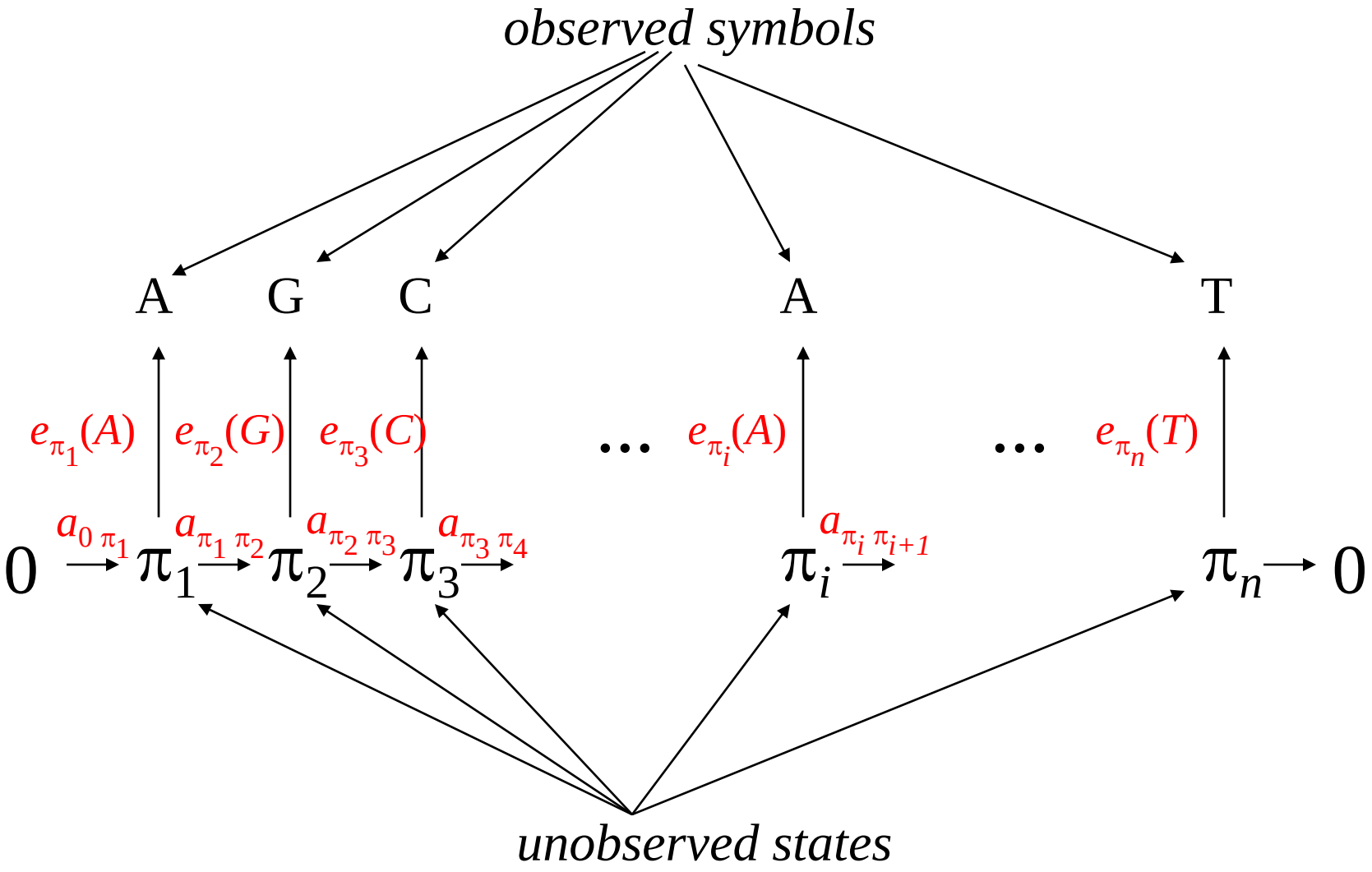
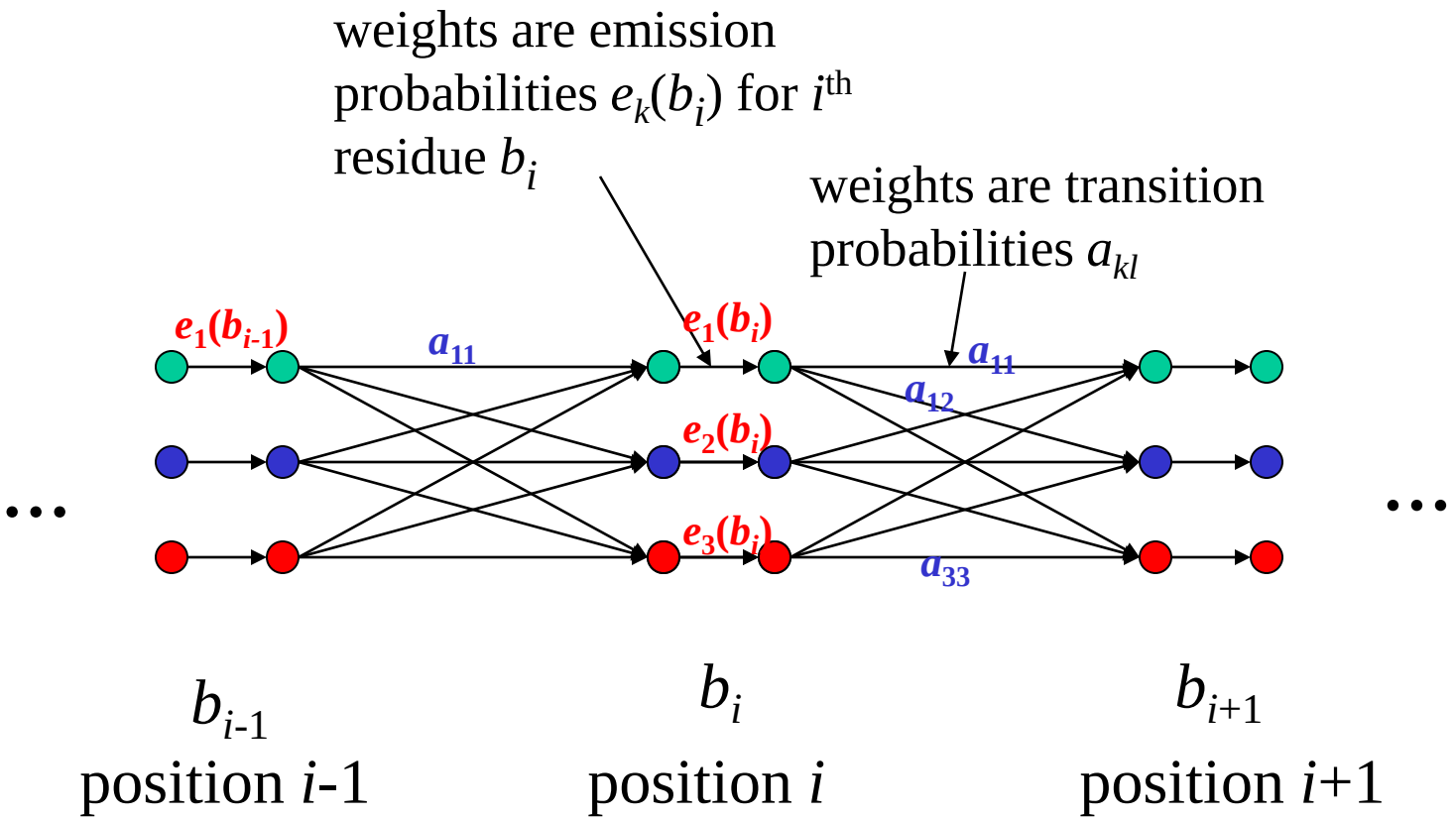
# Lecture 14

- Forward & forward/backward algorithms
- HMM parameter estimation
  - Viterbi training
  - Baum-Welch training

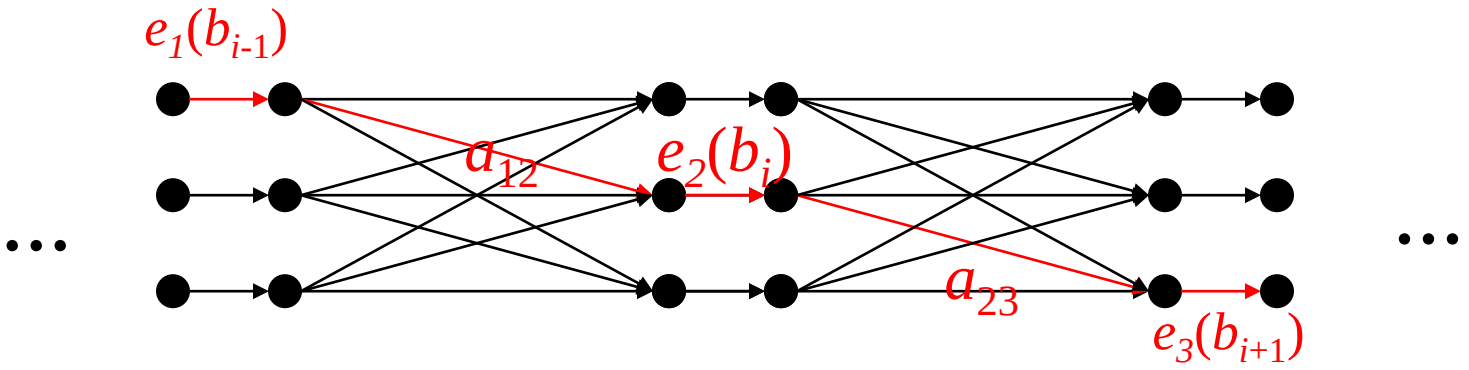
# Hidden Markov Model



# WDAG for 3-state HMM, length *n* sequence



# Path Weights



- ***Paths*** through graph from begin node to end node correspond to ***sequences of states***
- ***Product weight*** along path
  = ***joint probability*** of state sequence & observed symbol sequence
- ***Highest-weight path*** = ***highest probability state sequence***
- ***Sum*** *of (product) path weights*, ***over all paths***,
  = ***probability of observed sequence***
- ***Sum*** *of (product) path weights* ***over***
  - all paths *going through a particular node*, or
  - all paths *that include a particular edge*,

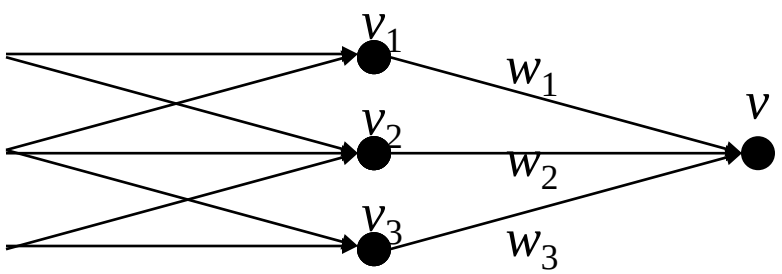
  ***divided by*** prob of observed sequence,
  = ***posterior probability*** of that edge or node

- use dynamic programming to find
  - sum of all product path weights
    = "forward algorithm" for probability of observed sequence
  - sum of all product path weights through particular node or particular edge
    = "forward/backward algorithm" to find posterior probabilities
- Now must use product weights and non-log-transformed probabilities
  - because need to *add* probabilities

- In each case, compute successively for each node (by increasing depth:  left to right)
  - the sum of the weights of all paths ending at that node
  - N.B. paths are constrained to begin at the begin node!
- In forward/backward algorithm,
  - work through all nodes a second time, in opposite direction
    - i.e. in reverse graph – constraining paths to start in rightmost column of nodes

For each vertex $v$, let $f(v) = \sum_{\text{paths } p \text{ ending at } v} \text{weight}(p)$, where weight($p$) = *product* of edge weights in $p$. Only consider paths starting at 'begin' node.

Compute $f(v)$ by dynam. prog: $f(v) = \sum_i w_i f(v_i)$, where
$v_i$ ranges over the parents of $v$, and
$w_i$ = weight of the edge from $v_i$ to $v$.

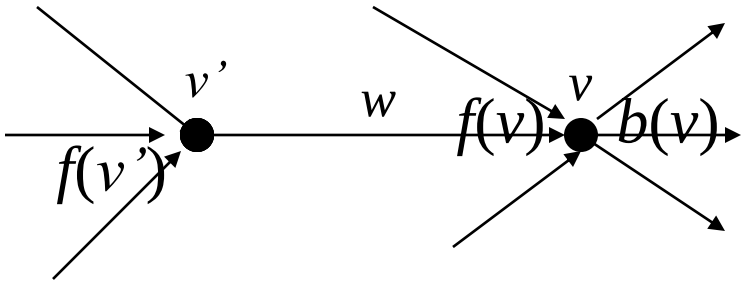



Similarly for $b(v) = \sum_{p \text{ beginning at } v} \text{weight}(p)$

The paths *beginning* at $v$ are the ones *ending* at $v$ in the *reverse (or inverted) graph*

# *from lecture 10 :*

- Can “invert” any WDAG: create graph with
  - same vertices & edge weights
  - direction of each edge reversed
- inverted WDAG has same paths & path weights, but in reverse order
- inverting does not necessarily “invert” depth structure




$f(v)b(v)$ = sum of the path weights of all paths *through v*.

$f(v')wb(v)$ = sum of the path weights of all paths *through the edge (v',v)*

# Forward/backward algorithm

- Work through graph in forward direction:
  - compute and store $f(v)$
- Then work through graph in backward direction:
  - compute $b(v)$
  - compute $f(v)$ $b(v)$ and $f(v)wb(v)$ as above, store in appropriate cumulative sums
  - only need to store $b(v)$ until have computed $b$'s at next position
- Posterior probability of being in state $s$ at position $i$ is $f(v)$ $b(v)$ / *total sequence prob*
  - where $v$ is the corresponding graph node

- Numerical issues: multiplying many small values can cause underflow. Remedies:
  - *Scale* weights to be close to 1 (affects all paths by same constant factor – which can be multiplied back later); or
  - (where possible) use log weights, so can add instead of multiplying.
  - see Rabiner & Tobias Mann links on web page

# HMM Parameter Estimation

- *Parameters* = transition & emission probs
  - *parameter values* ↔ *probability model*
- If unknown, estimate from set of training sequences
- *Maximum likelihood* (ML) estimation (= choice of param vals to maximize prob of training data) is preferred
  - optimality properties of ML estimates discussed in Ewens & Grant

↔ finding maximum value on a multi-dimensional surface

  - Hard problem! Can be many local maxima

# Parameter estimation when state sequence is *known*

- When underlying state sequence for each training sequence is *known*,
  - e.g.: site model

  then ML estimates are given by:
  - emission probabilities:

    $e_k(b)$^ = (# times symbol $b$ emitted by state $k$) / (# times state $k$ occurs) .
  - transition probabilities:

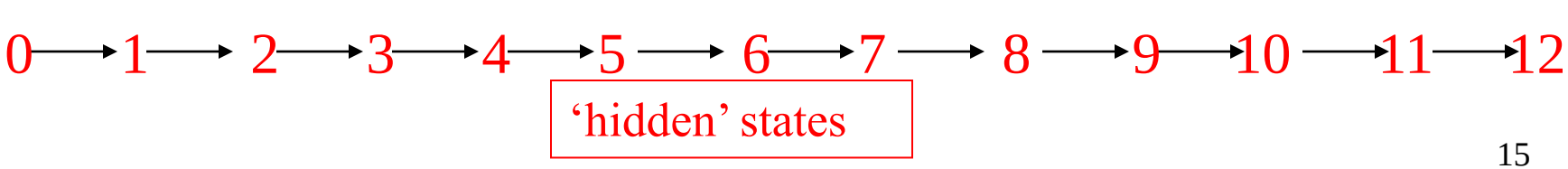
    $a_{kl}$ ^ = (# times state $k$ followed by state $l$) / (# times state $k$ occurs)
  - in denominator above, *omit occurrence at last position of sequence* (for transition probabilities)
    - But include it for emission probs
  - can include pseudocounts, to incorporate prior expectations/avoid small sample overfitting (Bayesian justification)

# HMM for *C. elegans* 3' Splice Sites


| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 3276 | 3516 | 2313 | 476 | 67 | 757 | 240 | 8192 | 0 | 3359 | 2401 | 2514 |
| C | 970 | 648 | 664 | 236 | 129 | 1109 | 6830 | 0 | 0 | 1277 | 1533 | 1847 |
| G | 593 | 575 | 516 | 144 | 39 | 595 | 12 | 0 | 8192 | 2539 | 1301 | 1567 |
| T | 3353 | 3453 | 4699 | 7336 | 7957 | 5731 | 1110 | 0 | 0 | 1017 | 2957 | 2264 |
| **CONSENSUS** | W | W | W | T | T | t | C | A | G | r | w | w |

Emission probabilities

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 0.400 | 0.429 | 0.282 | 0.058 | 0.008 | 0.092 | 0.029 | 1.000 | 0.000 | 0.410 | 0.293 | 0.307 |
| C | 0.118 | 0.079 | 0.081 | 0.029 | 0.016 | 0.135 | 0.834 | 0.000 | 0.000 | 0.156 | 0.187 | 0.225 |
| G | 0.072 | 0.070 | 0.063 | 0.018 | 0.005 | 0.073 | 0.001 | 0.000 | 1.000 | 0.310 | 0.159 | 0.191 |
| T | 0.409 | 0.422 | 0.574 | 0.896 | 0.971 | 0.700 | 0.135 | 0.000 | 0.000 | 0.124 | 0.361 | 0.276 |



# Parameter estimation when state sequence *unknown*

- *Viterbi training*

1. choose starting parameter values
   - must be valid probabilities; avoid 0 unless topology dictates
   - make them *biologically plausible* given state interpretation
2. find Viterbi highest weight paths for each sequence
3. estimate new emission and transition probs as above, *assuming* the Viterbi state sequence
4. iterate steps 2 and 3 until convergence
   - not guaranteed to occur – but nearly always does
5. repeat steps 1 – 4 with other starting values
   - choose values with highest total path score

- Viterbi training does ***not*** necessarily give ML estimates, but often are reasonably good

# Baum-Welch training

- Special case of EM ('expectation-maximization') algorithm
- like Viterbi training, but
  - uses *all* paths, each weighted by its probability

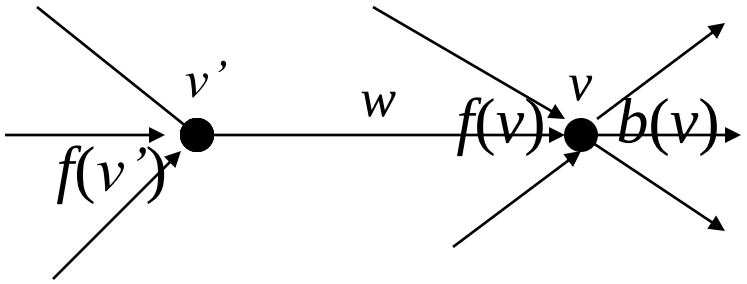
    rather than just highest probability path.
- sometimes give significantly better results than Viterbi
  - e.g. for PFAM

# Implementing Baum-Welch

– An edge in the WDAG contributes *fractional* (or *weighted*) *counts* given by its posterior probability:

– (*): $(\sum_{\text{all paths } p \text{ through edge } e} \text{weight}(p)) / (\sum_{\text{all paths } p} \text{weight}(p))$

(Fractional counts are computed using forward-backward algorithm)




$f(v)b(v)$ = sum of the path weights of all paths *through v*.

$f(v')wb(v)$ = sum of the path weights of all paths *through the edge (v',v)*

– Compute new param estimates

- $e_k(b)$^ = (frac. # times symbol $b$ emitted by state $k$) / (frac. # times state $k$ occurs)
- $a_{kl}$ ^ = (frac. # times state $k$ followed by state $l$) / (frac. # times state $k$ occurs)
  - (In denom,, omit frac counts at last position of sequence)

where “frac. # times” is given by (*) for appropriate edge type (emission or transition)

– New Baum-Welch parameter estimates have higher likelihood
  - general property of EM algorithm
  - not true in general for Viterbi training

– Iterate: get series of estimates converging to a *local* maximum on likelihood surface

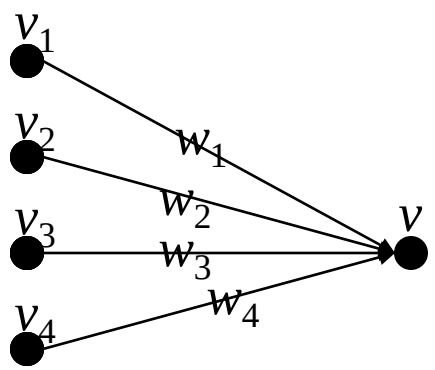
# Search of parameter space

- ML estimates correspond by definition to *global* maximum;
- but there may be many *local* maxima, and EM or Viterbi search can get "trapped" in one
- remedies:
  - Consider multiple starts (multiple choices for starting parameters)
  - use "reasonable values" to start search (e.g. unlikely transitions should be given small initial probabilities)

- Allow search to "jump" out of local maxima:
  - Add "noise" to counts at each iteration; gradually reduce the amount of noise
  - Use Viterbi-like training, but
    - sample paths probabilistically
      - » (in retracing Viterbi path, choose edge at random according to its prob, rather than taking highest prob parent);
    - use "temperature" T to adjust probabilities;
      - » initially with large T making all probs approximately equal;
      - » then gradually reduce T

# Probabilistic Viterbi Backtracking

reset all weights $w$ to $w^{1/T}$. For large T ( >> 1), this makes distinct $w$'s relatively close; for small T (<< 1), relatively far apart




choose parent $v_i$ with probability $w_i\, f(v_i) / f(v)$. For large T, all parents almost equally likely to be chosen; for small T, strongly favor largest (max) $w_i\, f(v_i)$

given choice of paths, re-estimate weights; iterate