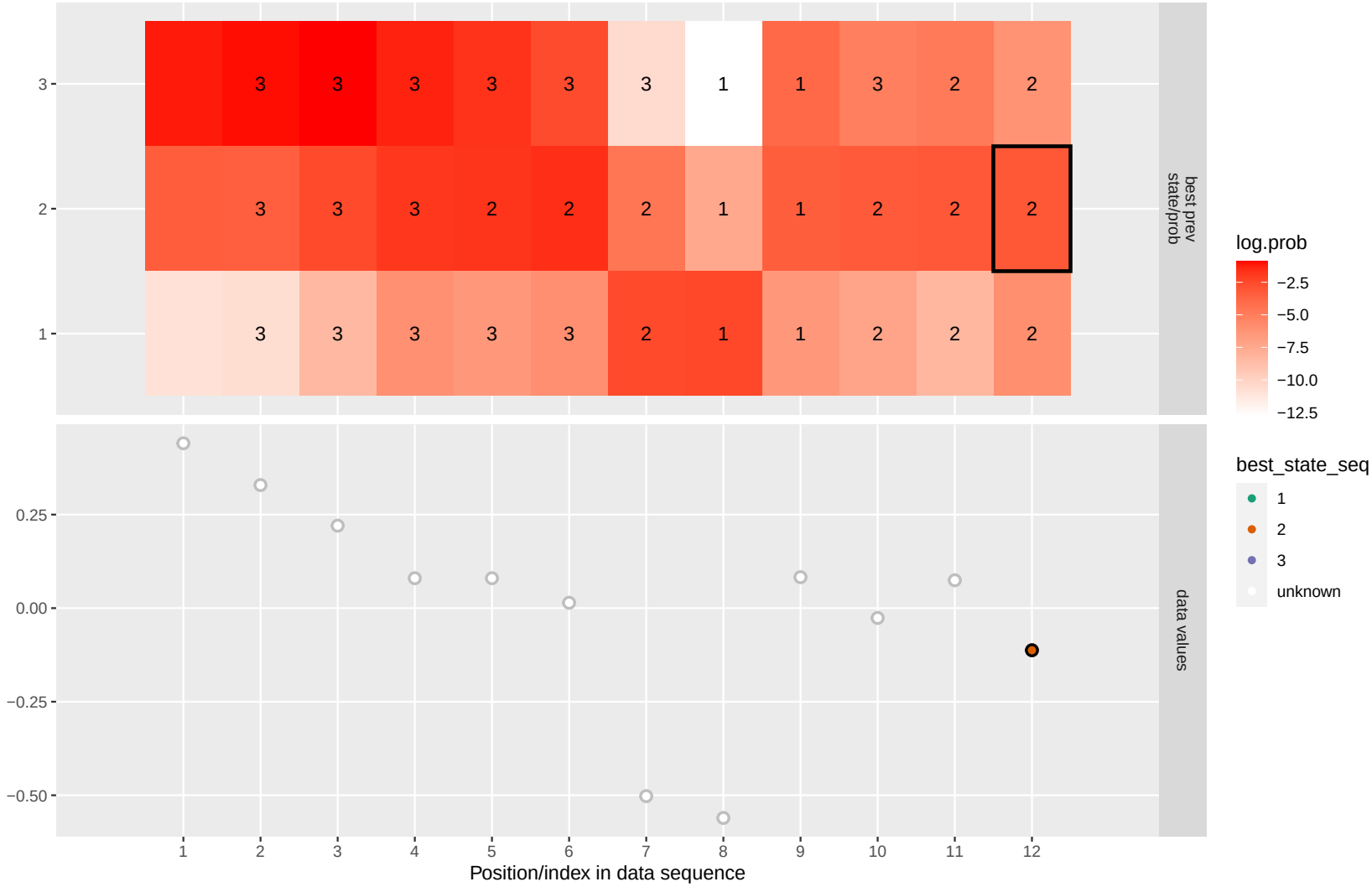


Viterbi backtracking



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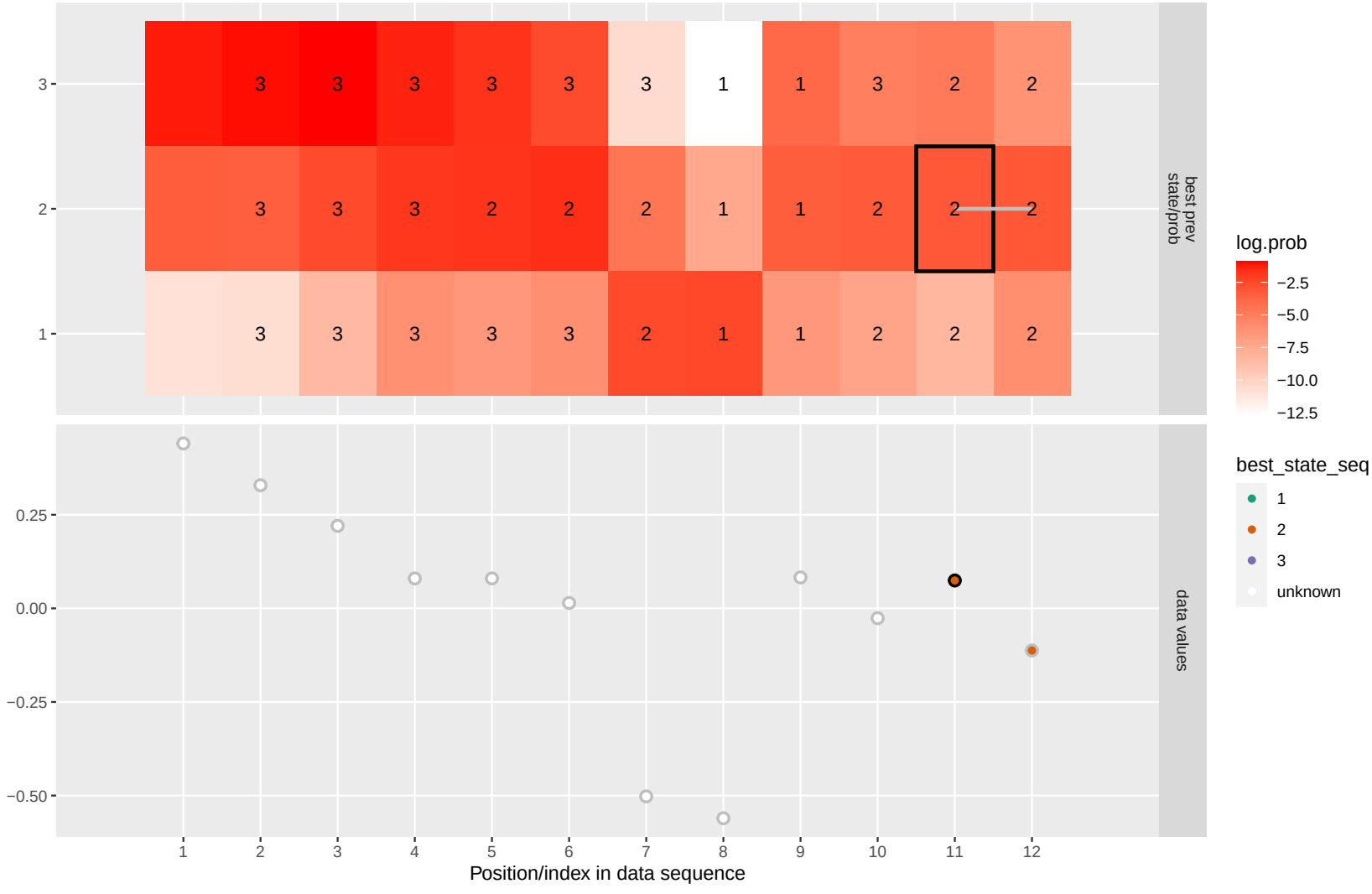

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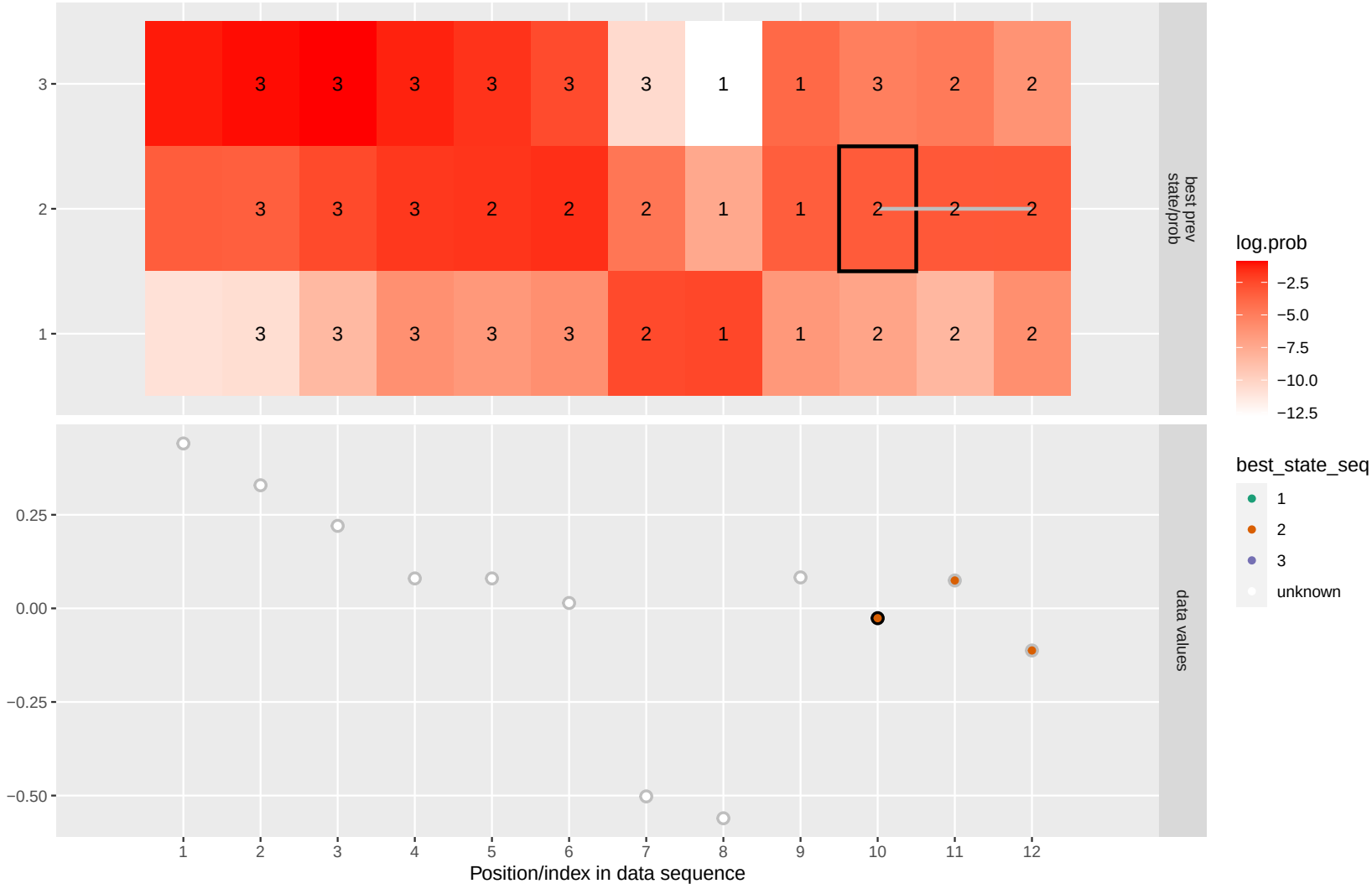

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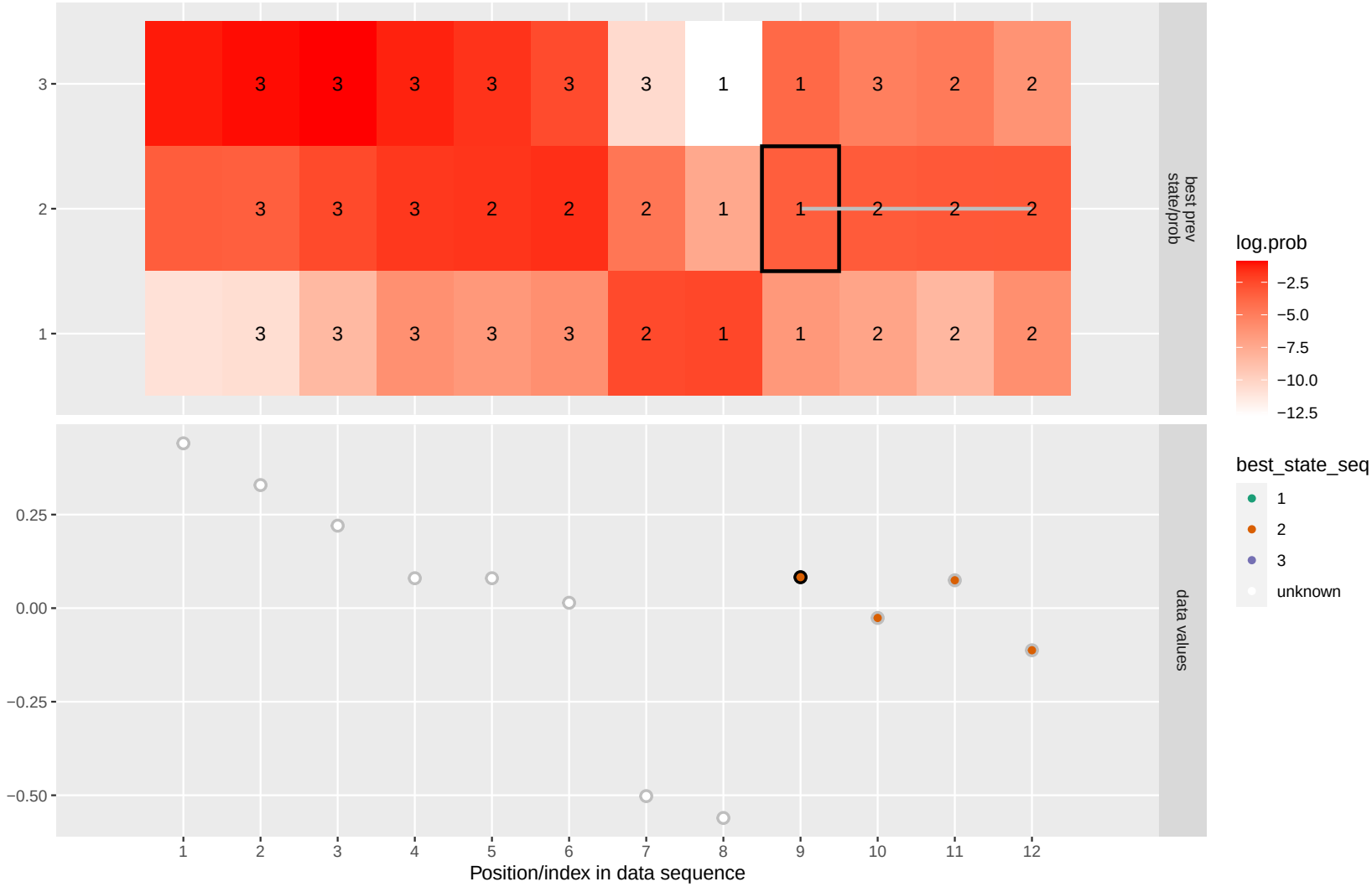

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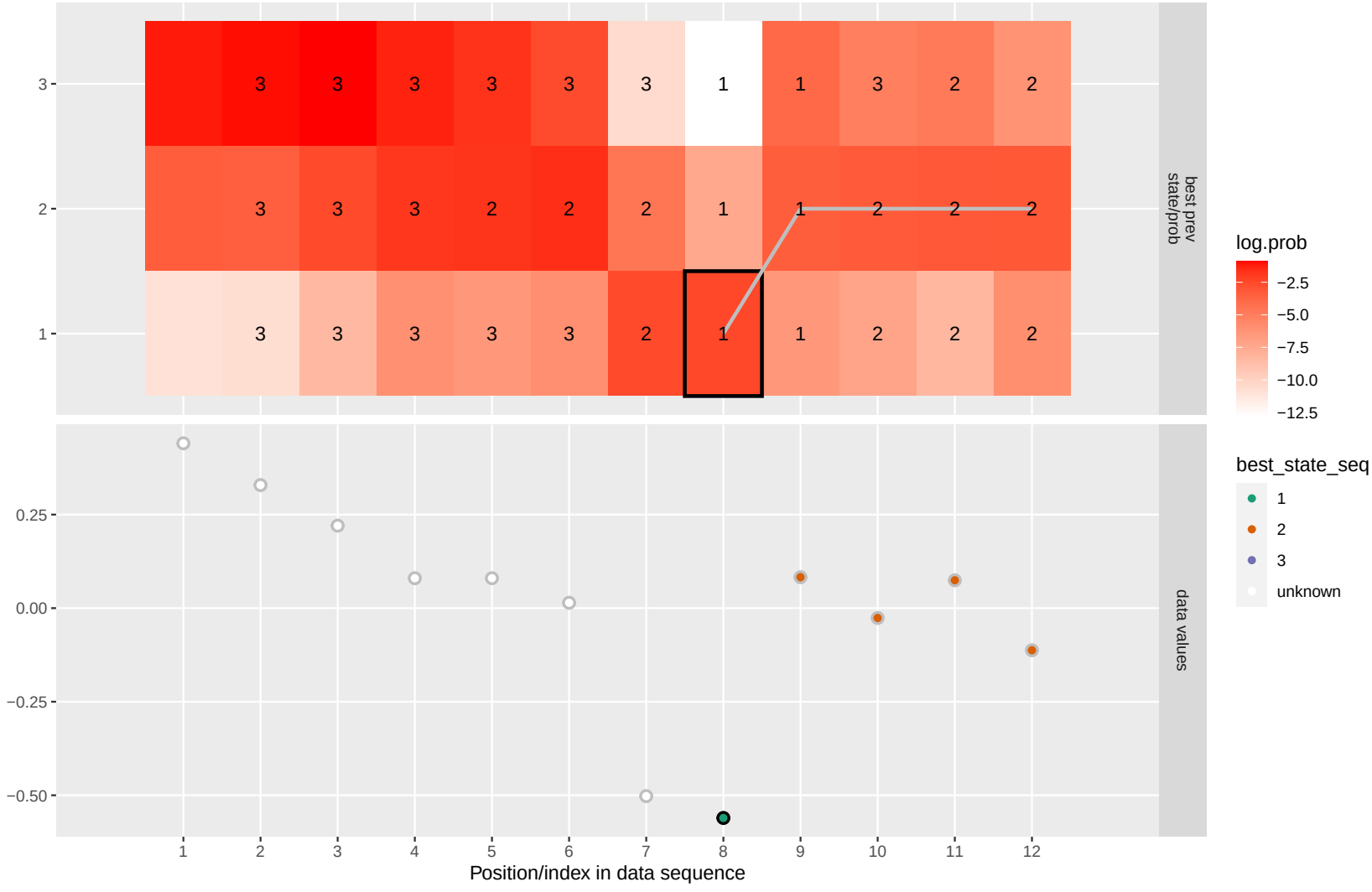

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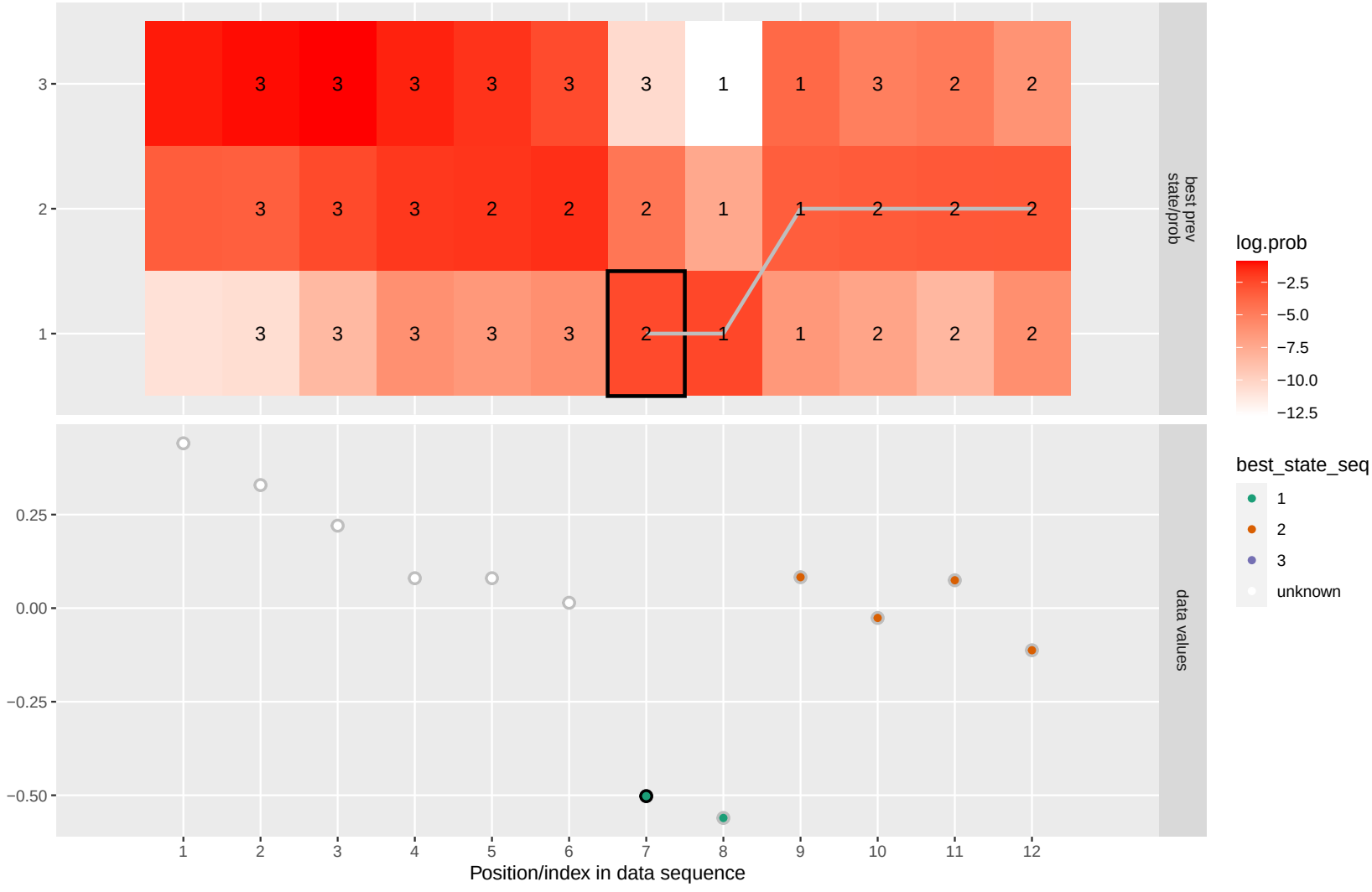

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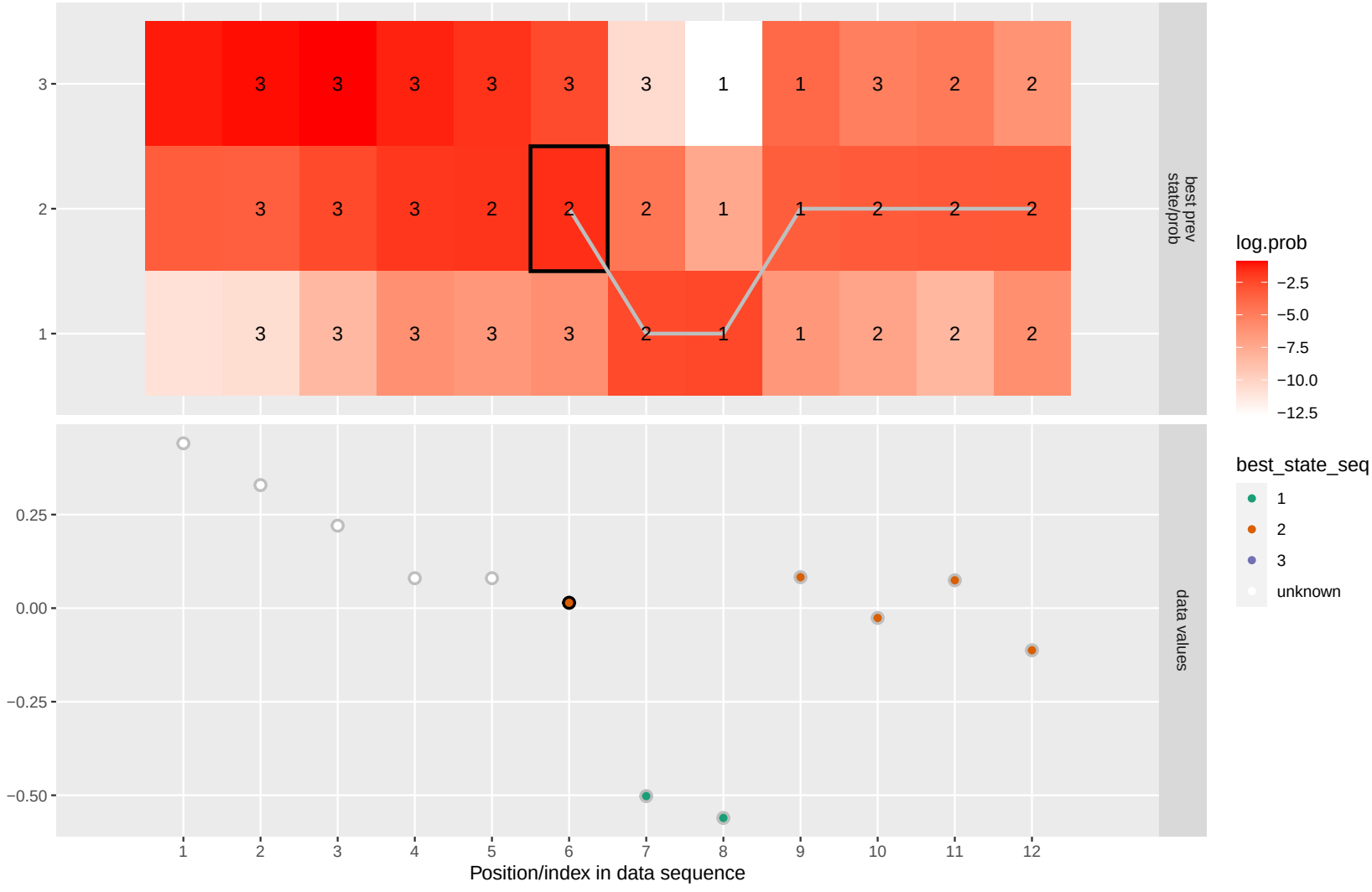

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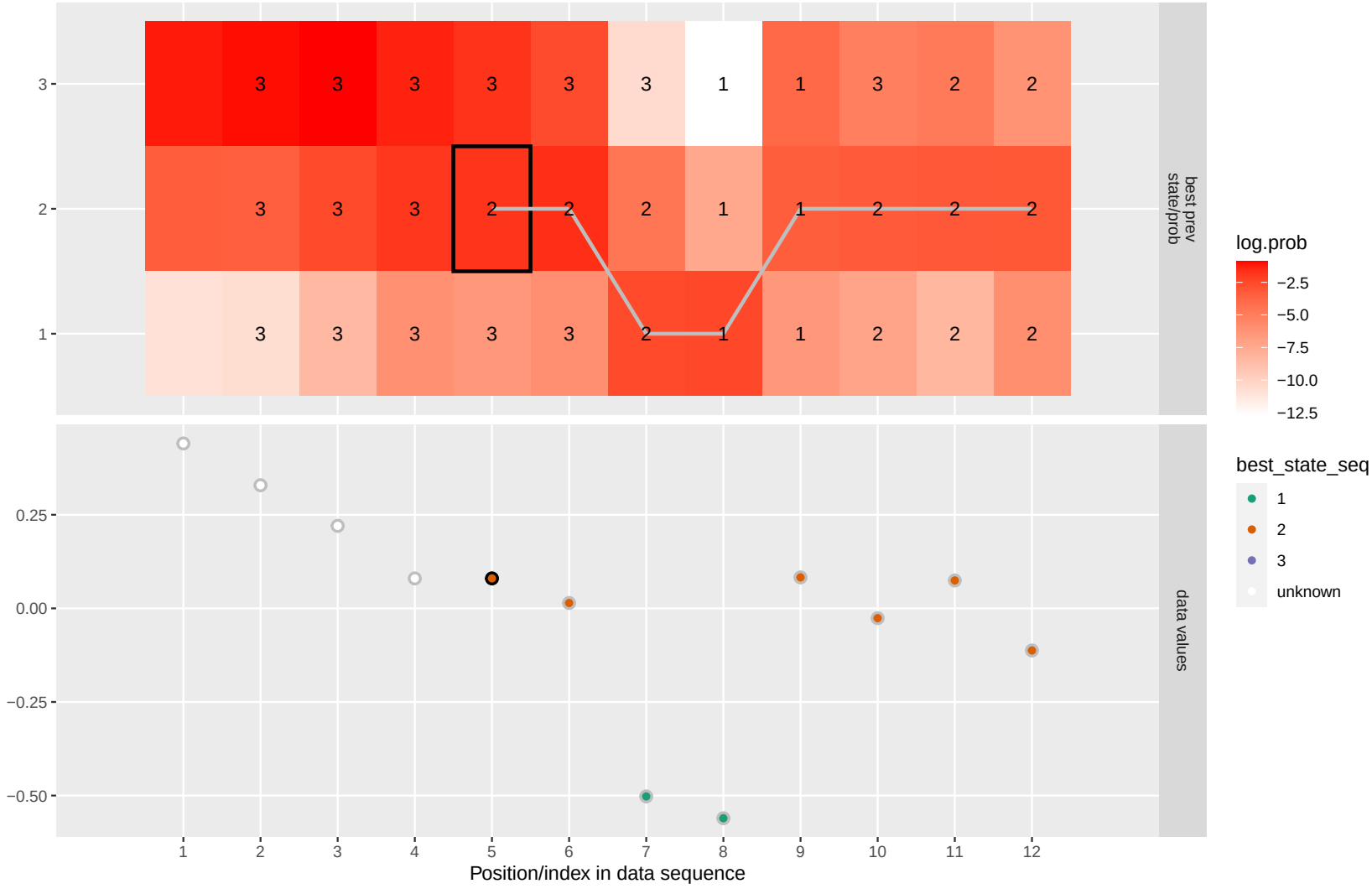

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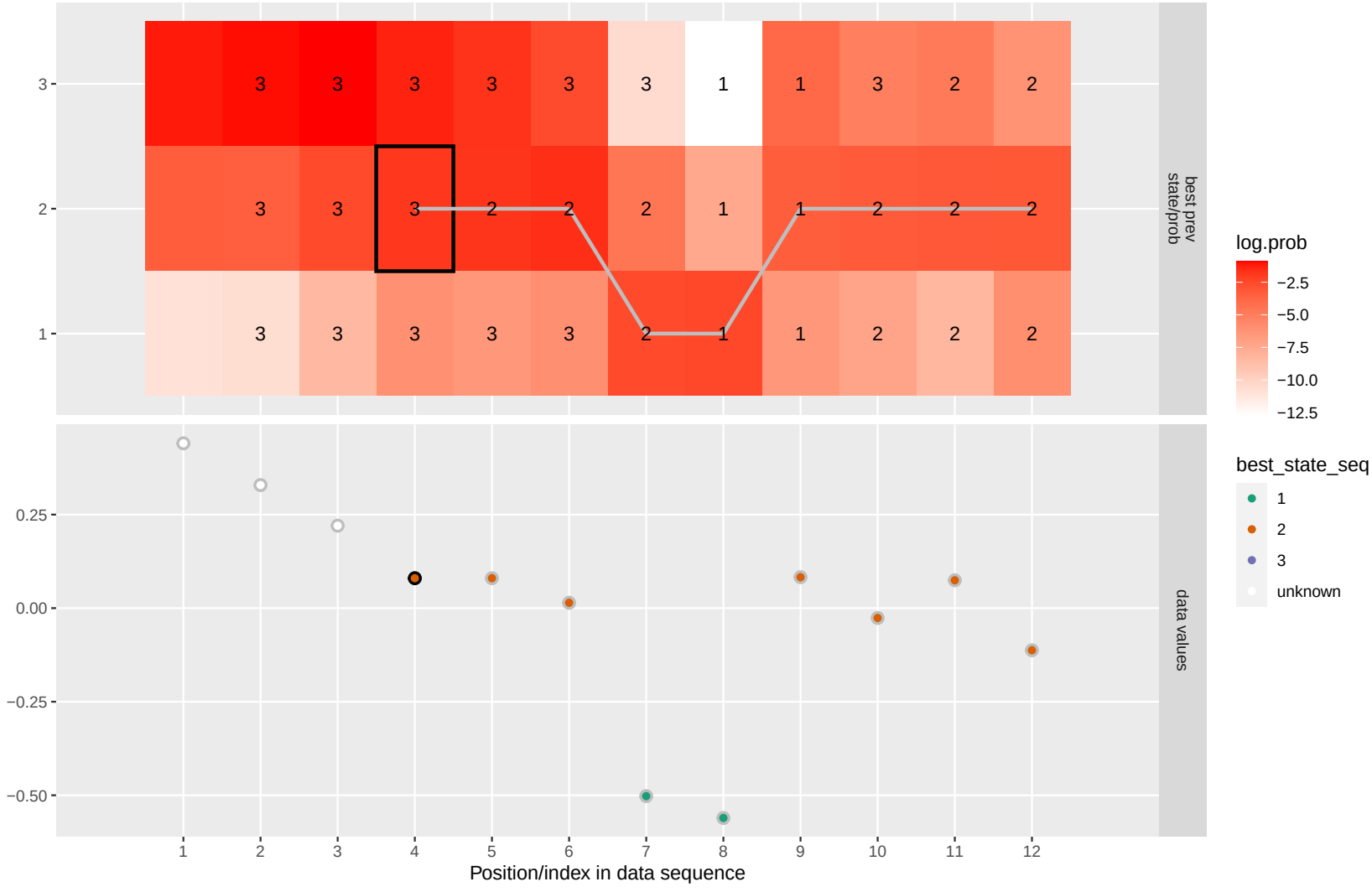

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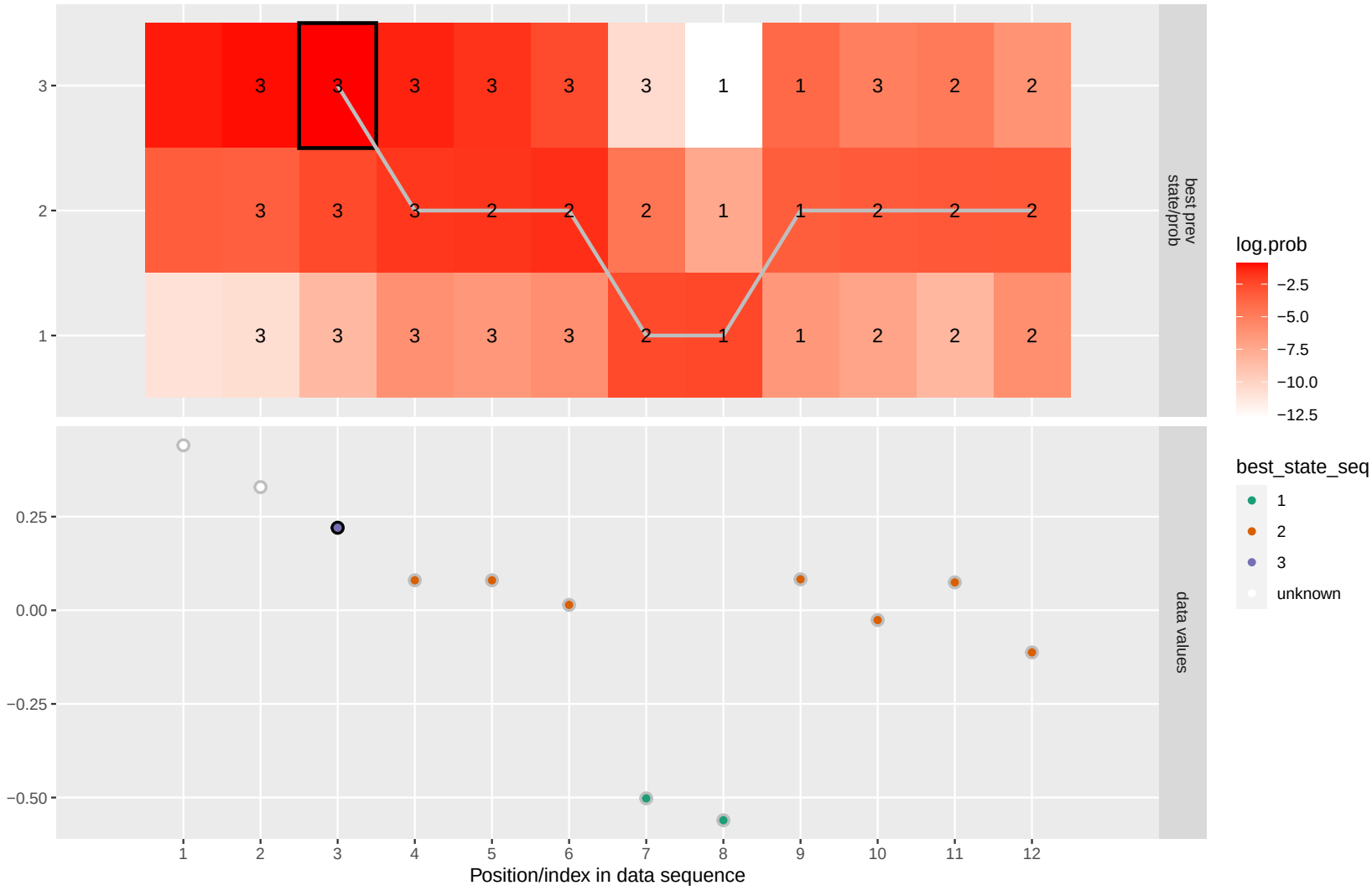

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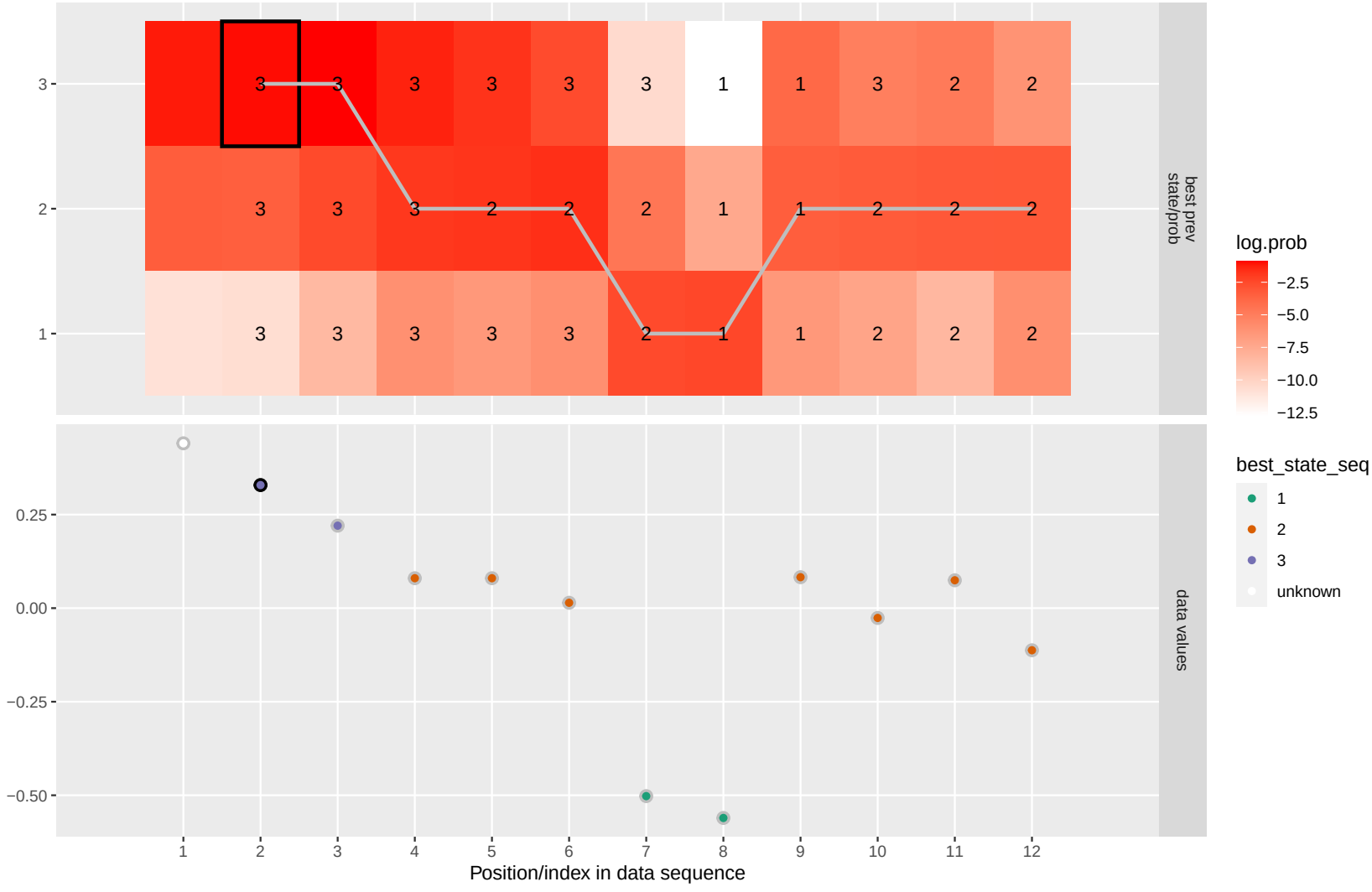

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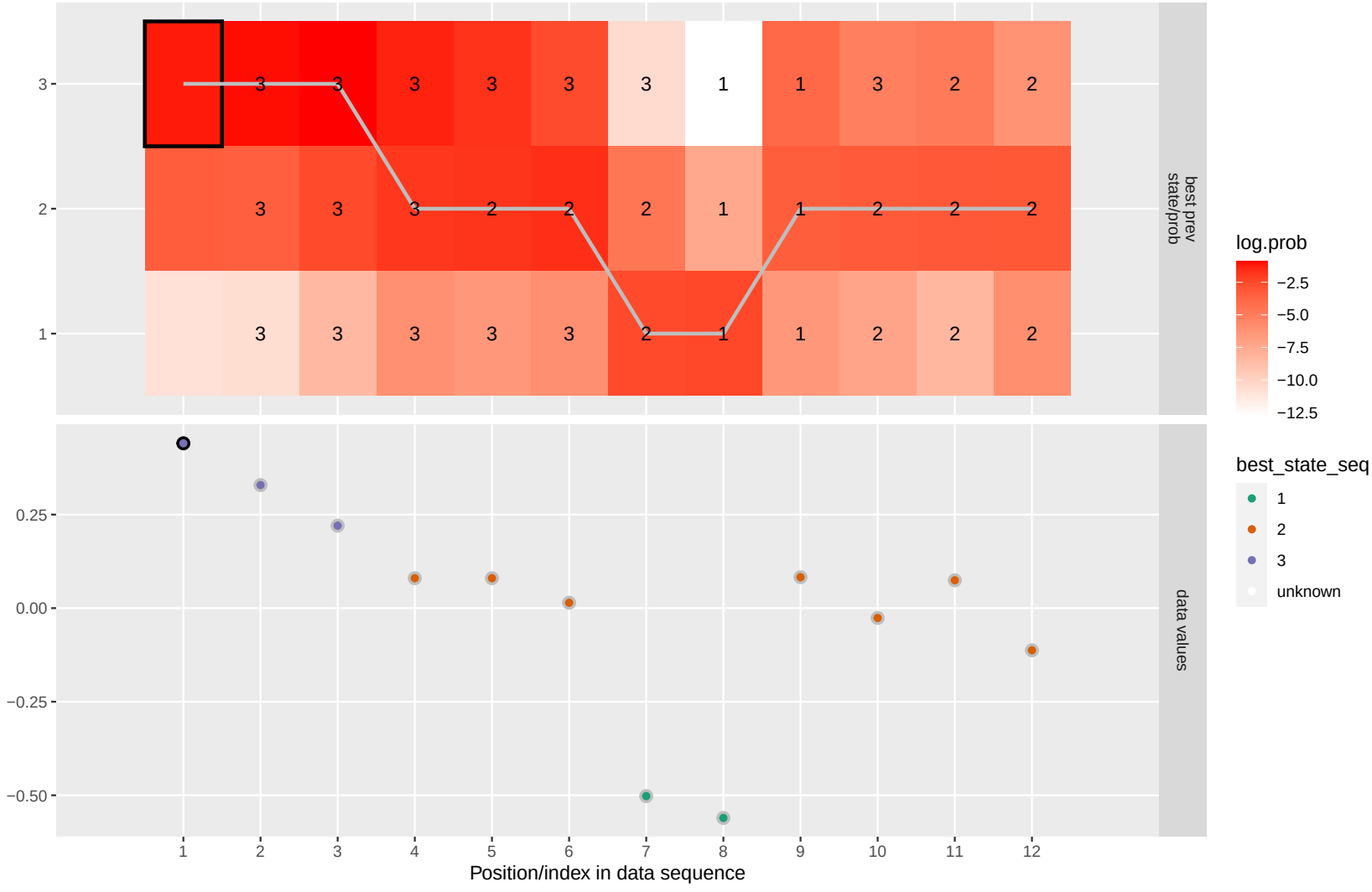
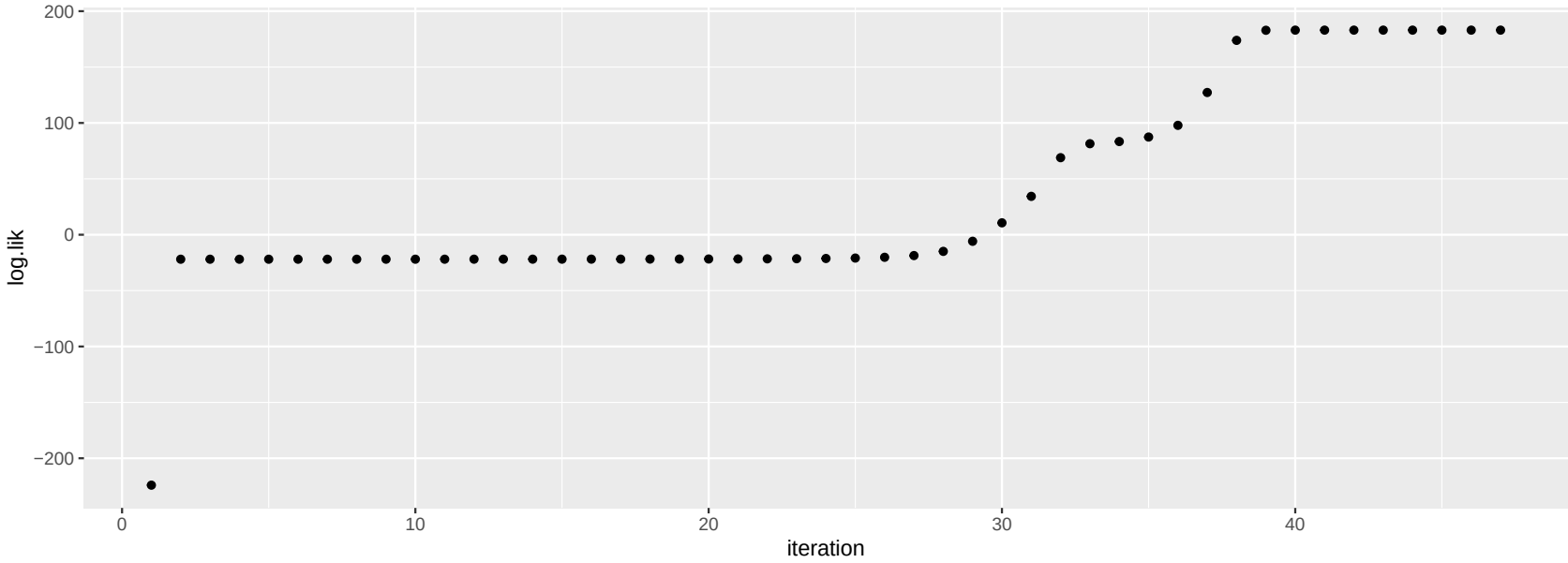
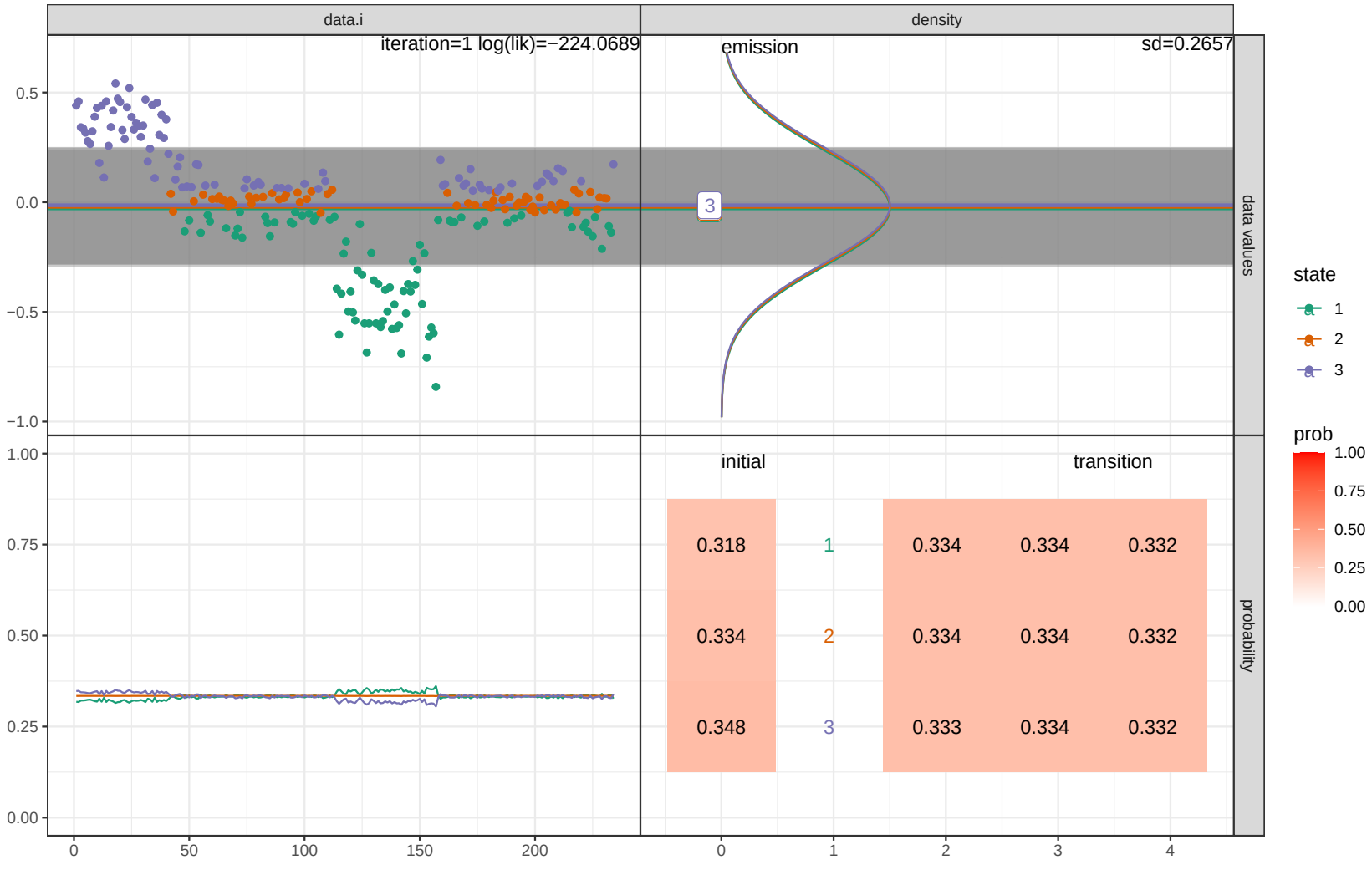


Baum-Welch learning algorithm

- Is an instance of Expectation-Maximization (EM), like the Gaussian Mixture Model learning algorithm.
- E step involves forward/backward passes over data sequences, to compute probability of each data point in each state.
- M step involves re-computing model parameters.
- Repeat until the log likelihood stops increasing.



Visualization of learning iterations



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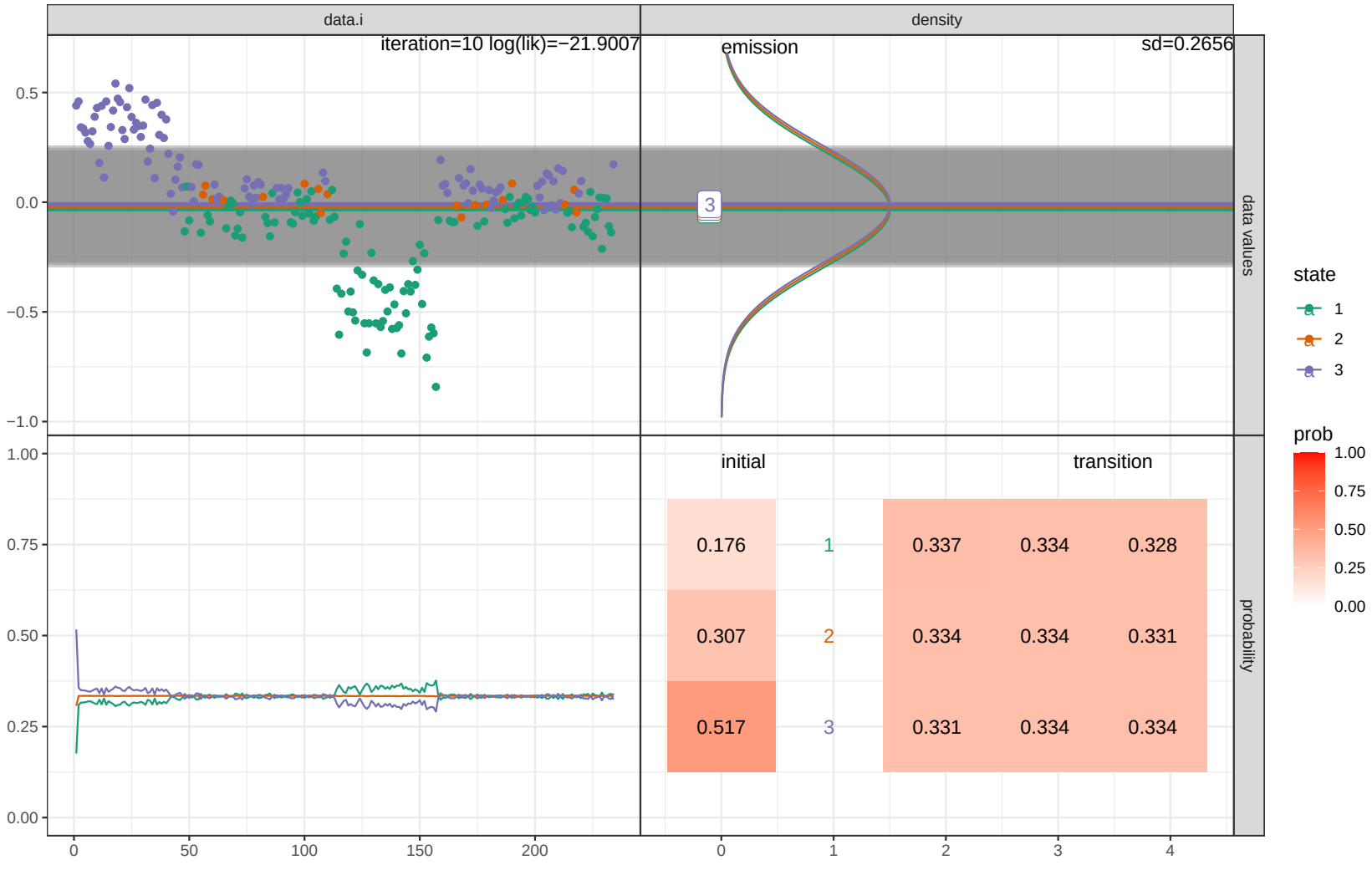

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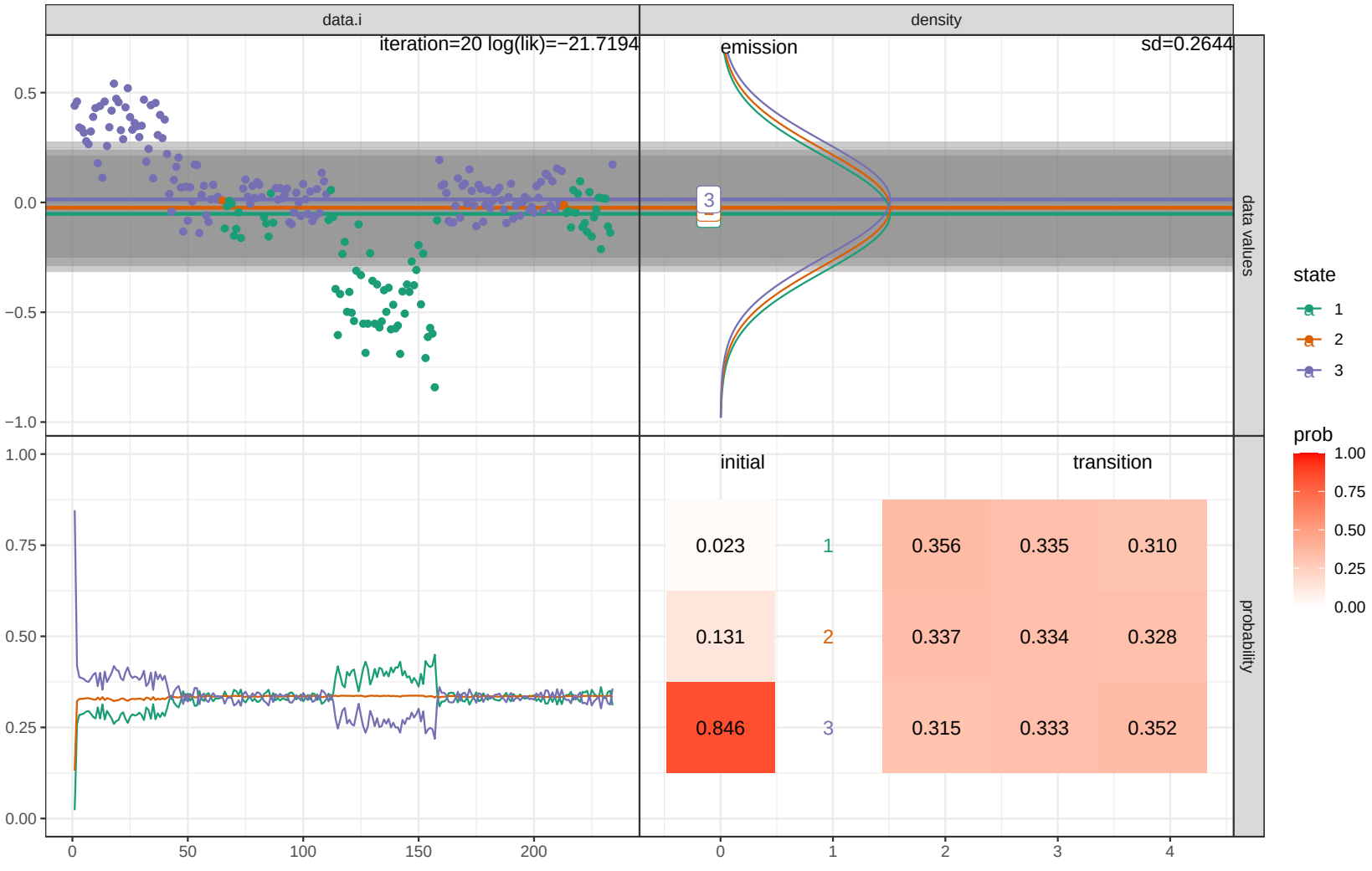

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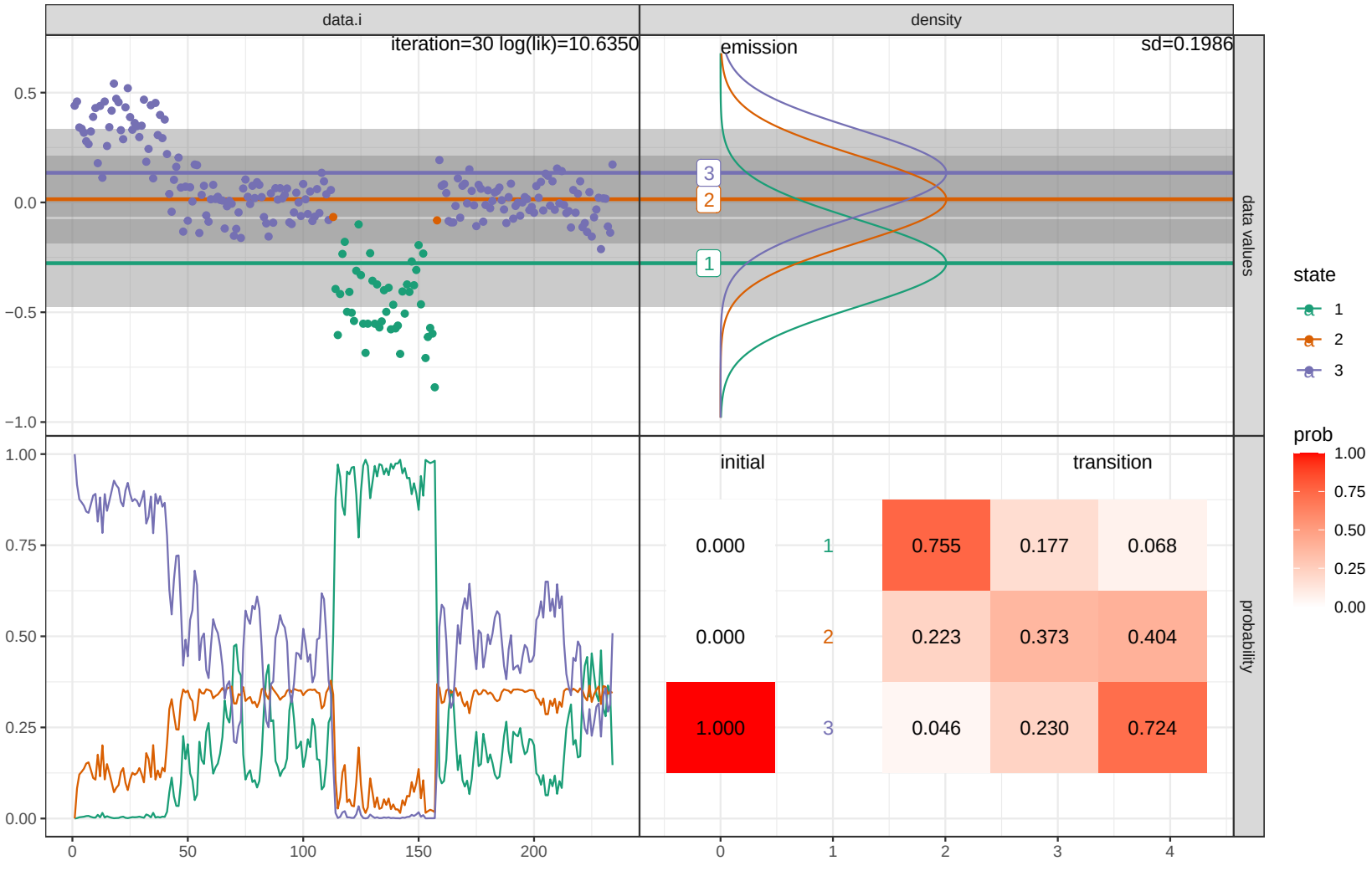

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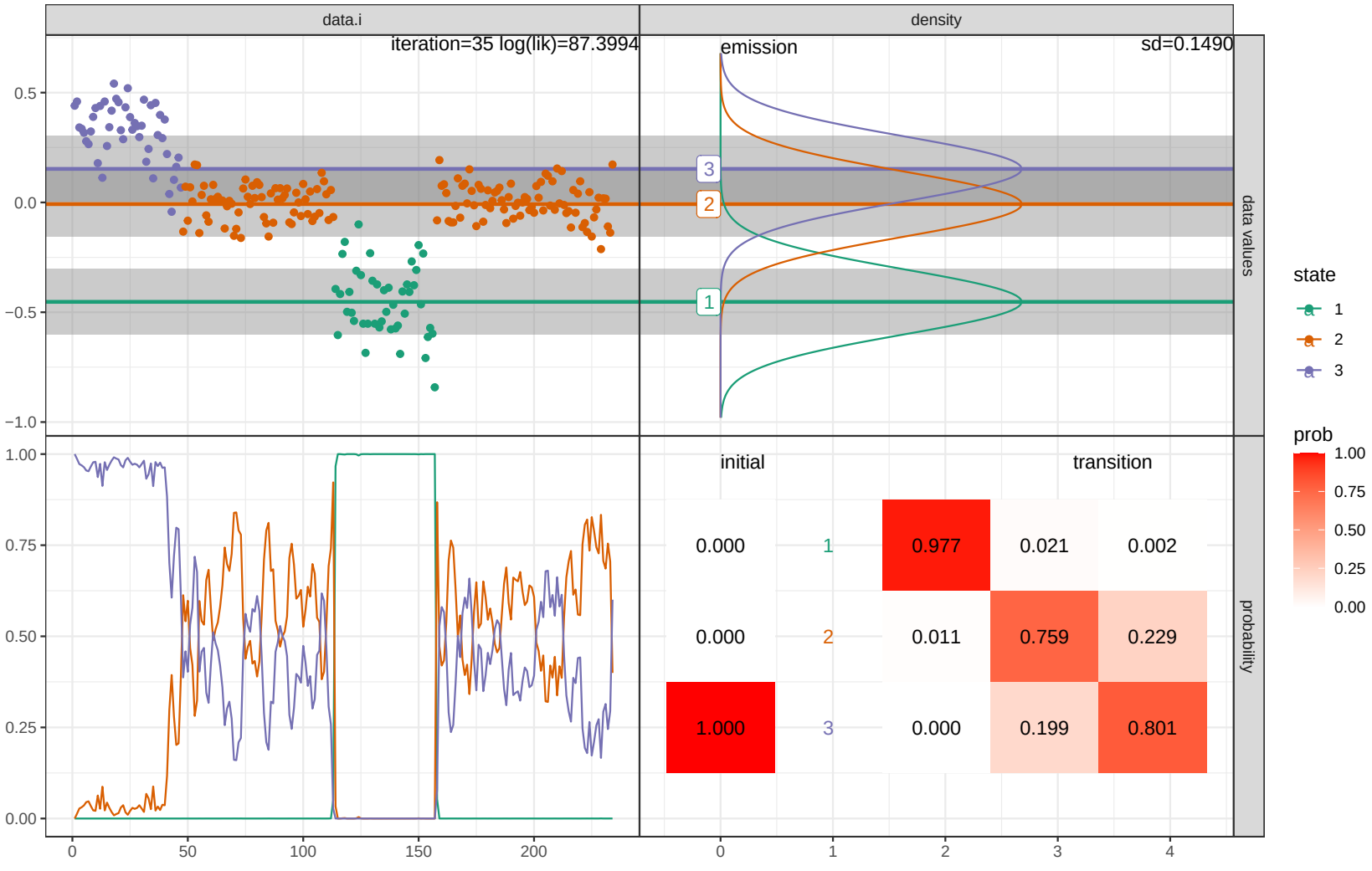

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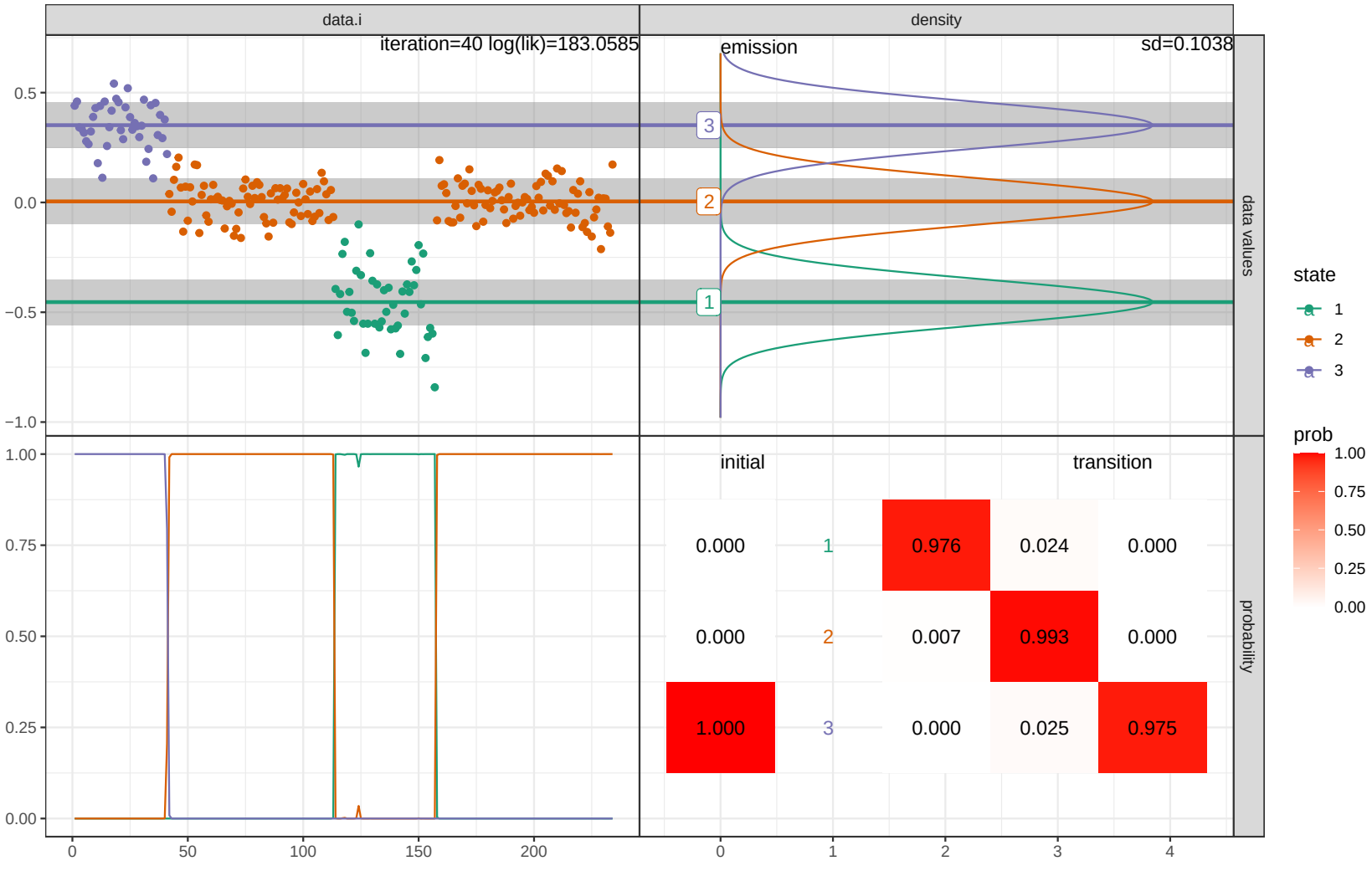
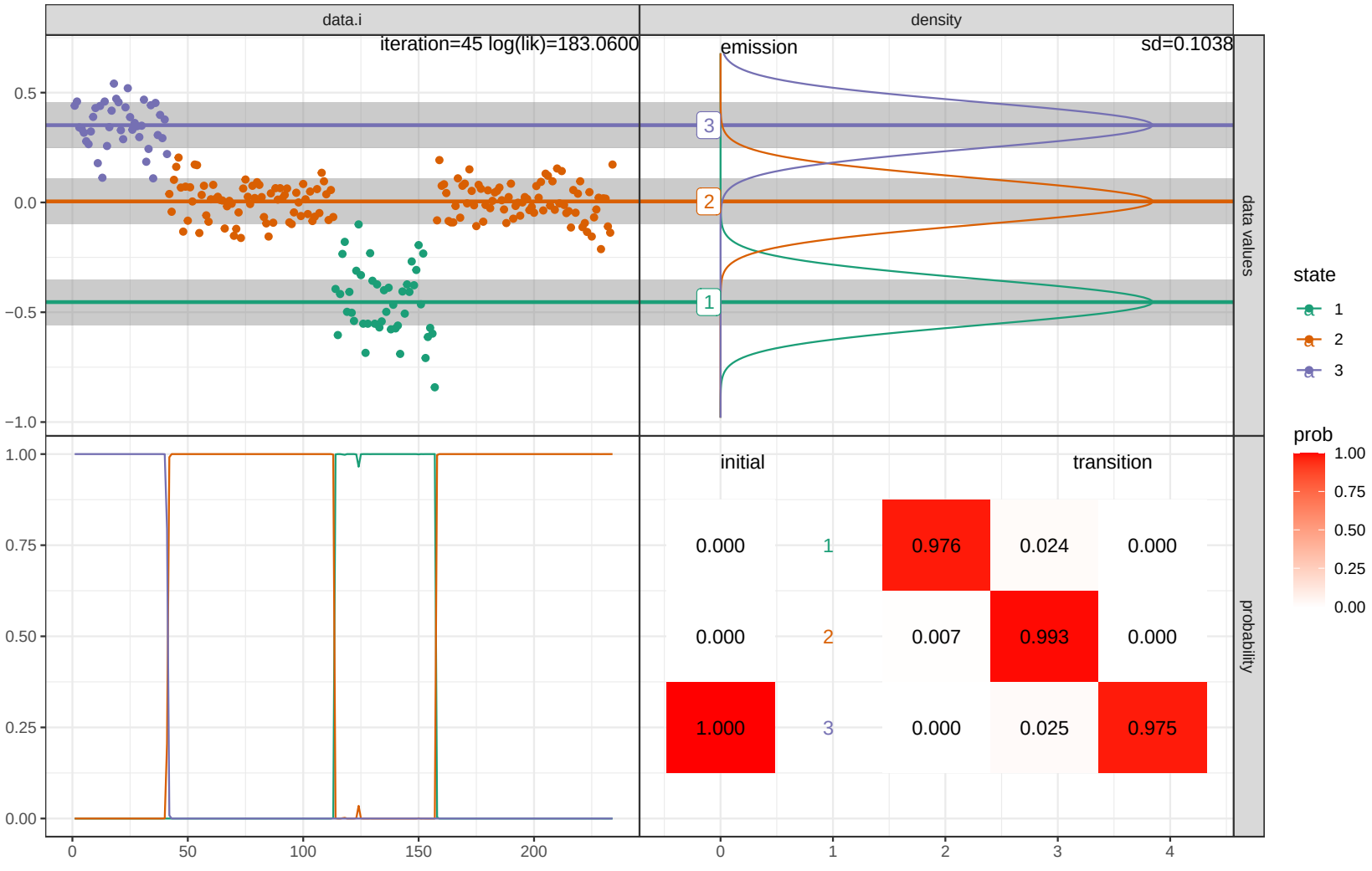
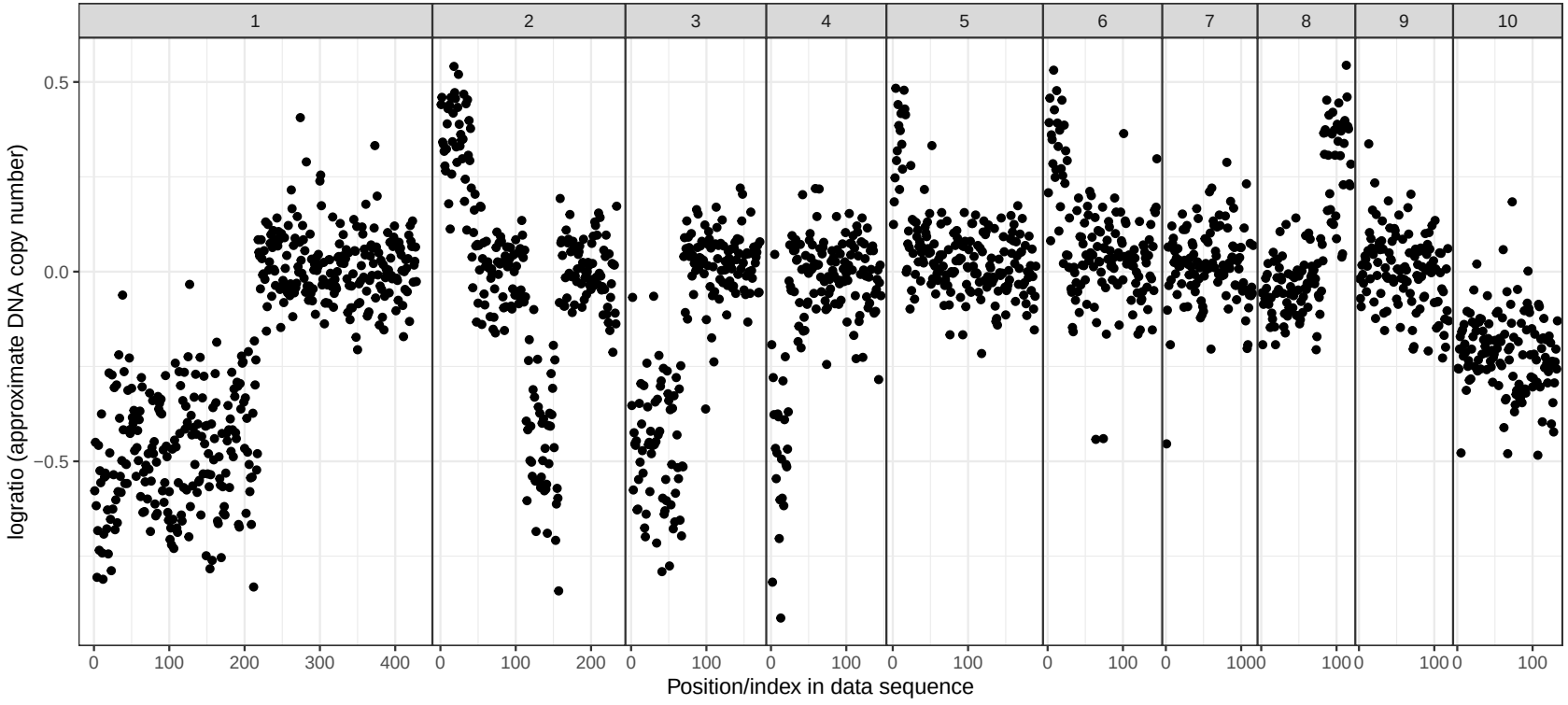


Visualization of learning iterations

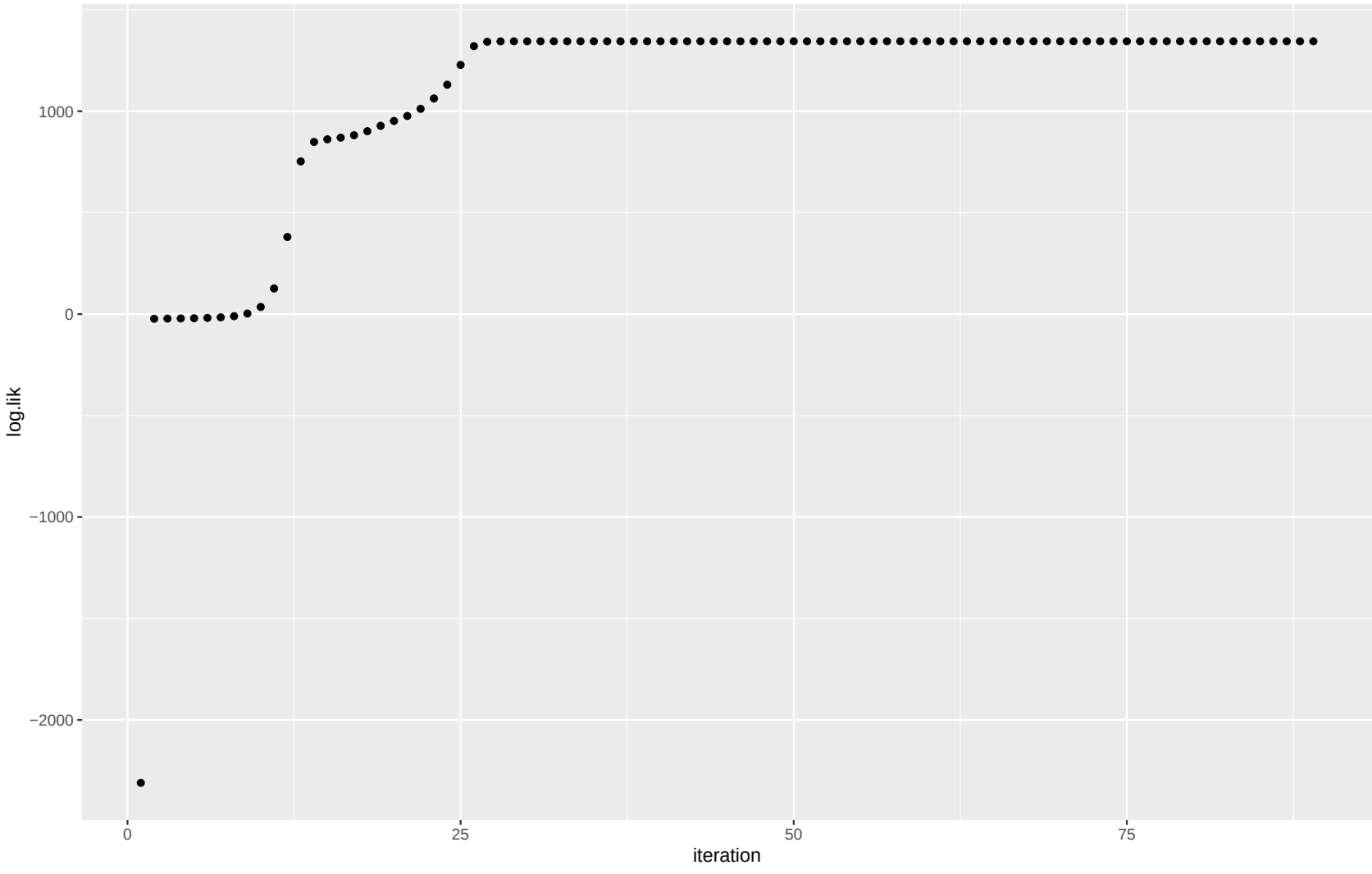


Shared states between chromosomes on a profile?

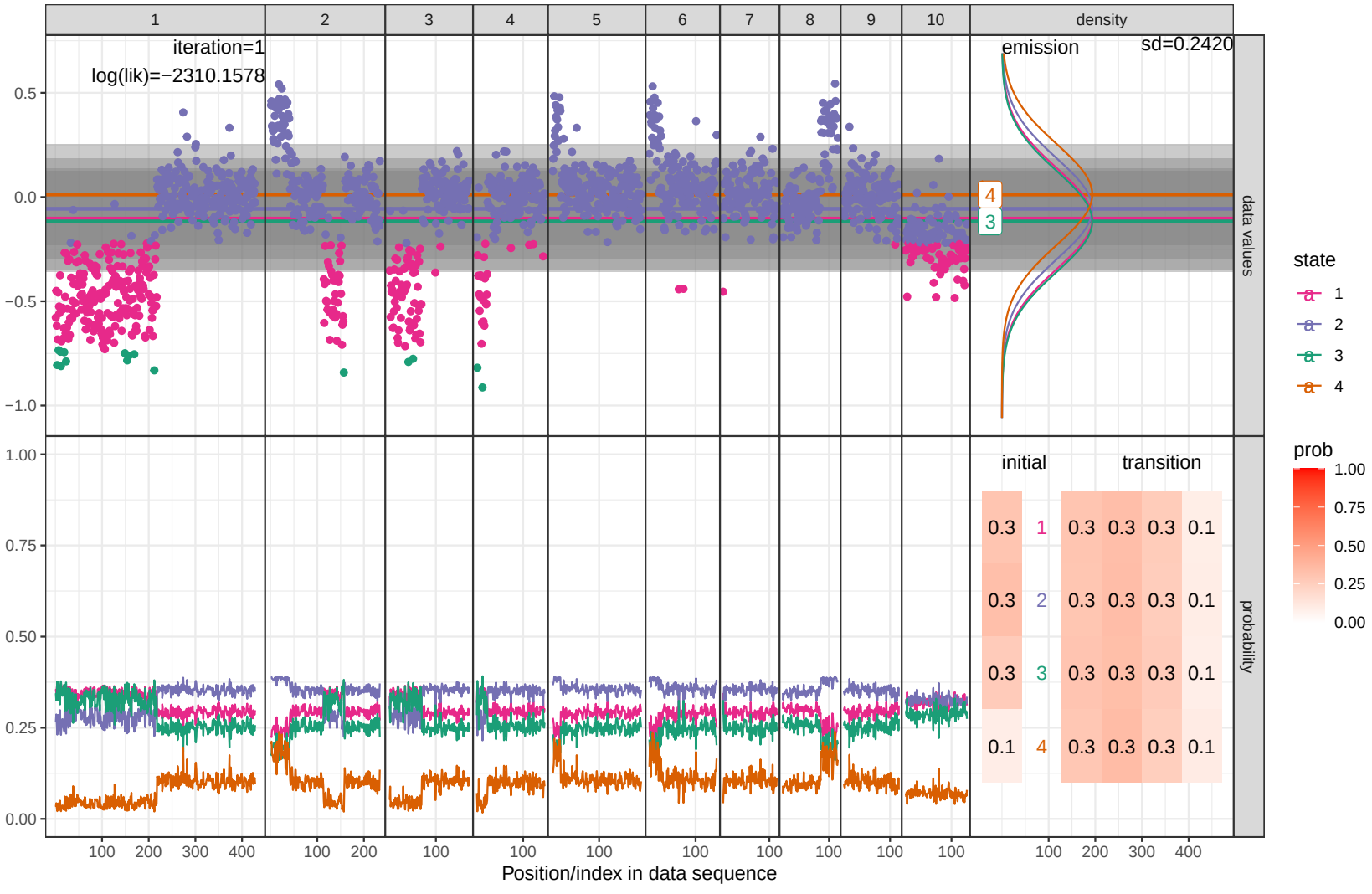
- Sometimes there are several data sequences which are assumed to have the same set of hidden states.
- In this case Baum-Welch can be used to fit HMM to all data at the same time (total log likelihood is summed over all data sequences).



HMM learned on whole profile



Learning iterations using multiple sequences



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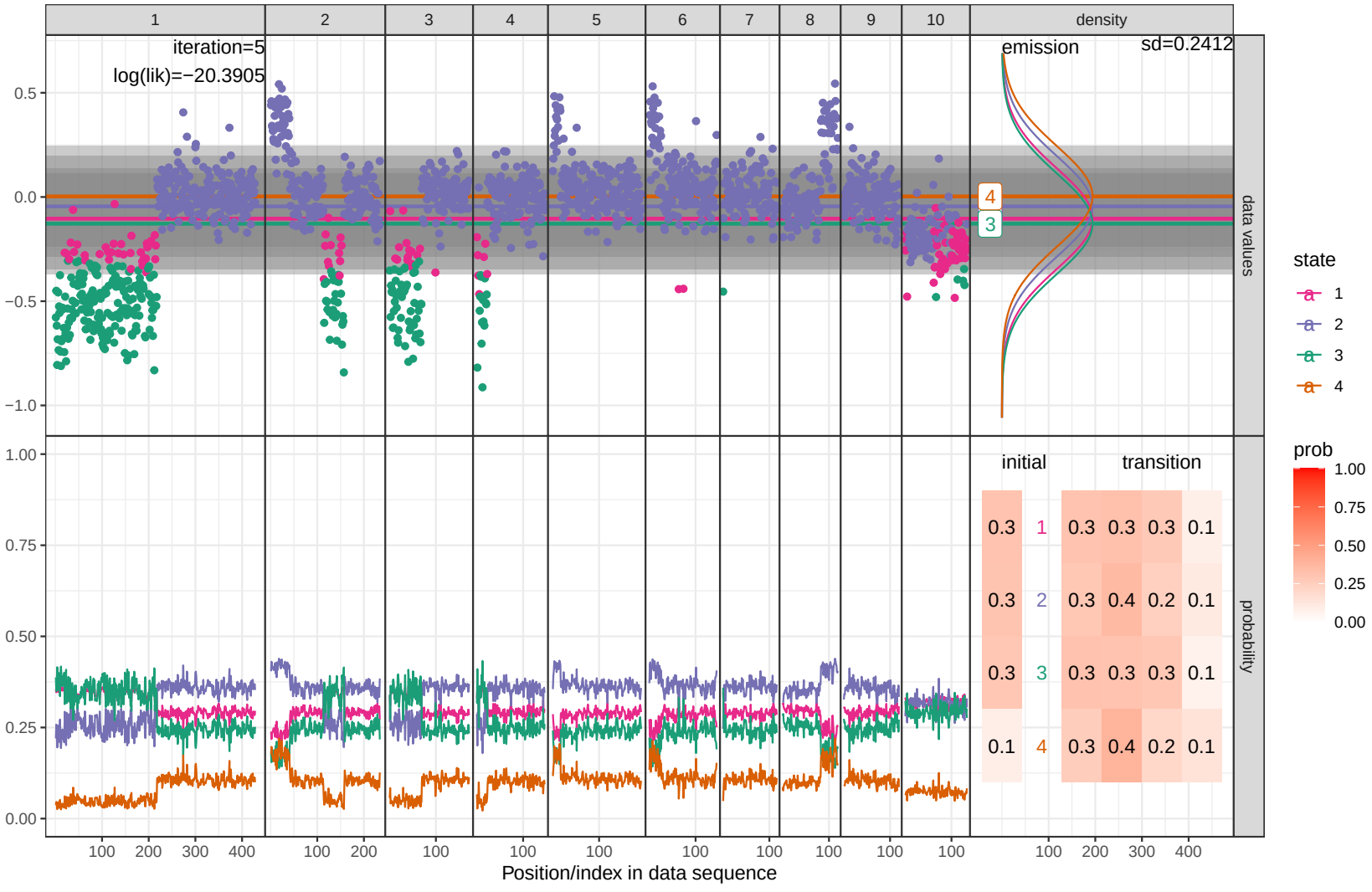

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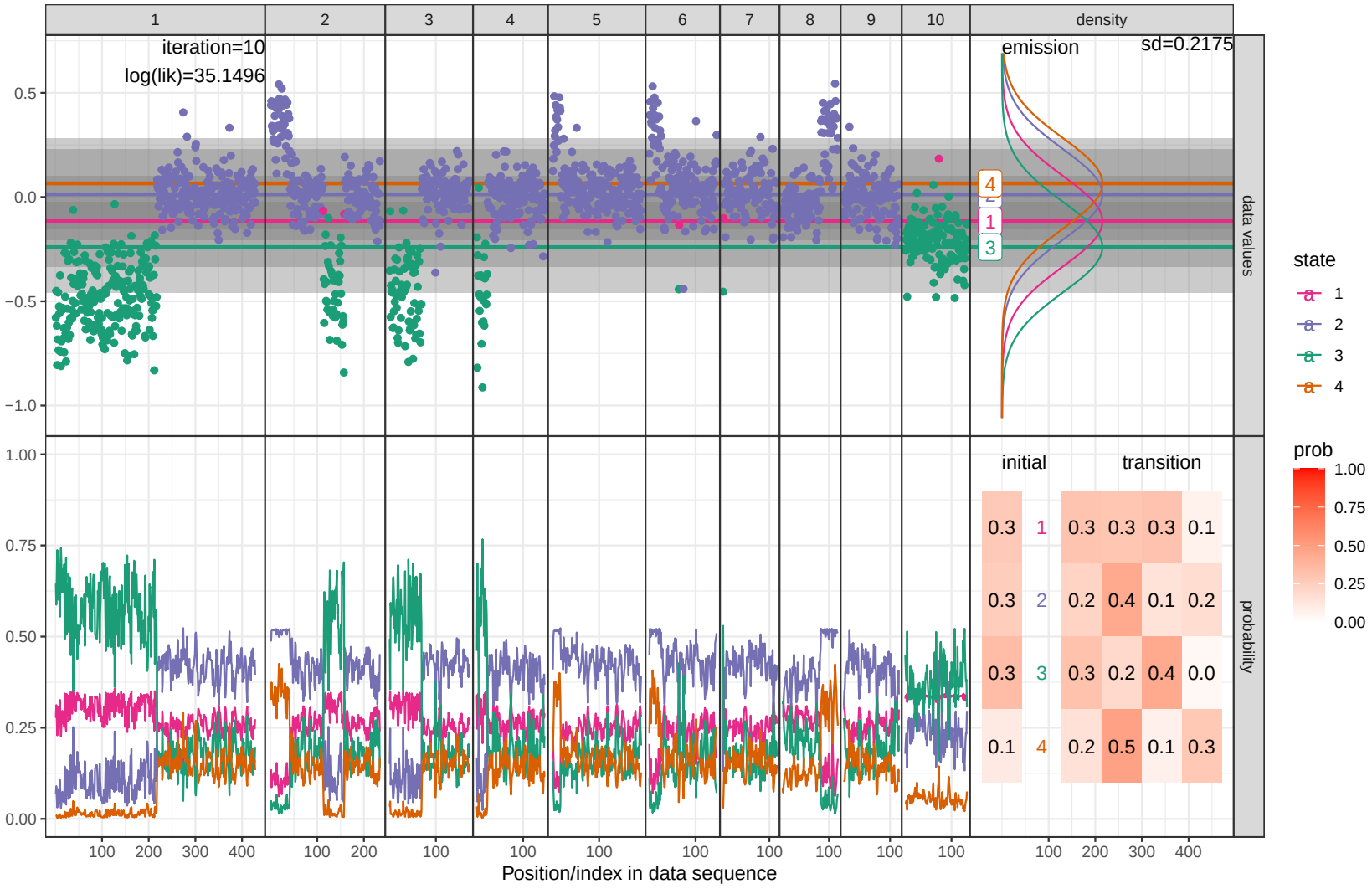

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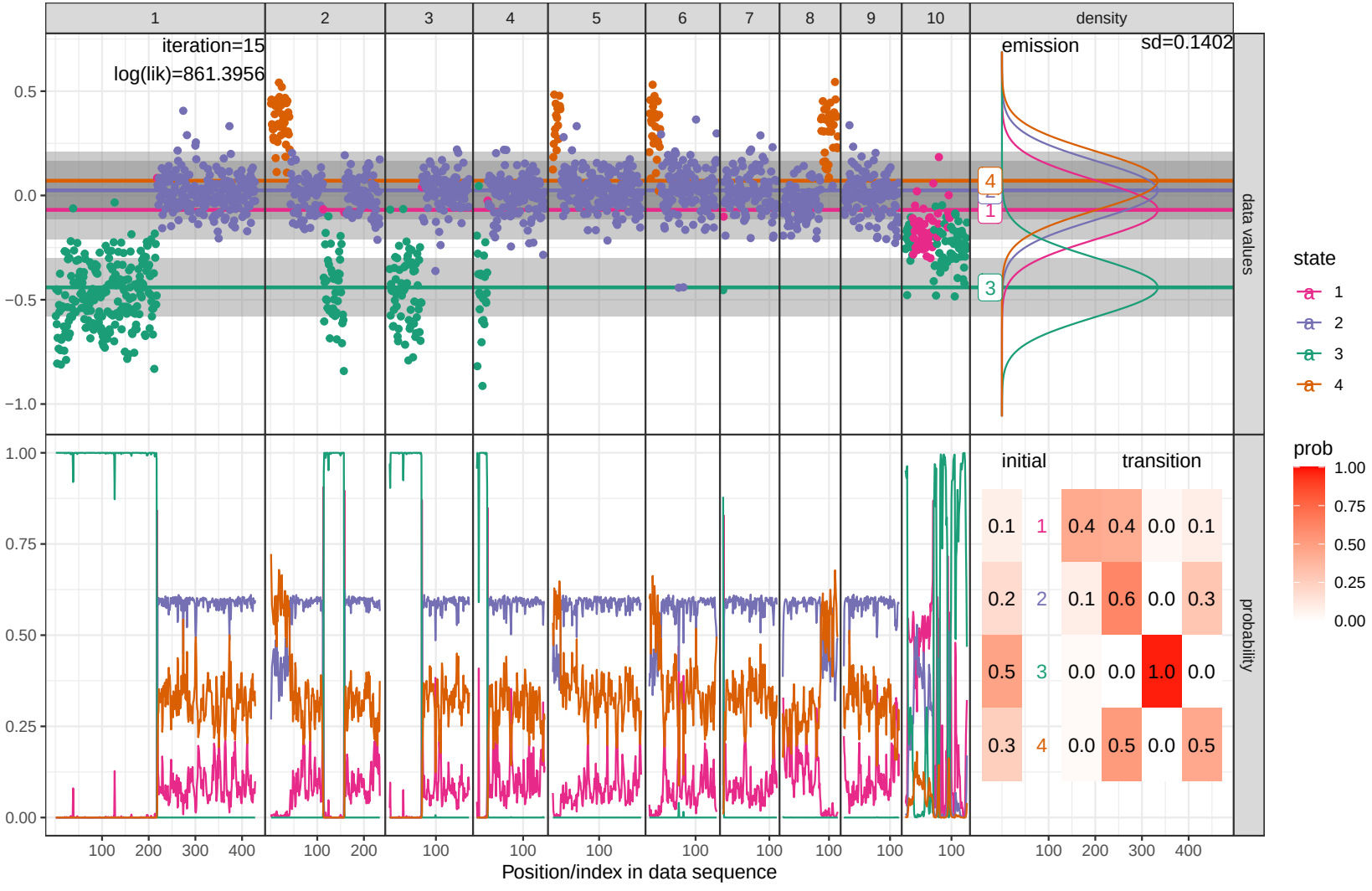

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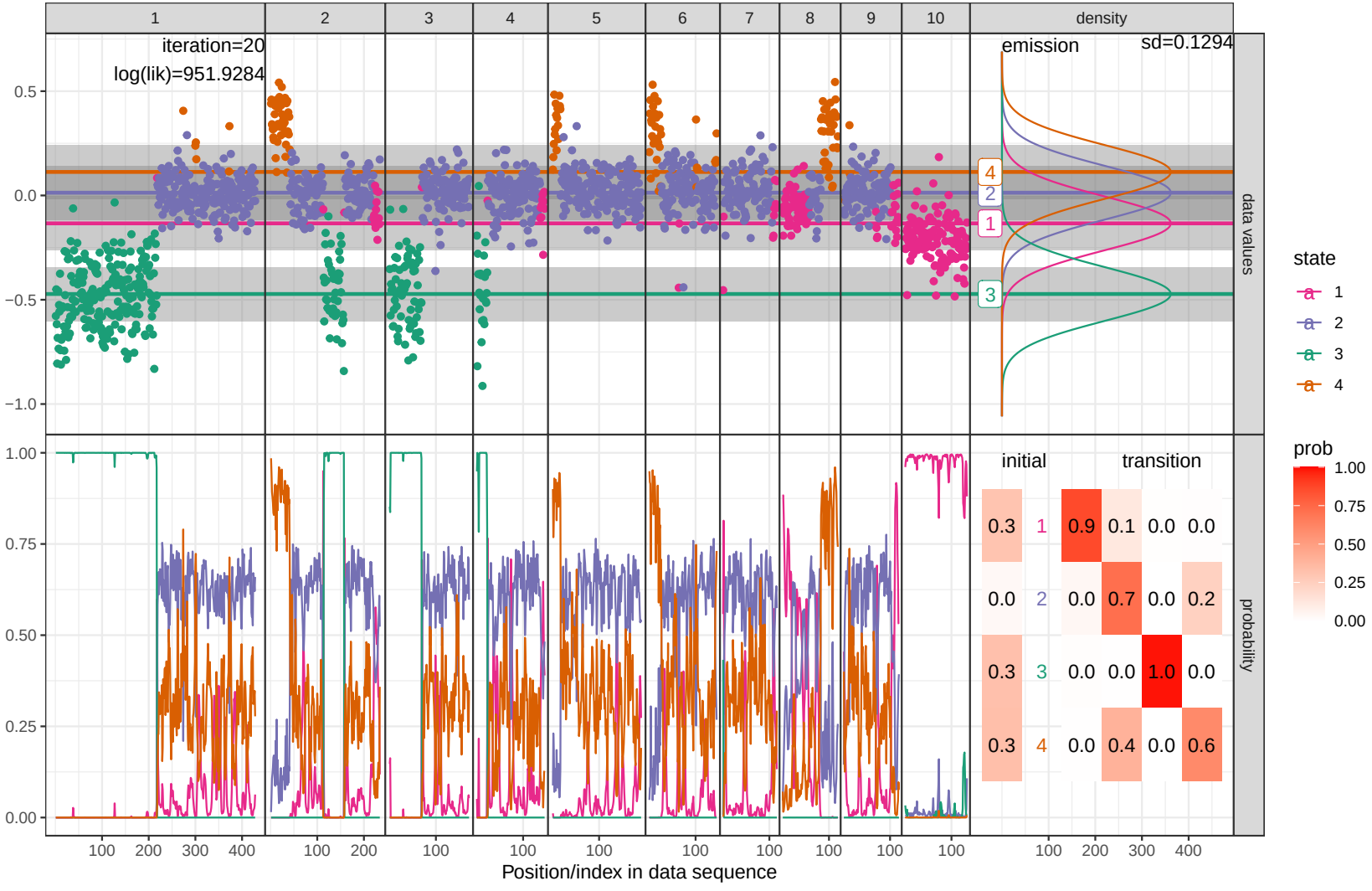

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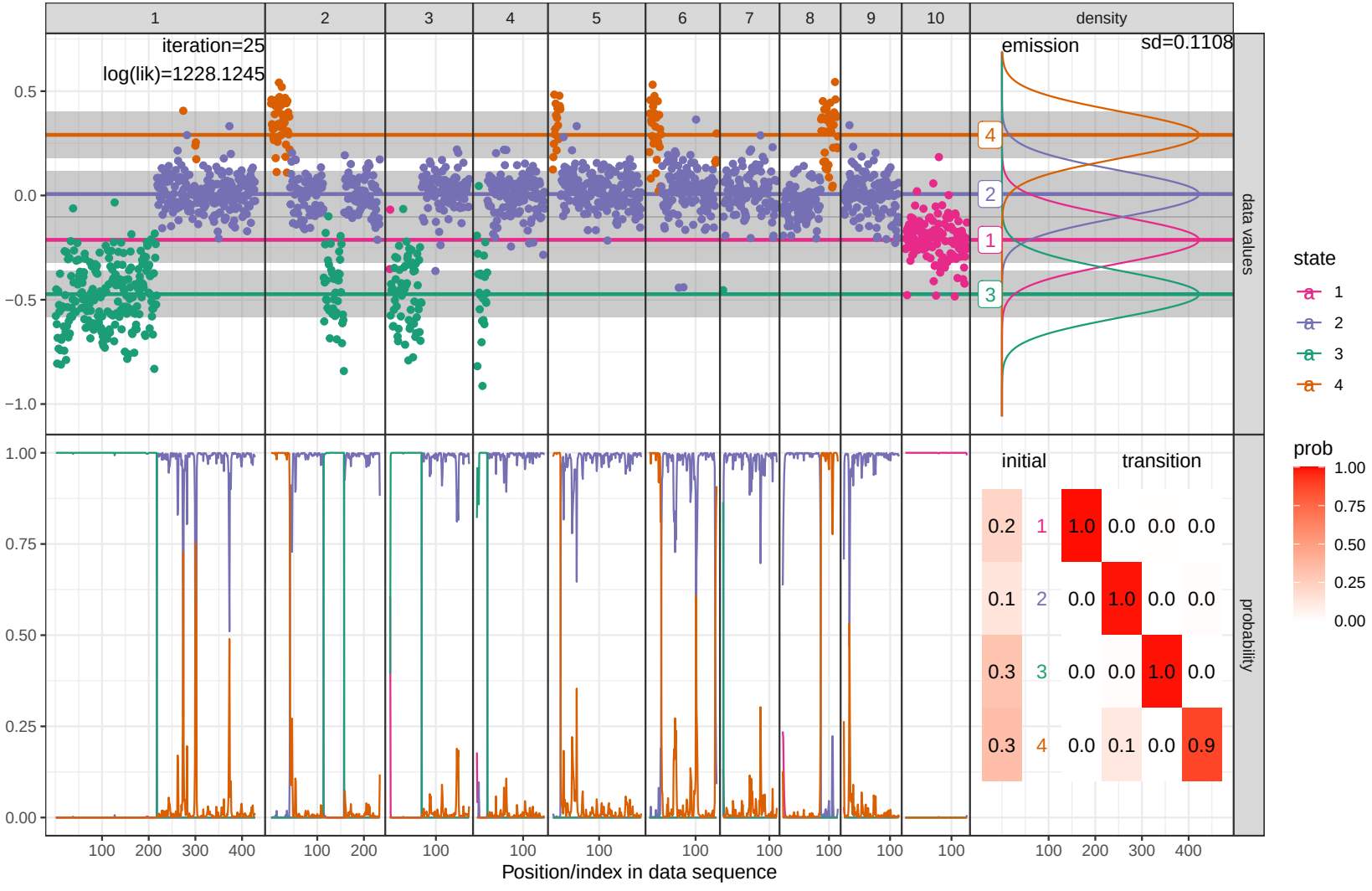
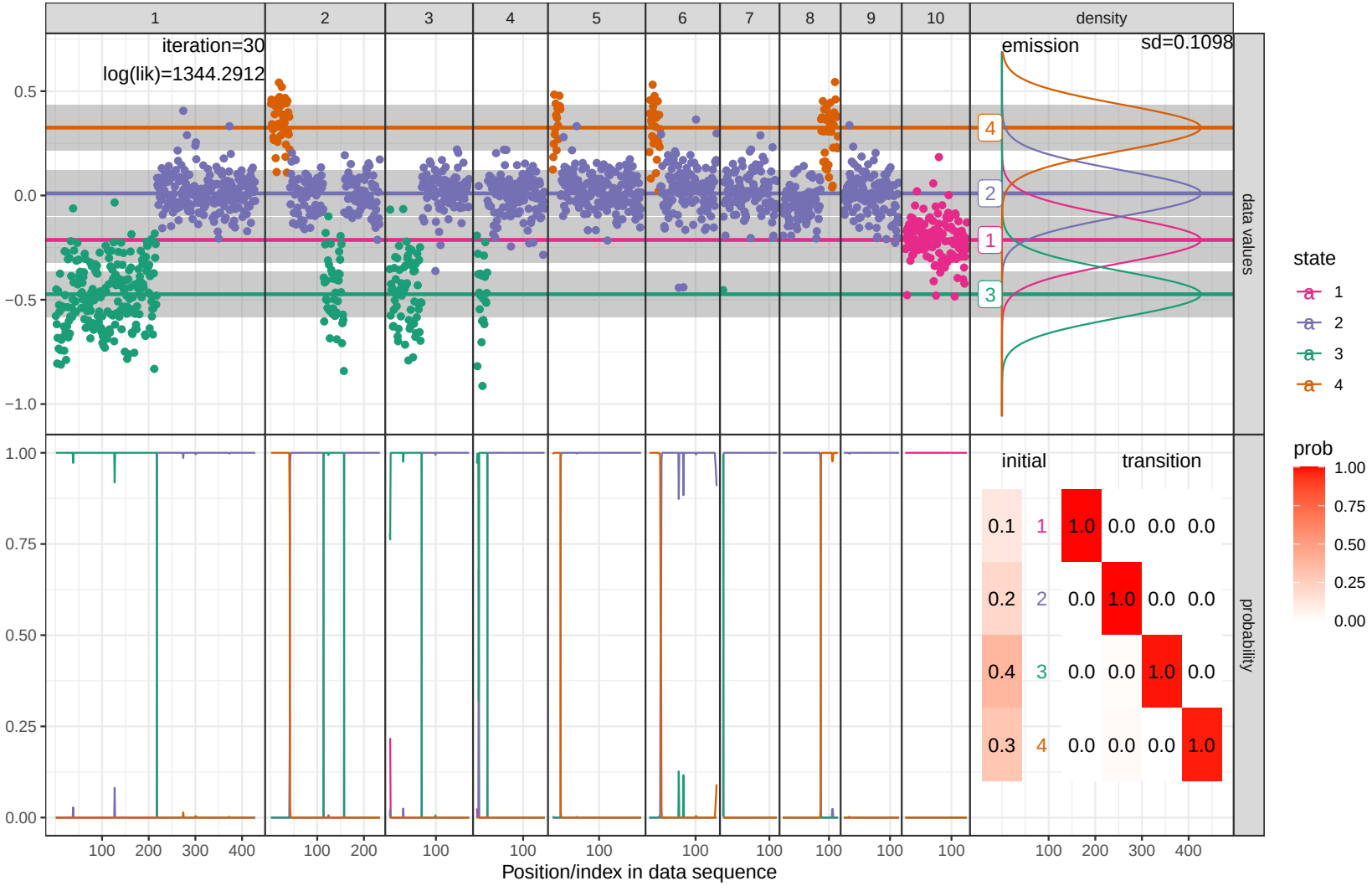
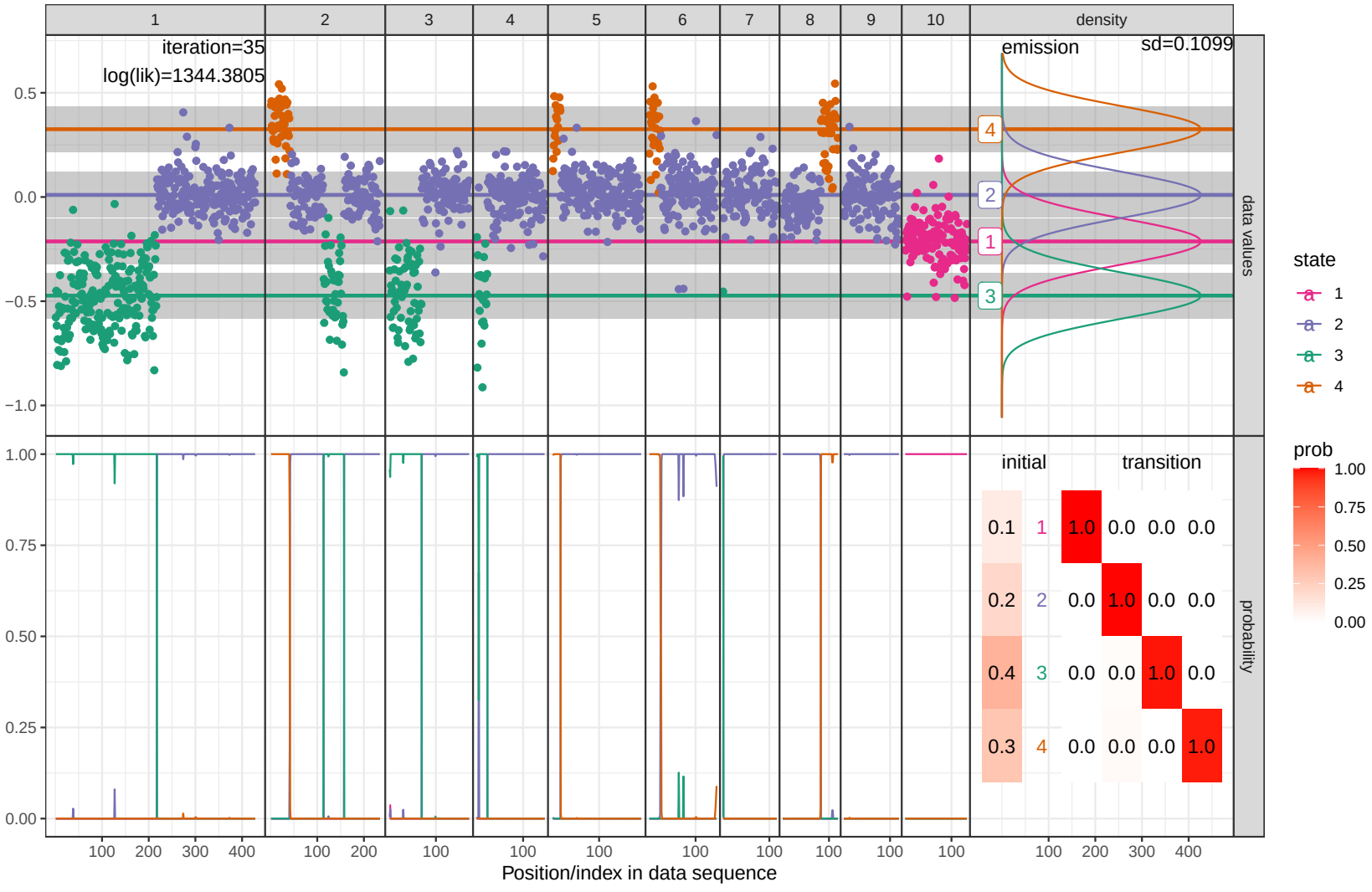


Learning iterations using multiple sequences



Learning iterations using multiple sequences



Time/space complexity

For K states and N data

- Forward/Viterbi: $O(K^2N)$ time, $O(K^2 + KN)$ space.
- Each iteration of Baum-Welch: $O(K^2N)$ time and space.
- Some asymptotic speedups are possible in special cases, for example sparse transition matrices, see Murphy book.

Comparison with other algorithms

- K-means and Gaussian mixture models also have cluster-specific parameters (mean, covariance, prior weight), but are not able to model sequential dependence.
- Binary/optimal segmentation require specification of number of segments/changepoints rather than number of hidden states.
- All segmentation models we studied had K mean parameters, and a single variance/sd parameter common to all segments.
- Binary/optimal segmentation always jump to a new mean parameter, whereas HMM may jump to a previously visited mean parameter.
- Binary/optimal segmentation with K segments can be interpreted as an HMM with a constrained transition matrix ($a_{ij} = 1$ if $j = i + 1$ else 0: always jump to the next state, never jump back to a previous state).
- Binary/optimal segmentation log likelihood only uses emission probabilities, whereas HMM also includes initial/transition probabilities.

Possible exam questions

- In the previous slides we saw $K = 3$ or 4 clusters. How many parameters of each type are there to learn in each case? (assume common sd parameter as in slides)
- How many parameters if each cluster has its own sd parameter?
- In the previous slides the data have a single feature (logratio). How many parameters if there are $P = 2$ real-valued features instead? (assume normal distribution with no constraints on covariance matrix)