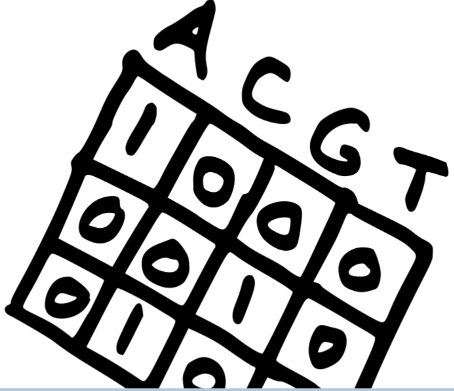
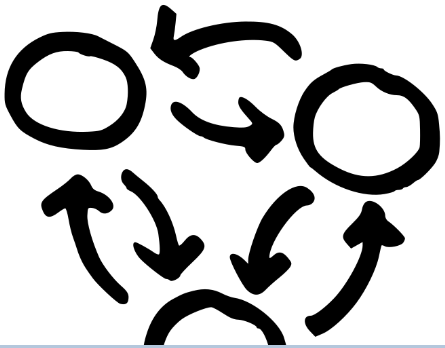
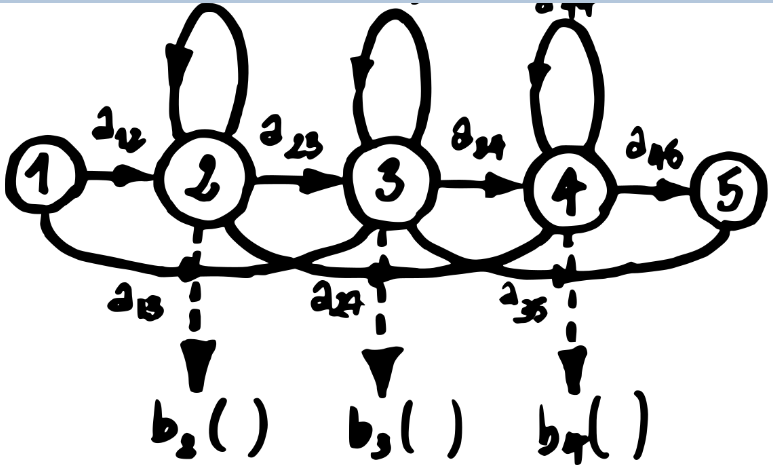
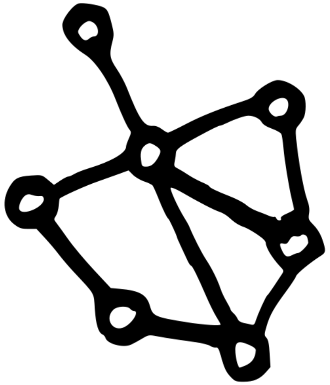




Sequence algorithms

DAG workshop, 2020
Cyril Matthey-Doret





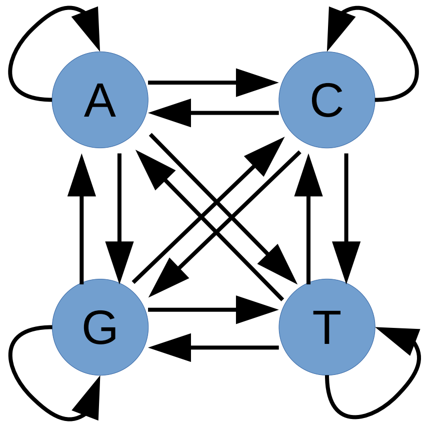
cyril.mattheydoret@gmail.com
cmdoret

Exercises from session 3

Working with sequences of states

- Different from classification: Input and output have an order
- Markov models: define states and transition probabilities
- Example: nucleotide transition matrix from DNA sequence

Input:
AACTTTGAGAC

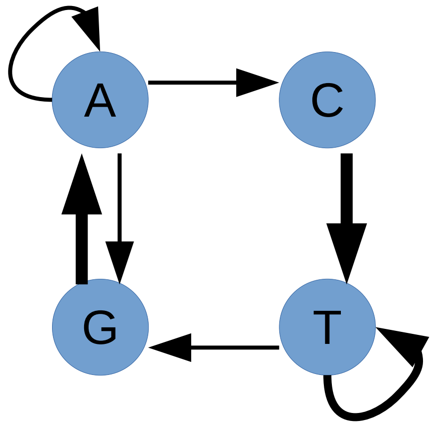


↗	A	C	G	T
A	1	1	1	0
C	0	0	0	1
G	2	0	0	0
T	0	0	1	2

Working with sequences of states

- Different from classification: Input and output have an order
- Markov models: define states and transition probabilities
- Example: nucleotide transition matrix from DNA sequence

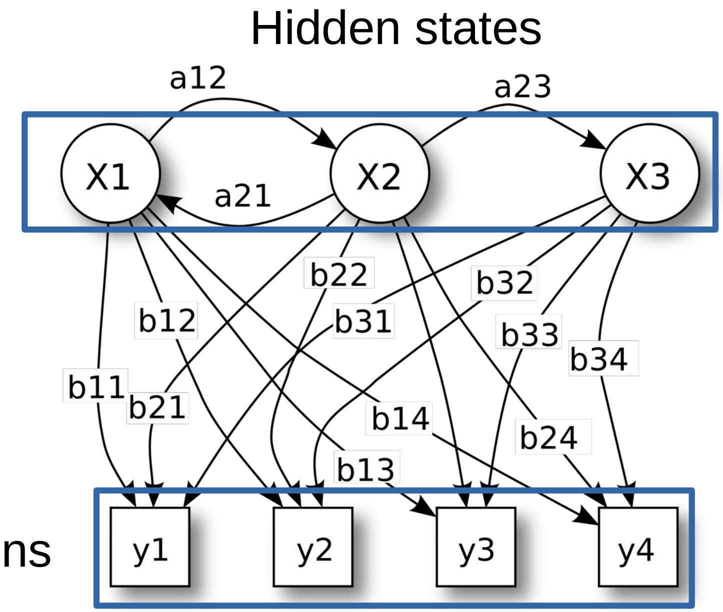
Input:
AACTTTGAGAC



↗	A	C	G	T
A	0.33	0.33	0.33	0
C	0	0	0	1
G	1	0	0	0
T	0	0	0.33	0.66

Predicting states from sequence

- Markov models by themselves have limited use in genomics
- Hidden Markov models (HMM) are more useful in genomics
    - Input: observations → DNA sequence
    - Output: states → gene / not gene



a = transition probabilities
b = emission probabilities

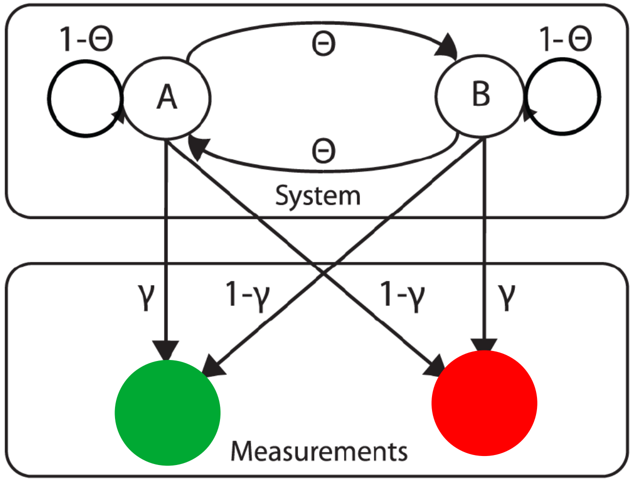
Observations

HMM: example

- A system switches between two (hidden) states A and B
- A device measures the system state, but it is error prone
- It shows 🟢 or 🔴 when it measures A or B, respectively

What we want to know →

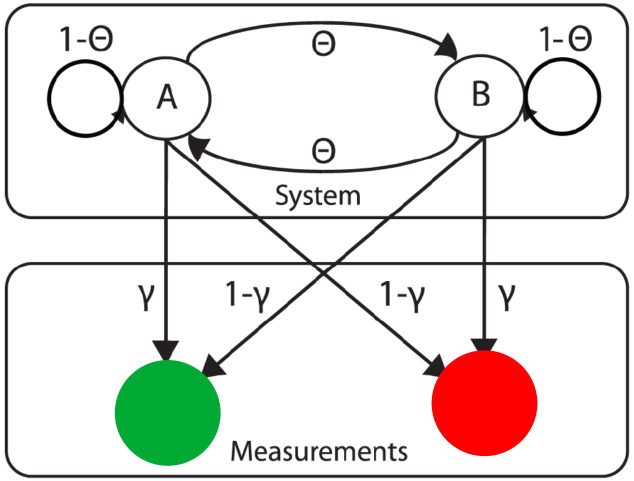
What we see →



Example from: Sunnåker et al., PloS Comp.Biol. 2013

HMM: example

- Given the measurement sequence: 🟢 🔴 🔴
- What is the probability of the observed measurement sequence ?
  - Naive: Sum probabilities of all possible state sequences



HMM: Naive sequence probability

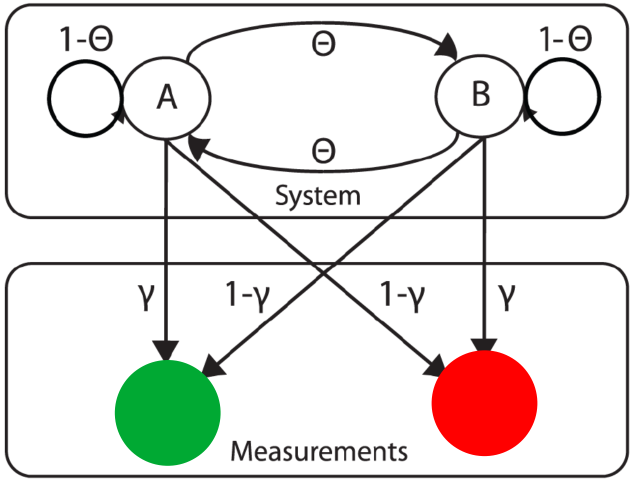
- Find the probability of measurements: 🟢 🔴 🔴
- Weighted sum probabilities of every single state sequence

With X different hidden states, the number of possible sequences **S** of length T is: **R=X^T (here: 8=2^3)**

State sequence of length T

$$p(M_T) = \sum_{r=1}^{R} p(M_T|S_T^r)p(S_T^r)$$

Measurement sequence of length T



HMM: Naive sequence probability

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State sequence of length T

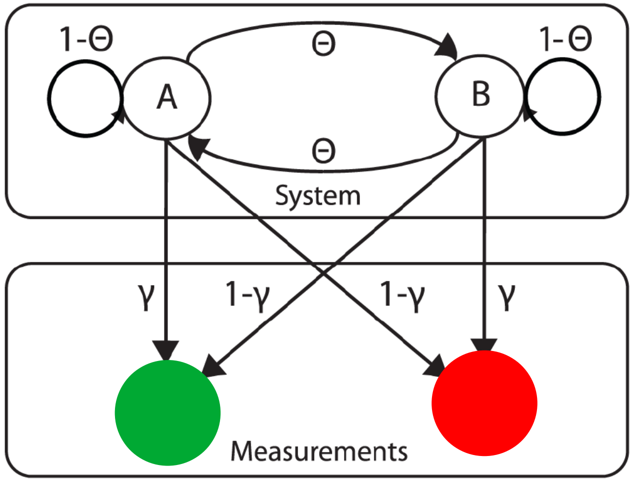
$$p(M_T) = \sum_{r=1}^{R} p(M_T|S_T^r)p(S_T^r)$$

🟢 🔴 🔴   🟢 🔴 🔴

AAA
AAB
ABB
...

AAA
AAB
ABB
...

Measurement sequence of length T



HMM: Naive sequence probability

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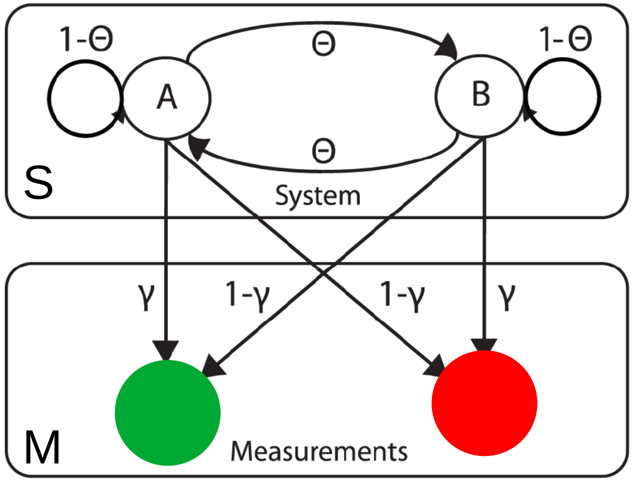
State sequence of length T

$$p(M_T) = \sum_{r=1}^{R} p(M_T|S_T^r)\underset{?}{}p(S_T^r)\underset{?}{}$$

Measurement sequence of length T



HMM: Naive sequence probability

- Find the probability of measurements: 🟢 🔴 🔴
- Weighted sum probabilities of every single sequences

Measurement at position t of M

$$p(M_T|S_r^T) = \prod_{t=1}^{T} p(m(t)|s(t))$$

State at position t of S

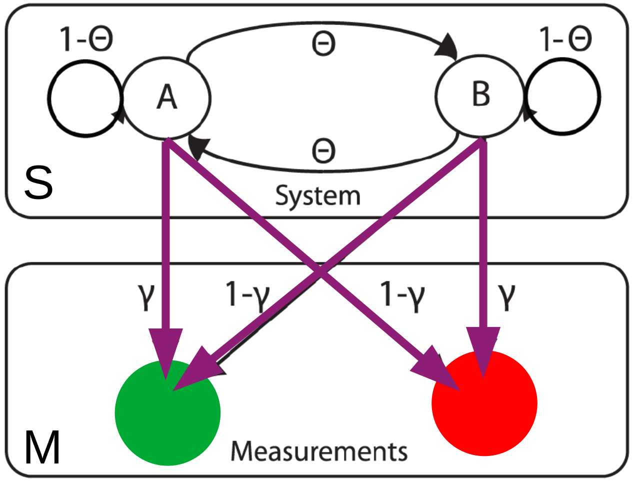
$$p(M_T) = \sum_{r=1}^{R} p(M_T|S_T^r)p(S_T^r)$$

HMM: Naive sequence probability

- Find the probability of measurements: 🟢 🔴 🔴
- Weighted sum probabilities of every single sequences

$$p(M_T|S_r^T) = \prod_{t=1}^{T} \underbrace{p(m(t)|s(t))}_{\text{Emission prob}}$$

$$p(M_T) = \sum_{r=1}^{R} p(M_T|S_T^r)p(S_T^r)$$



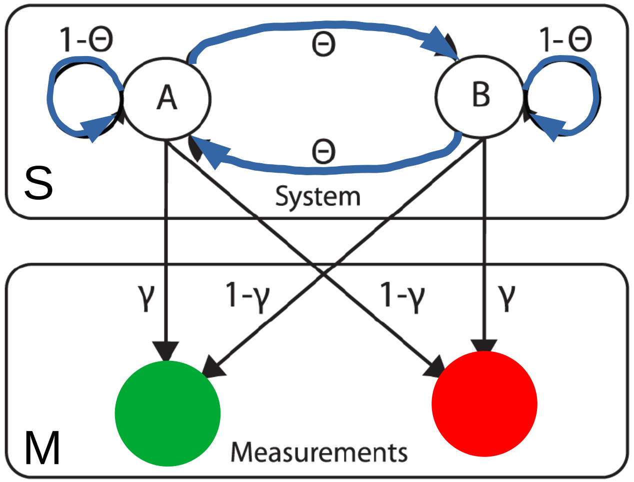
HMM: Naive sequence probability

- Find the probability of measurements: 🟢🔴🔴
- Weighted sum probabilities of every single sequences

$$p(M_T|S_r^T) = \prod_{t=1}^{T} \underbrace{p(m(t)|s(t))}_{\text{Emission prob}}$$

$$p(M_T) = \sum_{r=1}^{R} p(M_T|S_T^r)p(S_T^r)$$

$$p(S_T) = \prod_{t=1}^{T} p(s(t)|s(t-1))$$



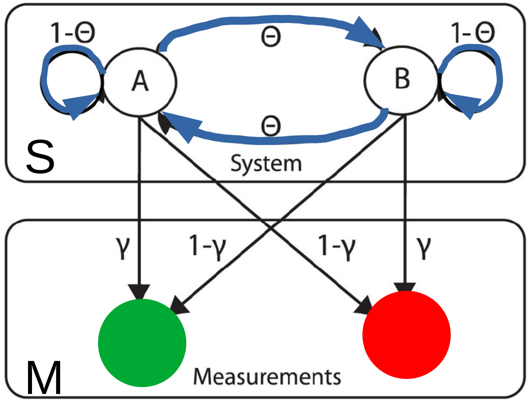
HMM: Naive sequence probability

- Find the probability of measurements: 🟢 🔴 🔴
- Weighted sum probabilities of every single sequences

$$p(M_T|S_r^T) = \prod_{t=1}^{T} \underbrace{p(m(t)|s(t))}_{\text{Emission prob}}$$

$$p(M_T) = \sum_{r=1}^{R} p(M_T|S_T^r)p(S_T^r)$$

$$p(S_T) = \prod_{t=1}^{T} \overbrace{p(s(t)|s(t-1))}^{\text{Transition prob}}$$



HMM: Naive sequence probability

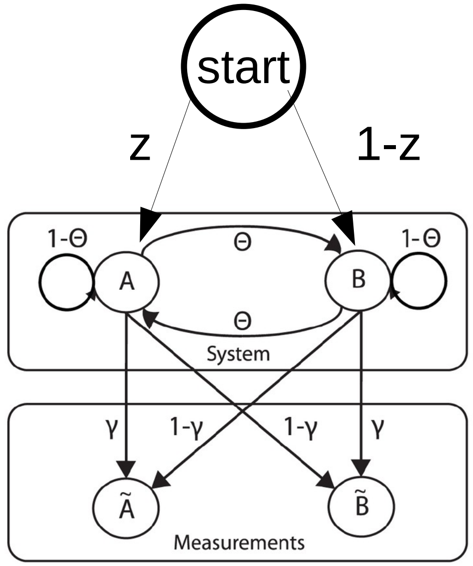
- Find the probability of measurements: 🟢 🔴 🔴
- Sum probabilities of every single sequences

$$p(M_T) = \sum_{r=1}^{R} \prod_{t=1}^{T} p(m(t)|s(t))p(s(t)|s(t-1))$$

What if t=0 and t-1 = -1 ?

HMM: Naive sequence probability

- Find the probability of measurements: 🟢 🔴 🔴
- Sum probabilities of every single sequences



$$p(M_T) = \sum_{r=1}^{R} \prod_{t=1}^{T} p(m(t)|s(t))p(s(t)|s(t-1))$$

What if t=0 and t-1 = -1 ?

HMM: Naive sequence probability

- Find the probability of measurements: 🟢 🔴 🔴
- Sum probabilities of every single sequences

Example:

P(GRR) = Σ |
p(GRR|AAA) = p(G1|A1) * z * p(R2|A2) * p(A2|A1) * p(R3|A3) * p(A3|A2)
= Ɣ * z * (1-Ɣ) * (1-Θ) * (1-Ɣ) * (1-Θ)
p(GRR|AAB) = ...
p(GRR|ABB) = …
…

$$p(M_T) = \sum_{r=1}^{R} \prod_{t=1}^{T} p(m(t)|s(t))p(s(t)|s(t-1))$$

HMM: Naive sequence probability

- Find the probability of measurements: 🟢 🔴 🔴
- Sum probabilities of every single sequences
- What is the time complexity according to T and X (number of states) ?

$$p(M_T) = \sum_{r=1}^{R} \prod_{t=1}^{T} p(m(t)|s(t))p(s(t)|s(t-1))$$

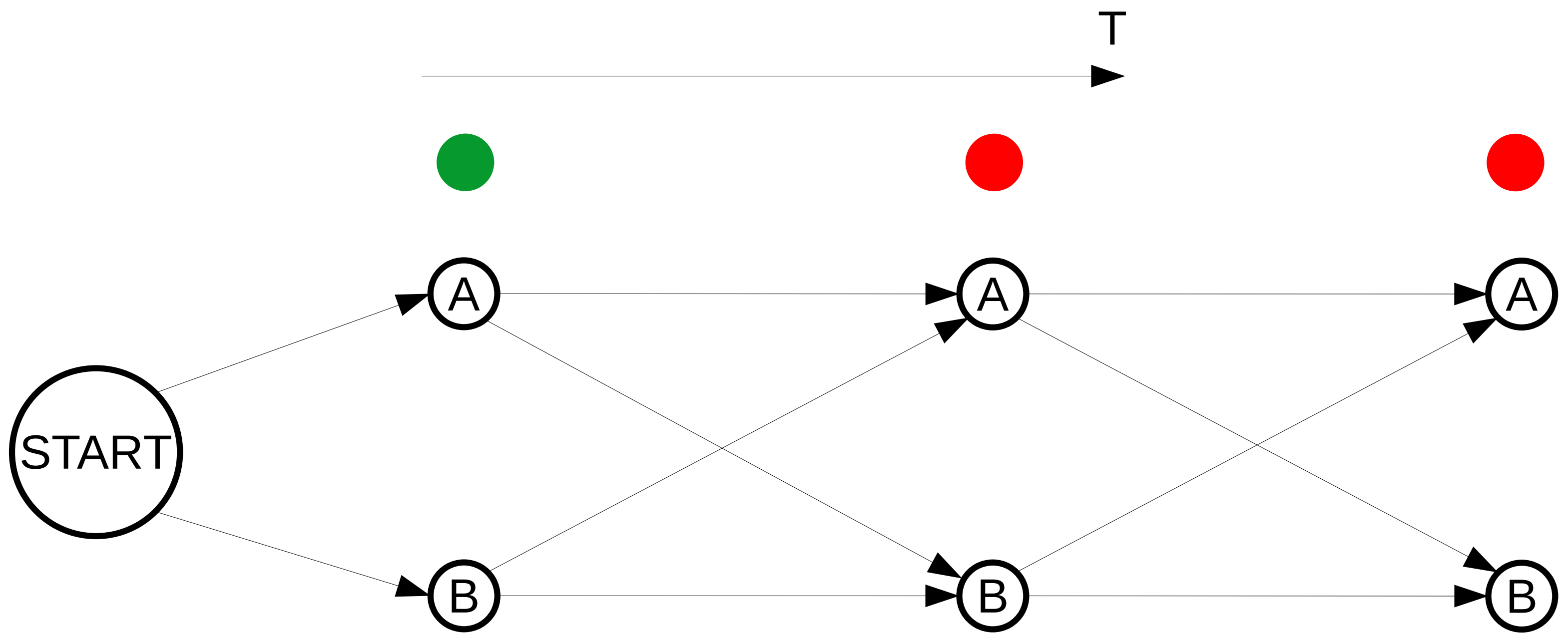
HMM: Naive sequence probability

- Find the probability of measurements: 🟢 🔴 🔴
- Sum probabilities of every single sequences
- What is the time complexity according to T and X (number of states) ? **O(X^T T)**

$$p(M_T) = \sum_{r=1}^{R} \prod_{t=1}^{T} p(m(t)|s(t))p(s(t)|s(t-1))$$

HMM: Forward algorithm

- Sequence probability can be solved using dynamic programming
- Avoid recomputing the same products many time



HMM: Forward algorithm

- Sequence probability can be solved using dynamic programming
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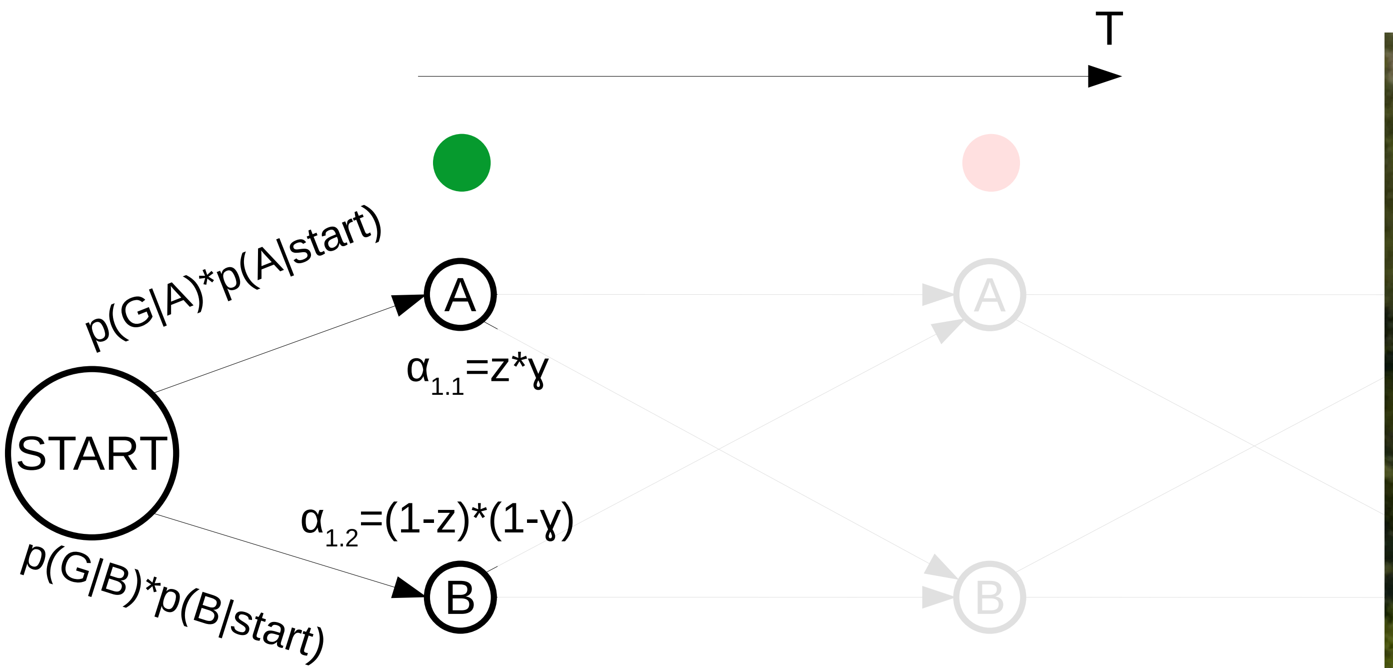

HMM: Forward algorithm

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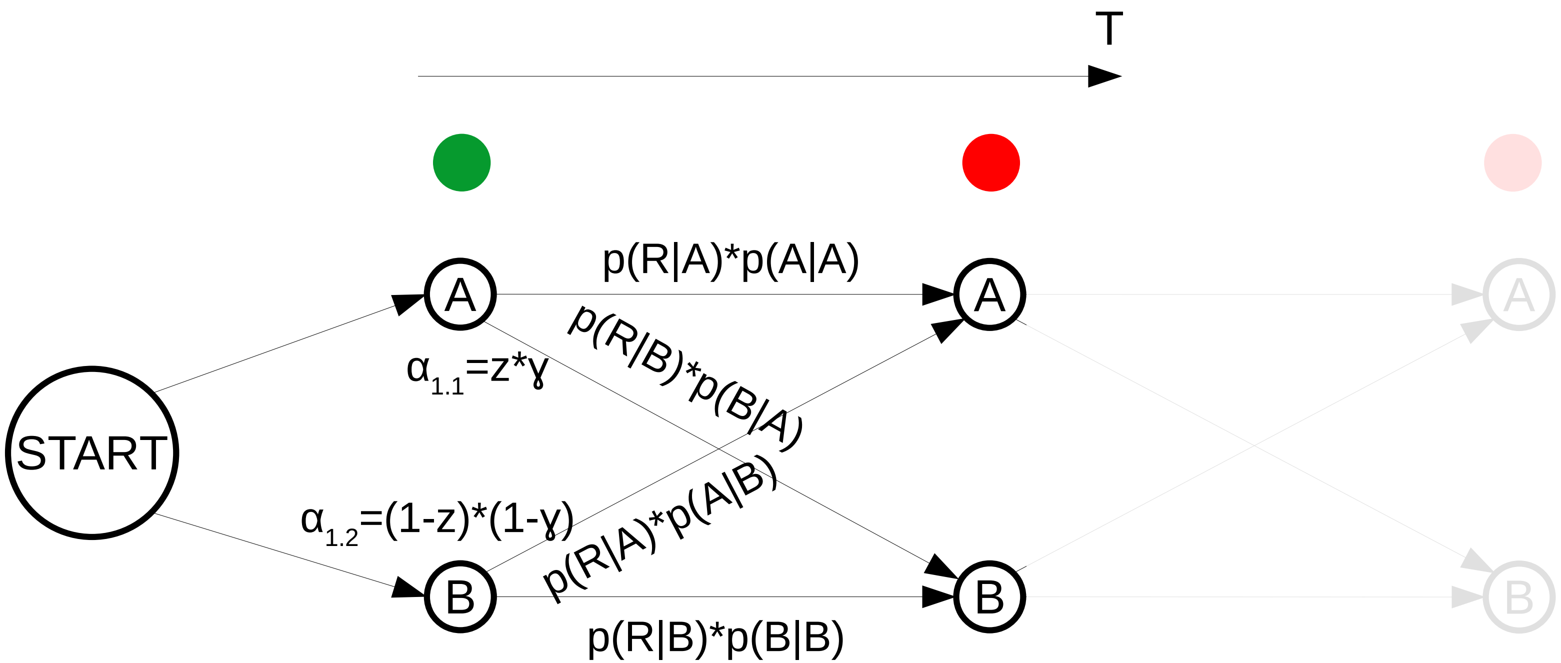

HMM: Forward algorithm

- Sequence probability can be solved using dynamic programming
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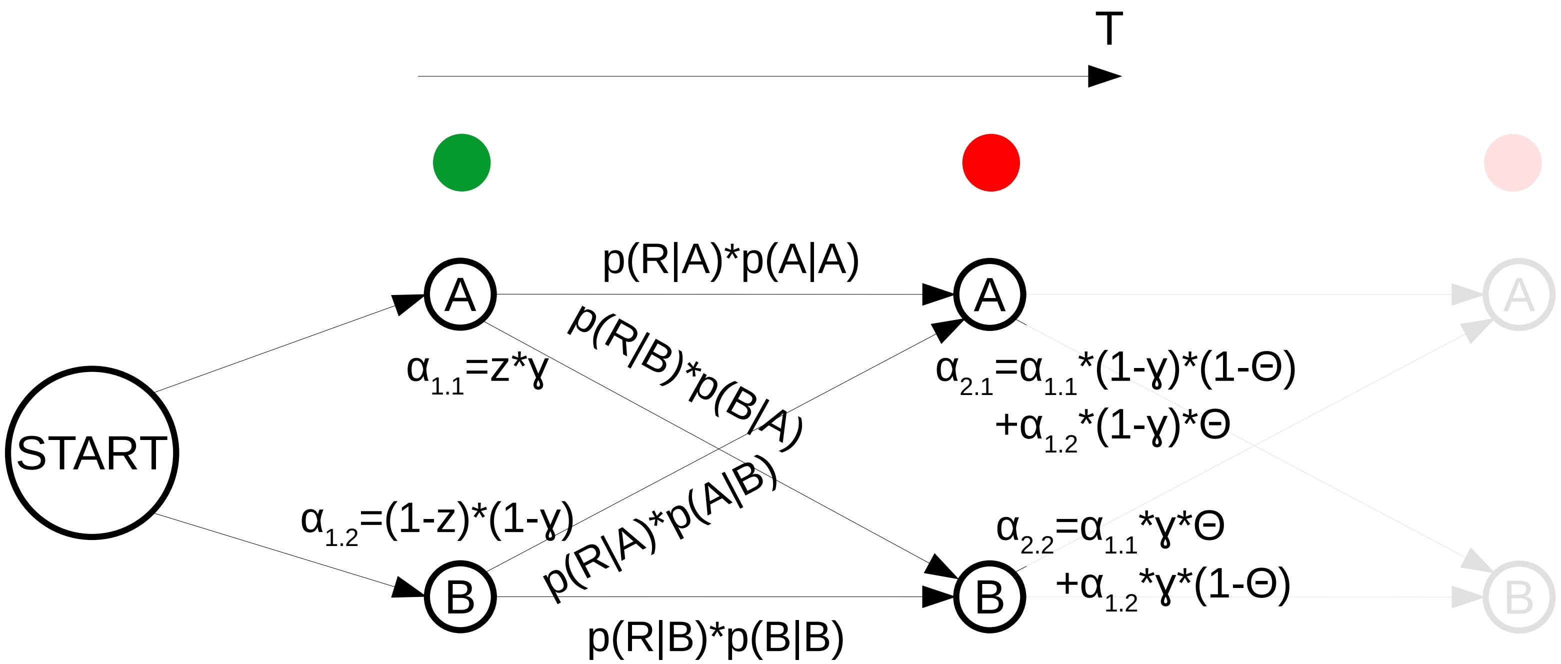
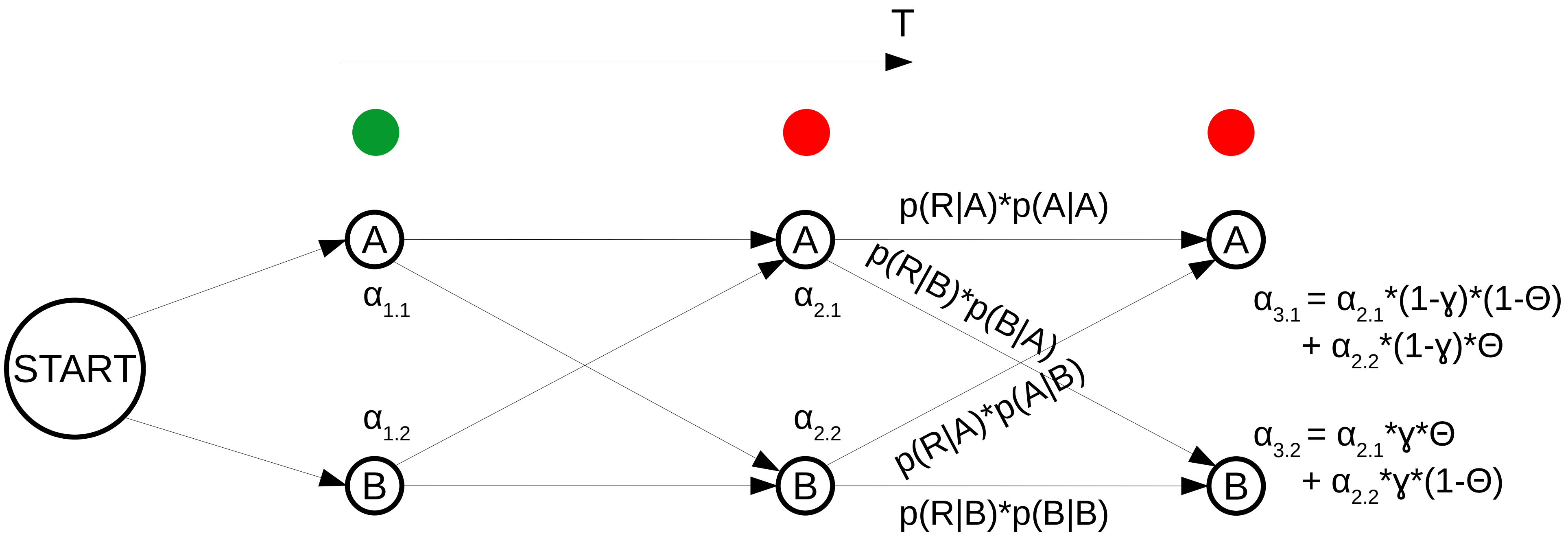

T
START
A
B
A
B
A
B
p(R|A)*p(A|A)
p(R|B)*p(B|A)
p(R|A)*p(A|B)
p(R|B)*p(B|B)
$\alpha_{1.1}=z*\gamma$
$\alpha_{1.2}=(1-z)*(1-\gamma)$
$\alpha_{2.1}=\alpha_{1.1}*(1-\gamma)*(1-\Theta)+\alpha_{1.2}*(1-\gamma)*\Theta$
$\alpha_{2.2}=\alpha_{1.1}*\gamma*\Theta+\alpha_{1.2}*\gamma*(1-\Theta)$

HMM: Forward algorithm

- Sequence probability can be solved using dynamic programming
- Avoid recomputing the same products many time

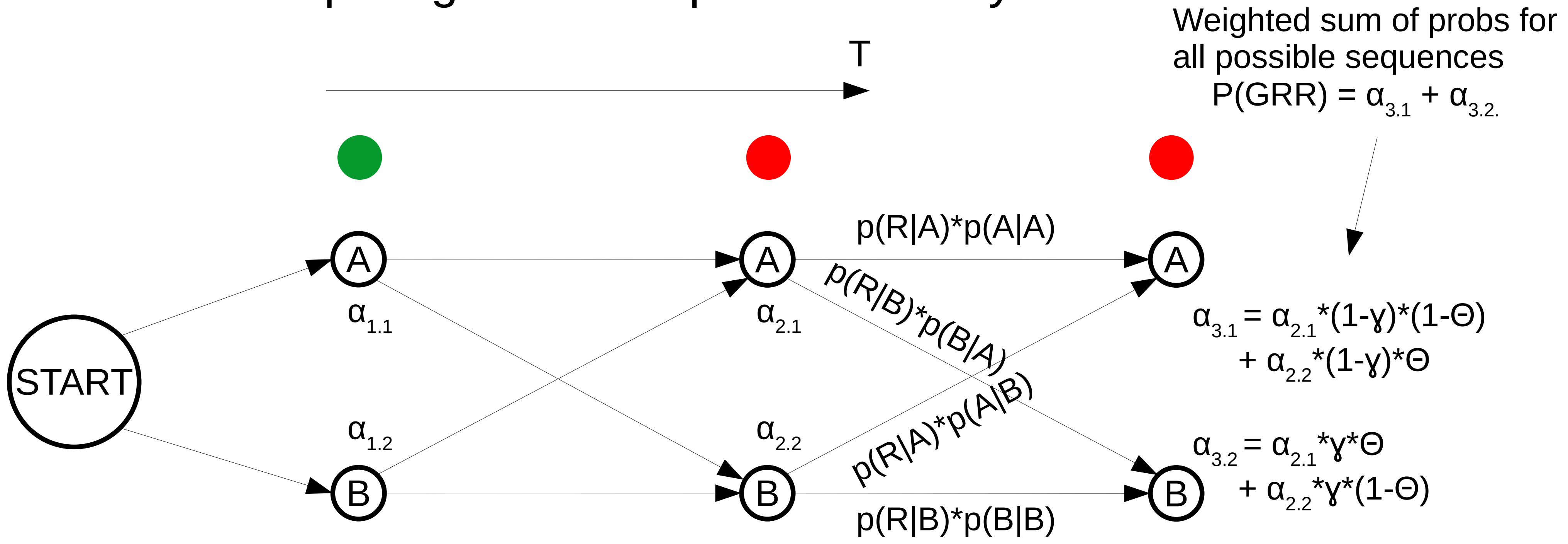


$\alpha_{3.1} = \alpha_{2.1} * (1-\gamma) * (1-\Theta)$
$+ \alpha_{2.2} * (1-\gamma) * \Theta$

$\alpha_{3.2} = \alpha_{2.1} * \gamma * \Theta$
$+ \alpha_{2.2} * \gamma * (1-\Theta)$

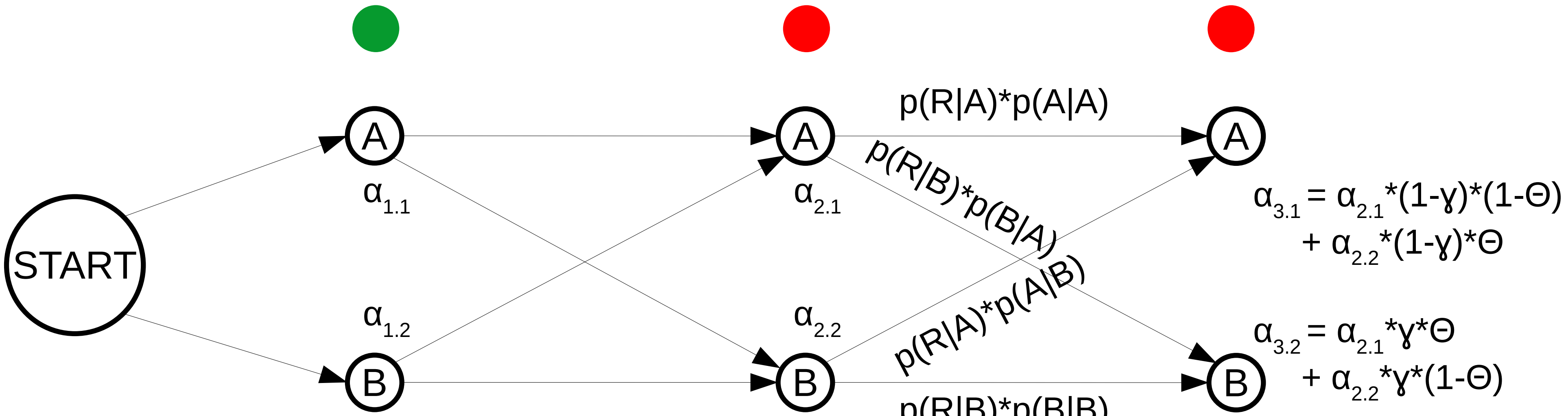
HMM: Forward algorithm

- Sequence probability can be solved using dynamic programming
- Avoid recomputing the same products many time


Weighted sum of probs for all possible sequences
$P(GRR) = \alpha_{3.1} + \alpha_{3.2.}$
T
START
A
B
$\alpha_{1.1}$
$\alpha_{1.2}$
$\alpha_{2.1}$
$\alpha_{2.2}$
p(R|A)*p(A|A)
p(R|B)*p(B|A)
p(R|A)*p(A|B)
p(R|B)*p(B|B)
$\alpha_{3.1} = \alpha_{2.1}*(1-\gamma)*(1-\Theta) + \alpha_{2.2}*(1-\gamma)*\Theta$
$\alpha_{3.2} = \alpha_{2.1}*\gamma*\Theta + \alpha_{2.2}*\gamma*(1-\Theta)$

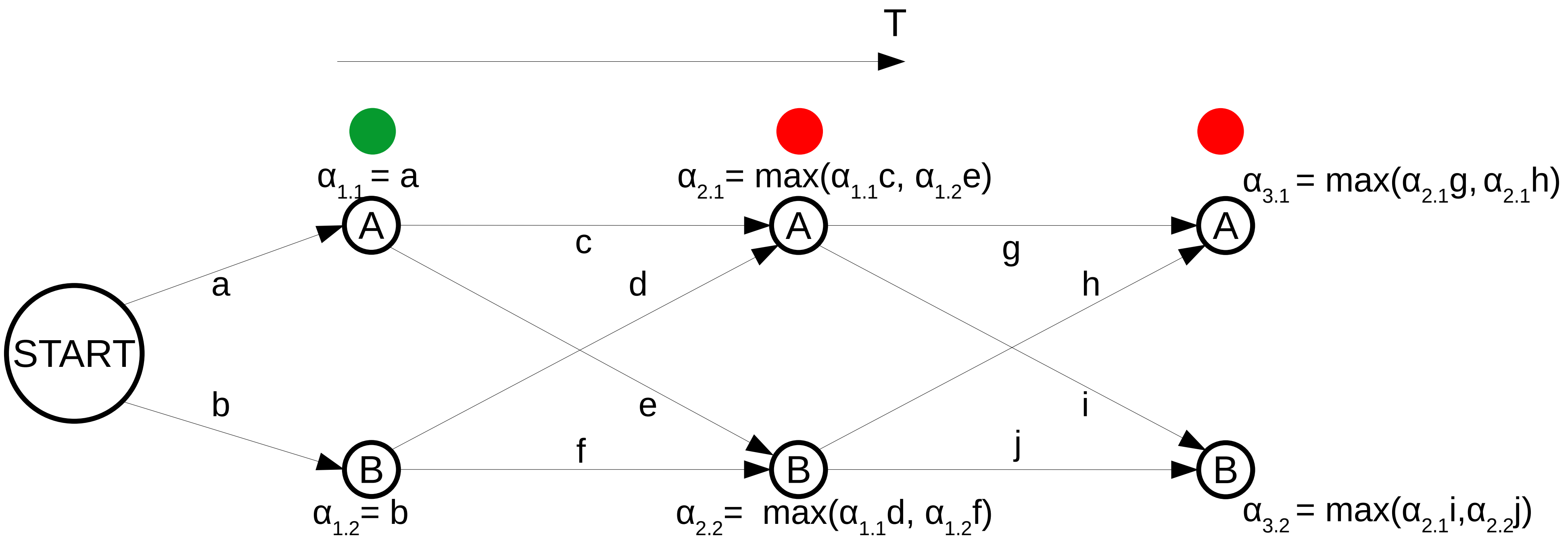
HMM: Forward algorithm

- Complexity of the forward algorithm is $O(TX^2)$ which is $<< O(TX^T)$
- Example use: Distinguishing between two models
  - e.g. Is my sequence more probable with a strand-aware model ?


START
A
B
$\alpha_{1.1}$
$\alpha_{1.2}$
$\alpha_{2.1}$
$\alpha_{2.2}$
p(R|A)*p(A|A)
p(R|B)*p(B|A)
p(R|A)*p(A|B)
p(R|B)*p(B|B)
$\alpha_{3.1} = \alpha_{2.1}*(1-\gamma)*(1-\Theta) + \alpha_{2.2}*(1-\gamma)*\Theta$
$\alpha_{3.2} = \alpha_{2.1}*\gamma*\Theta + \alpha_{2.2}*\gamma*(1-\Theta)$

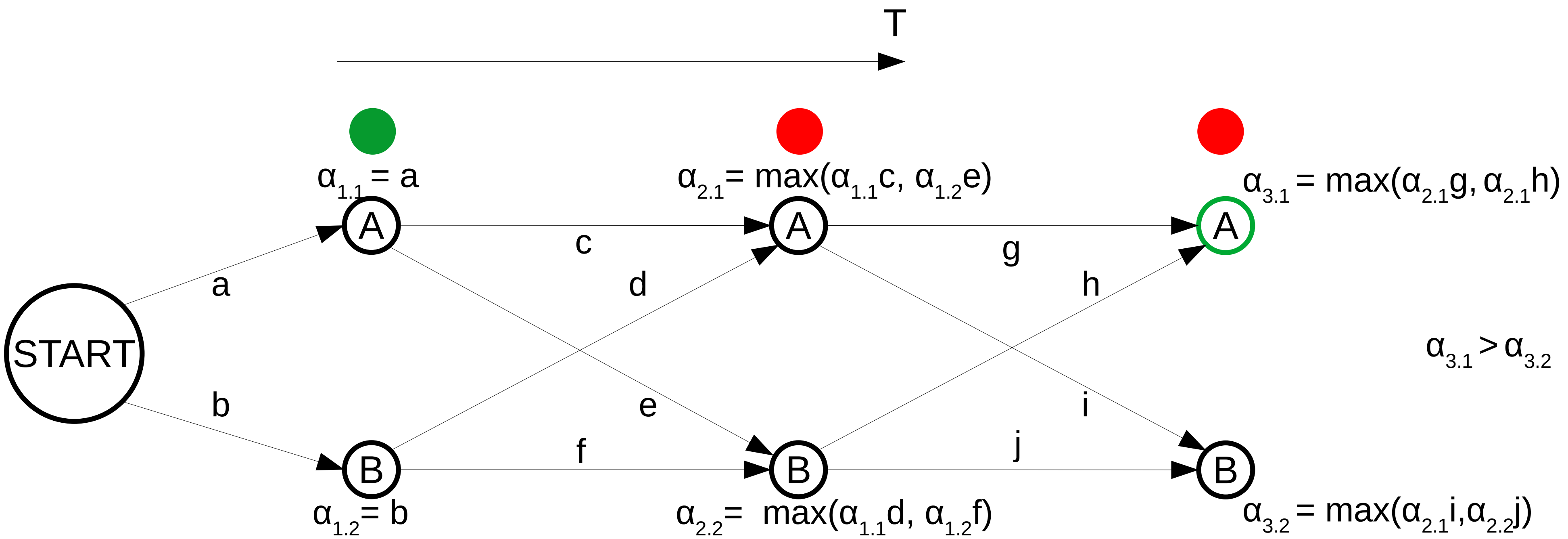
HMM: Viterbi algorithm

- What is the most likely sequence of states, given the observations ?
- Just like the forward algorithm, but using max() instead of sum()


T
$\alpha_{1.1} = a$
$\alpha_{2.1} = \max(\alpha_{1.1}c, \alpha_{1.2}e)$
$\alpha_{3.1} = \max(\alpha_{2.1}g, \alpha_{2.1}h)$
START
A
A
A
B
B
B
a
b
c
d
e
f
g
h
i
j
$\alpha_{1.2} = b$
$\alpha_{2.2} = \max(\alpha_{1.1}d, \alpha_{1.2}f)$
$\alpha_{3.2} = \max(\alpha_{2.1}i, \alpha_{2.2}j)$

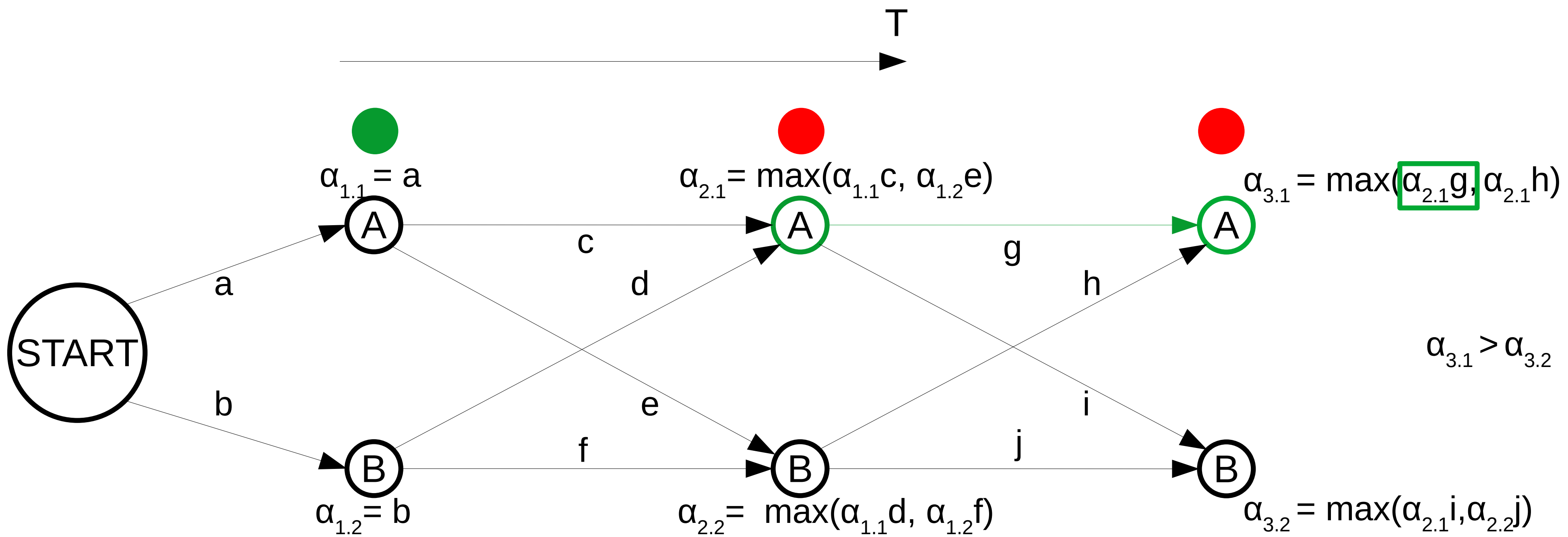
HMM: Viterbi algorithm

- Backtrack from T to 0 (similar to Needleman-Wunsch)


T
$\alpha_{1.1} = a$
$\alpha_{2.1} = \max(\alpha_{1.1}c, \alpha_{1.2}e)$
$\alpha_{3.1} = \max(\alpha_{2.1}g, \alpha_{2.1}h)$
START
A
B
a
b
c
d
e
f
g
h
i
j
$\alpha_{3.1} > \alpha_{3.2}$
$\alpha_{1.2} = b$
$\alpha_{2.2} = \max(\alpha_{1.1}d, \alpha_{1.2}f)$
$\alpha_{3.2} = \max(\alpha_{2.1}i, \alpha_{2.2}j)$

HMM: Viterbi algorithm

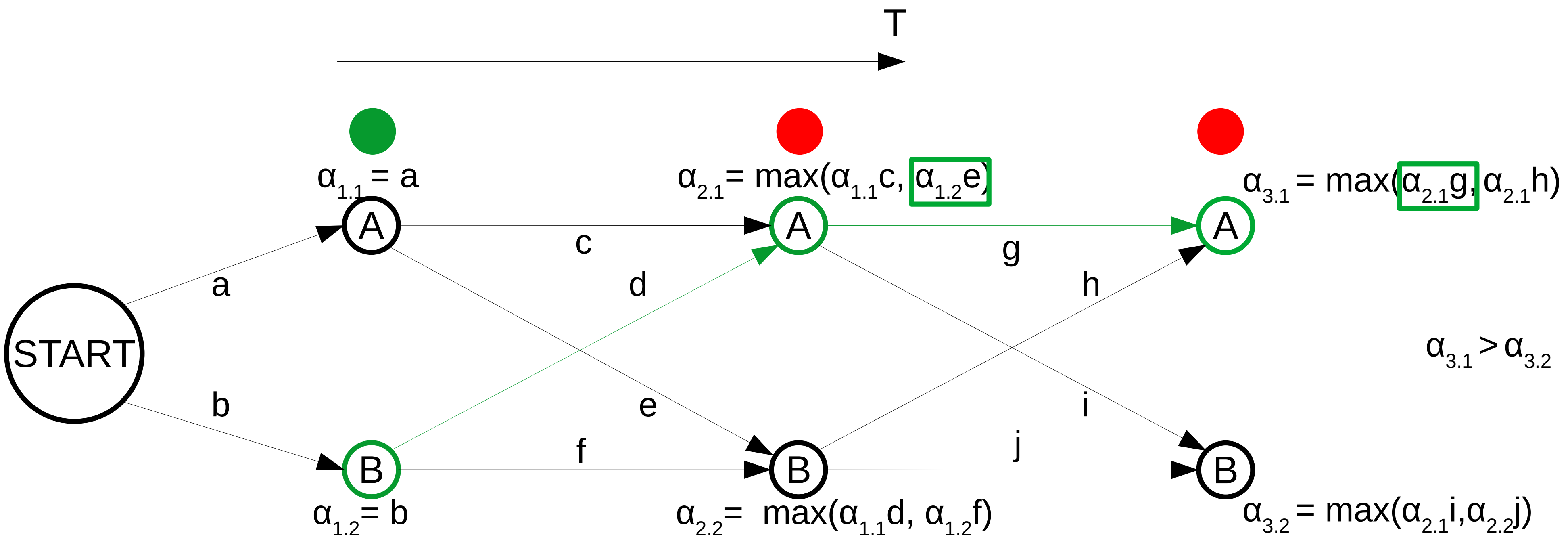
- Backtrack from T to 0 (similar to Needleman-Wunsch)



T
$\alpha_{1.1} = a$
$\alpha_{2.1} = \max(\alpha_{1.1}c, \alpha_{1.2}e)$
$\alpha_{3.1} = \max(\boxed{\alpha_{2.1}g,} \alpha_{2.1}h)$
START
A
A
A
B
B
B
a
b
c
d
e
f
g
h
i
j
$\alpha_{3.1} > \alpha_{3.2}$
$\alpha_{1.2} = b$
$\alpha_{2.2} = \max(\alpha_{1.1}d, \alpha_{1.2}f)$
$\alpha_{3.2} = \max(\alpha_{2.1}i, \alpha_{2.2}j)$

HMM: Viterbi algorithm

- Backtrack from T to 0 (similar to Needleman-Wunsch)



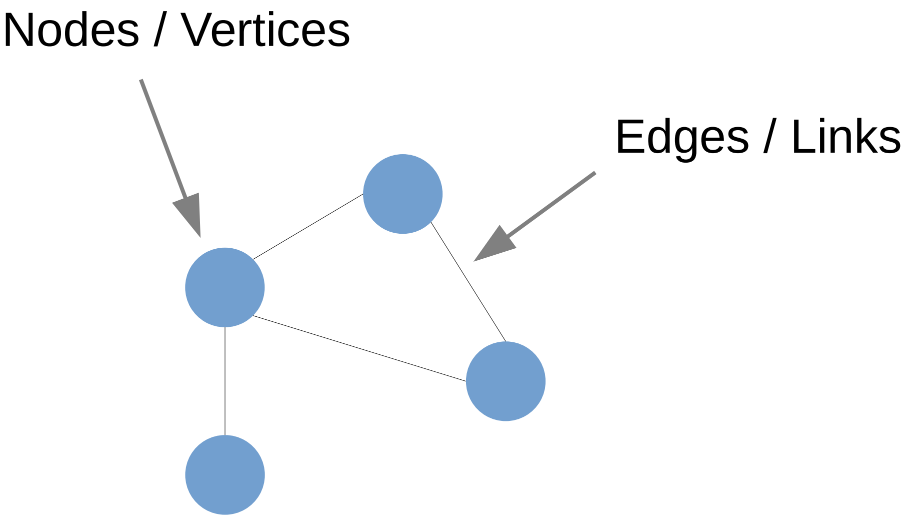
T
$\alpha_{1.1} = a$
$\alpha_{2.1} = \max(\alpha_{1.1}c, \boxed{\alpha_{1.2}e})$
$\alpha_{3.1} = \max(\boxed{\alpha_{2.1}g,} \alpha_{2.1}h)$
START
A
A
A
B
B
B
a
b
c
d
e
f
g
h
i
j
$\alpha_{3.1} > \alpha_{3.2}$
$\alpha_{1.2} = b$
$\alpha_{2.2} = \max(\alpha_{1.1}d, \alpha_{1.2}f)$
$\alpha_{3.2} = \max(\alpha_{2.1}i, \alpha_{2.2}j)$

HMM: Applications

- Gene annotation: Genome sequence → Intron/exon/splice site
  - AUGUSTUS
- Long read correction: Noisy long reads → most probable sequence
  - HERCULES
- Sequence alignment: Sequences → Insertion/Deletion/(Mis)match
  - HMMER
- Chromatin states: Histone marks → regulatory state
  - ChromHMM

Graph theory

- Many biological systems can be represented with graphs
  - Protein interactions, gene regulation, residues in proteins
- Nodes and edges (Markov models are also graphs)



Graph theory

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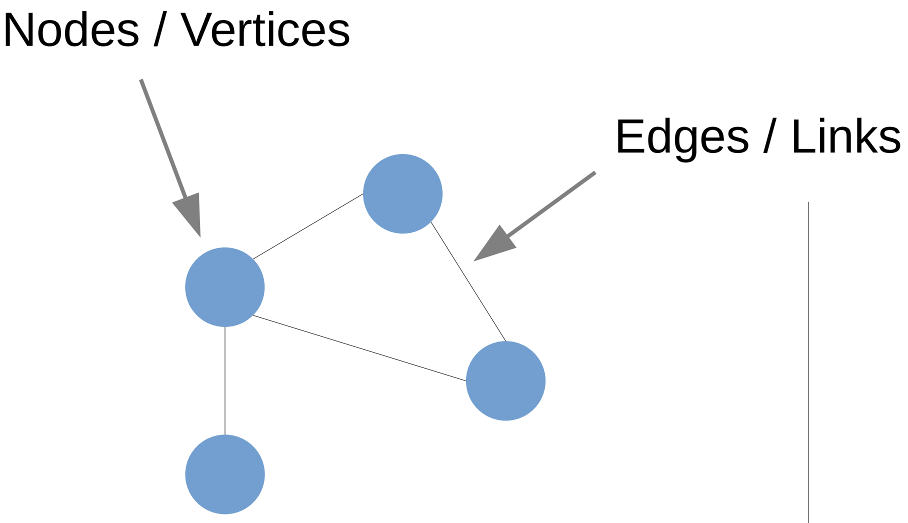
  - Protein interactions, gene regulation, residues in proteins
- Nodes and edges (Markov models are also graphs)

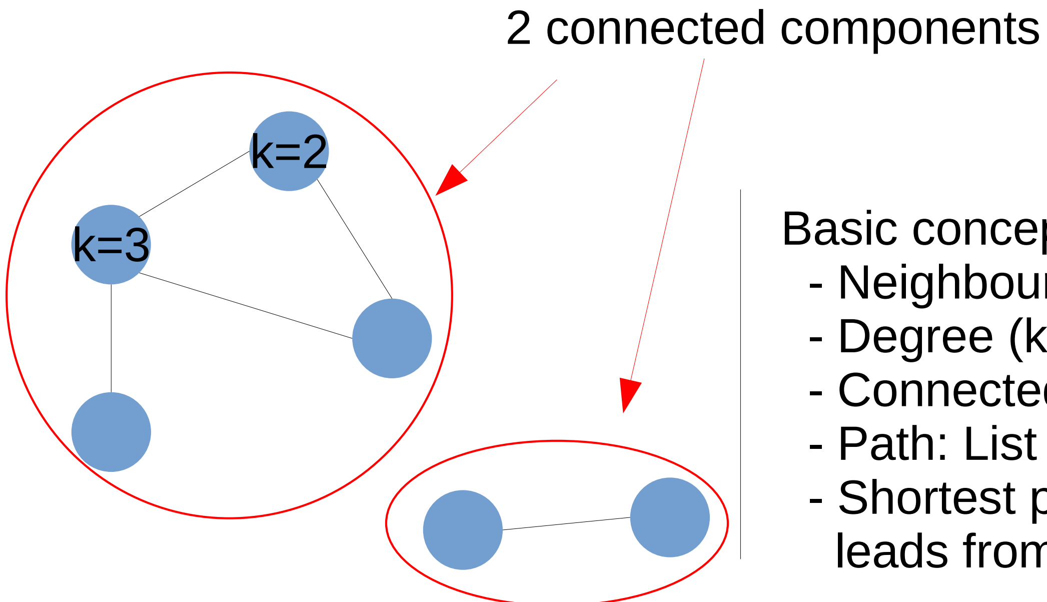


A graph is a set of nodes V and edges E: $G = (V, E)$

Number of nodes: $|V| = N$
Number of edges: $|E|$

Graph theory

- Various metrics can give information about a graph or its nodes

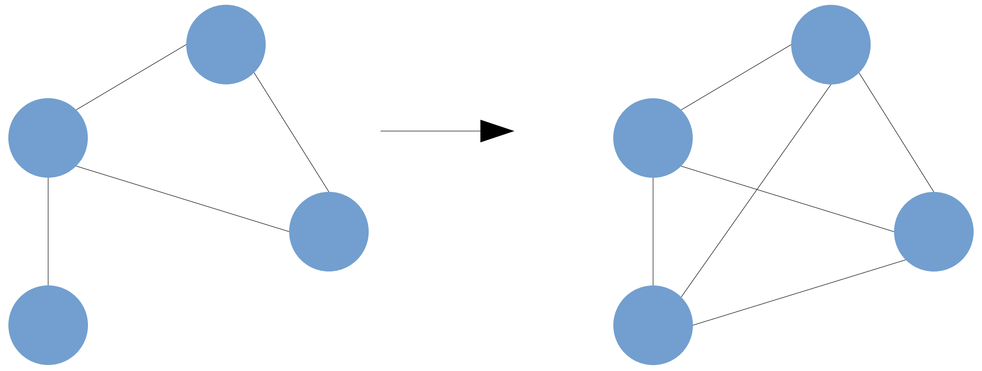


Basic concepts:
- Neighbours: adjacent nodes
- Degree (k): Number of neighbours
- Connected component: Group of connected nodes
- Path: List of adjacent nodes
- Shortest path: Shortest list of adjacent nodes which leads from one node to another

Graph theory

- Maximum number of edges in a network of N nodes ?
  - Hint: How many max edges / node ?

Example with 4 nodes:

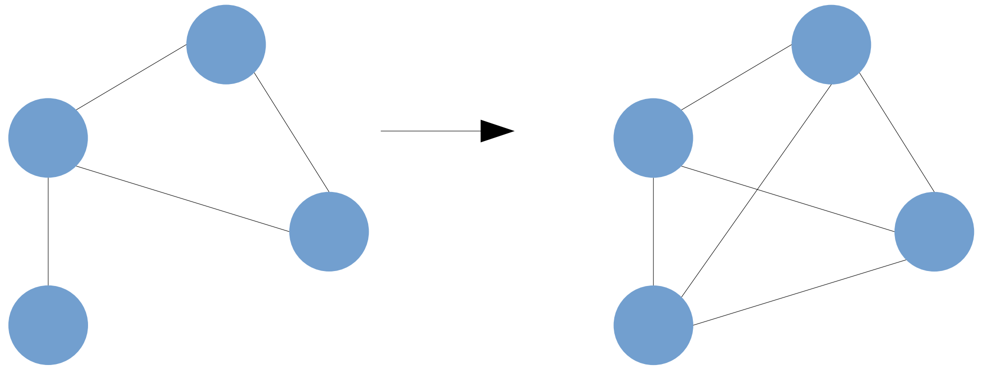


Fully connected:
4 Nodes, 6 edges

Graph theory

- Maximum number of edges in a network of N nodes ? **(N-1)!**
  - Hint: How many max edges / node ?
- In practice, edges scale in O(N) for most networks (“sparse”)

Example with 4 nodes:

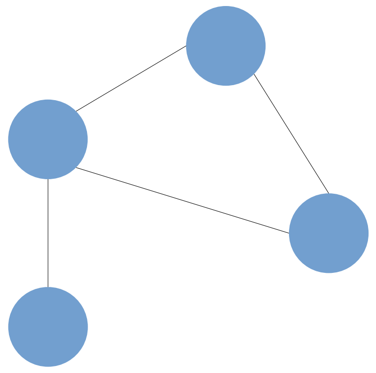


Fully connected:
4 Nodes, 6 edges

Graph theory

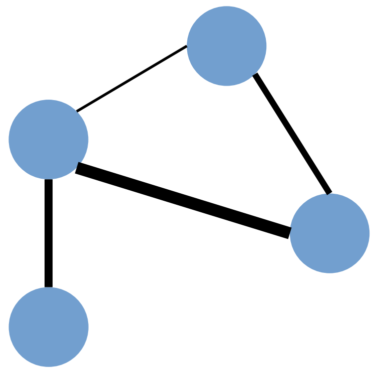
- Edges can be 0/1 or have weights or even directions
- This allows to model different types of processes

Undirected



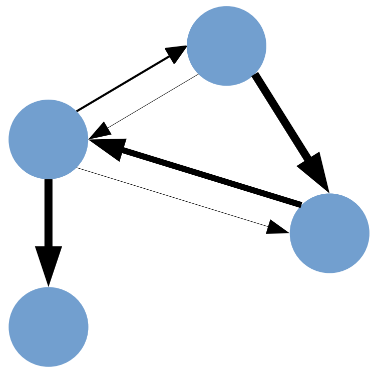
Ex: interacts

Weighted



Ex: binding affinity

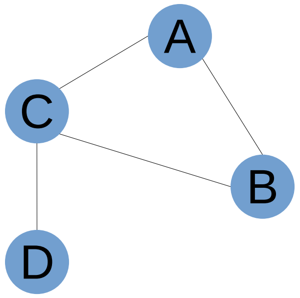
Directed



Ex: promotes/inhibits

Mathematical representation of graphs

- To work with graph, we need to use a formal representation
- There are 3 common representations:



Adjacency list

A – B
A – C
B – C
C – D

Adjacency matrix

$$\begin{array}{ccccc} & A & B & C & D \\ A & 0 & 1 & 1 & 0 \\ B & 1 & 0 & 1 & 0 \\ C & 1 & 1 & 0 & 1 \\ D & 0 & 0 & 1 & 0 \end{array}$$

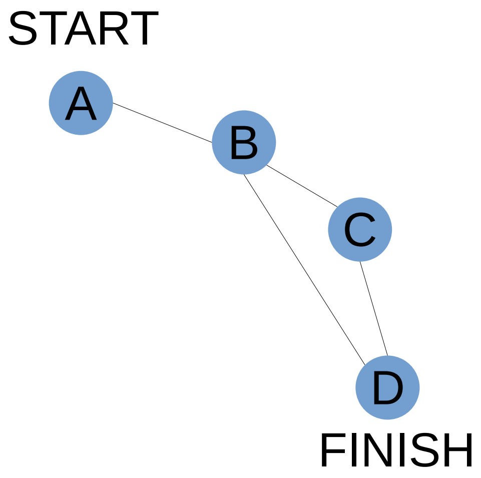
Note: for undirected graphs: $A[i, j] = A[j,i]$

Neighbour list

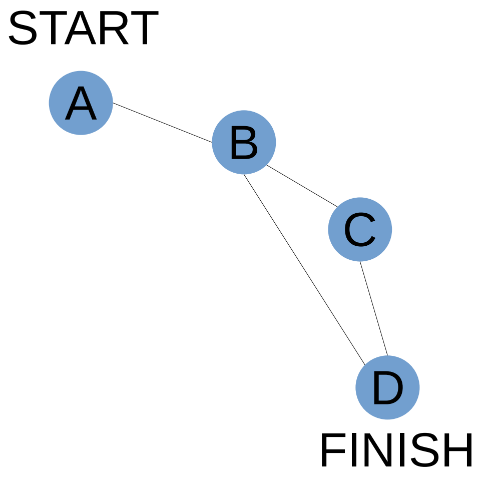
A – B,C
B – A,B
C – A,B,D
D – C

Random walks on a graph

- Imagine you move randomly on the graph
- Probability to go from node A to D in 2 steps ?



Random walks on a graph

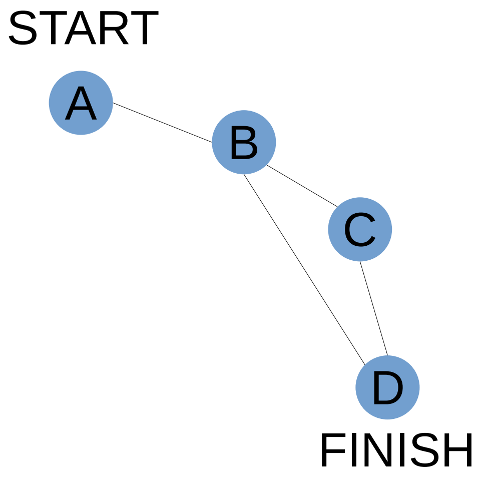


- Imagine you move randomly on the graph
- Probability to go from node A to D in 2 steps ?

All possible paths:

ABA
ABC
ABD 1 success / 3 paths = 0.33

Random walks on a graph

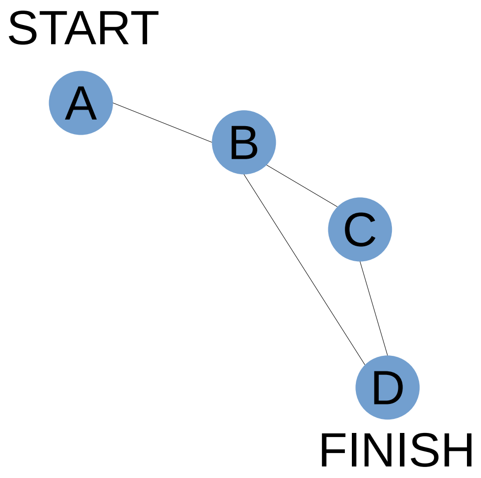


- As the graph grows larger, it becomes infeasible to list each path
- There are $O(K^T)$ paths of length T where K is the average degree

All possible paths:

ABA
ABC
ABD 1 success / 3 paths = 0.33

Random walks, but faster



- All neighbours of A $\rightarrow$ X^1
- All the neighbours of X^1 $\rightarrow$ X^2

1) Probability of A $\rightarrow$ X^1: $\boxed{P(A, X^1)}$
2) Probability of X^1 $\rightarrow$ X^2: $P(X^1, X^2)$
3) Sum $P(A, X^1)$ x $\boxed{P(X^1, D)}$, all cases reaching D

4) Generalization to N steps:

$$\sum P(A, X^1)P(X^1, X^2)...P(X^{N-1}, D)$$

Random walks, but faster

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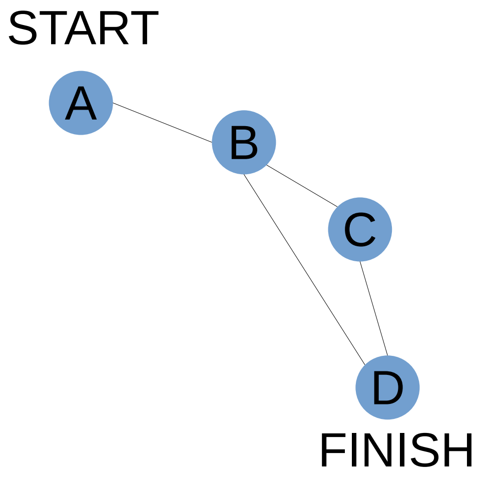

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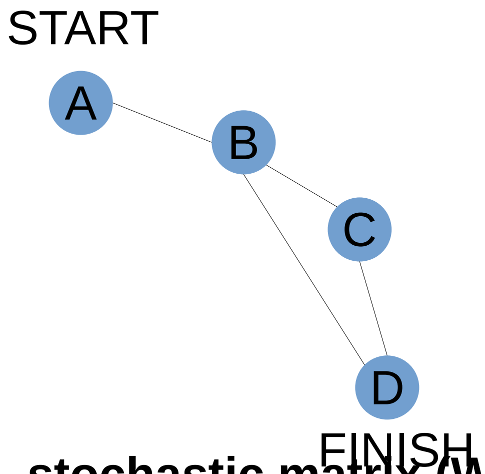
	A	B	C	D
A	0	1	0	0
B	1	0	1	1
C	0	1	0	1
D	0	1	1	0

Random walks, but faster



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Adjacency → stochastic matrix (W)

	A	B	C	D
A	0	1	0	0
B	0.33	0	0.33	0.33
C	0	0.5	0	0.5
D	0	0.5	0.5	0

Random walks, but faster

- The T'th power of the stochastic matrix gives the probability of going from node i to j in T steps
- Scales with O(T) instead of O(K^T)

P(A, D) in 1 step: W[A, D]
P(A, D) in 2 steps: W^2[A,D]
P(A, D) in T steps: W^T[A, D]

	A	B	C	D
A	0	1	0	0
B	0.33	0	0.33	0.33
C	0.	0.5	0	0.5
D	0	0.5	0.5	0

X

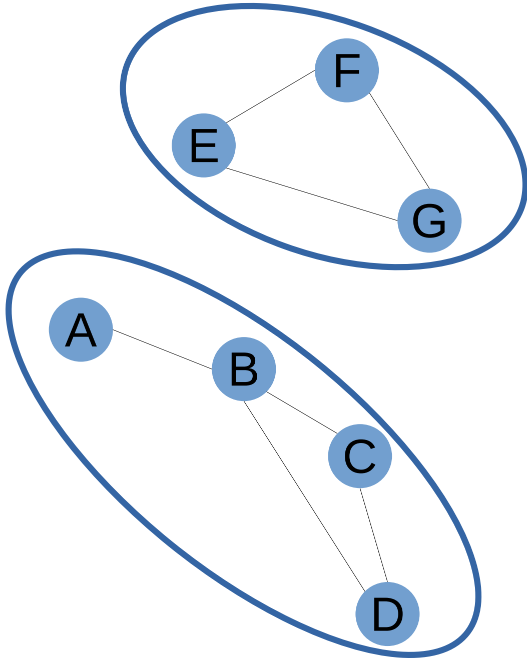
	A	B	C	D
A	0	1	0	0
B	0.33	0	0.33	0.33
C	0.	0.5	0	0.5
D	0	0.5	0.5	0

=

	A	B	C	D
A	0.33	0	0.33	0.33
B	0	0.66	0.17	0.17
C	0.17	0.5	0.42	0.17
D	0.17	0.5	0.17	0.42

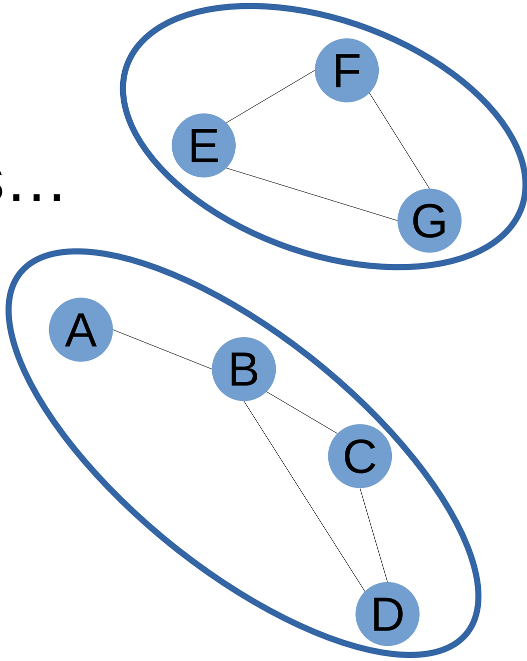
Network clustering

- Easiest scenario: Identify all disconnected components
- How would you do it ?



Identification of disconnected components

- Easiest scenario: Identify all disconnected components
- How would you do it ?
  - Start from any node
  - Explore neighbours, neighbours of neighbours…
  - Skip nodes already visited



Identification of disconnected components

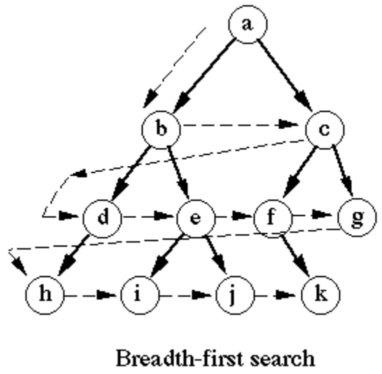
- Breadth first search

```
visited = []
queue = [initial]

while queue:
    node = queue.pop(0)

    if node not in visited:
        visited.append(node)
        neighbours = graph[node]

            for neighbour in neighbours:
                queue.append(neighbour)
```



Repeat with the remaining nodes, if any

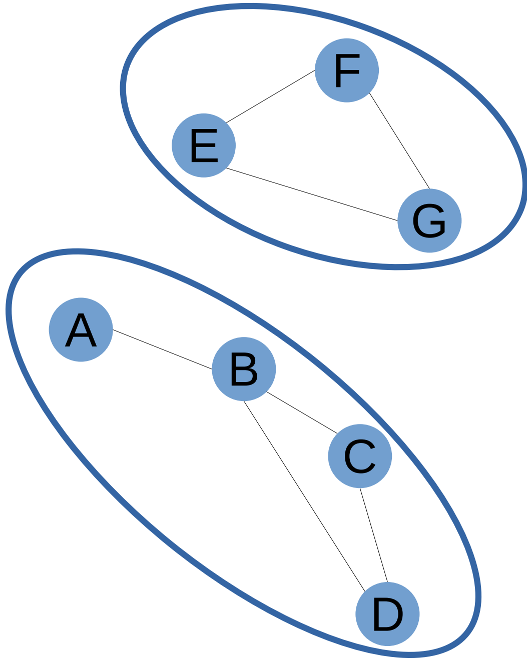


Image: https://www.cse.unsw.edu.au/~billw/Justsearch.html

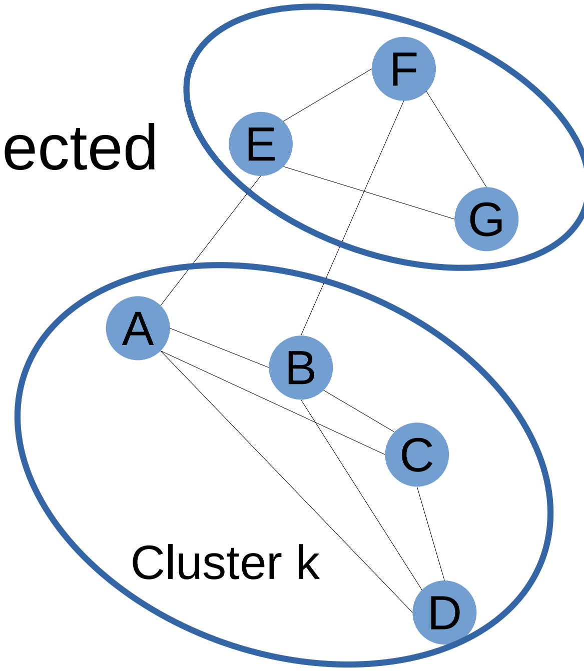
How to define clusters within a network ?

- We need a metric to quantify the accuracy of clusters
- We use modularity
  - Nodes in a cluster should have more edges among them than with other nodes than expected by chance

Number of edges among nodes in k: $l_k = 6$

Number of edges between k and outside: $o_k = 2$

Sum of nodes degrees in k: $d_k = 2l_k + o_k = 14$



How to define clusters within a network ?

- We need a metric to quantify the accuracy of clusters
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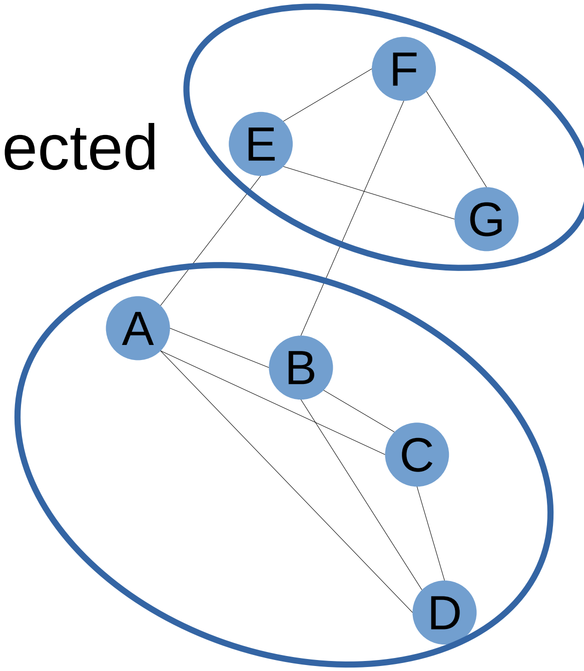
  - Nodes in a cluster should have more edges among them than with other nodes than expected by chance

Probability that one edge is in cluster:

$$\frac{d}{2|E|}$$

Number of possible edges in k

Number of possible edges in the whole network



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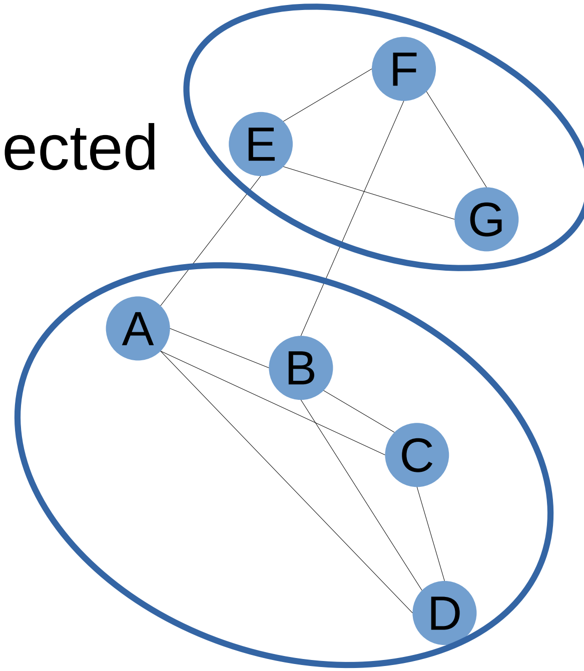


Expected number of internal nodes in a cluster:

$$\frac{d}{2|E|} \cdot d \cdot \frac{1}{2} = \frac{d^2}{4|E|}$$

How to define clusters within a network ?

- We need a metric to quantify the accuracy of clusters
- We use modularity
  - Nodes in a cluster should have more edges among them than with other nodes than expected by chance

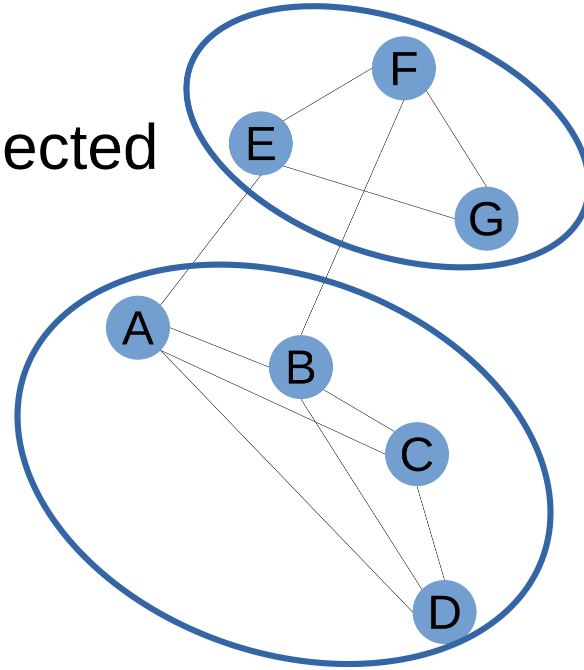
Normalizing factor

# expected internal edges

Network modularity:

$$Q = \frac{1}{|E|} \sum_{k=1}^{K} \left(l_k - \frac{d_k^2}{4|E|} \right)$$

# observed internal edges

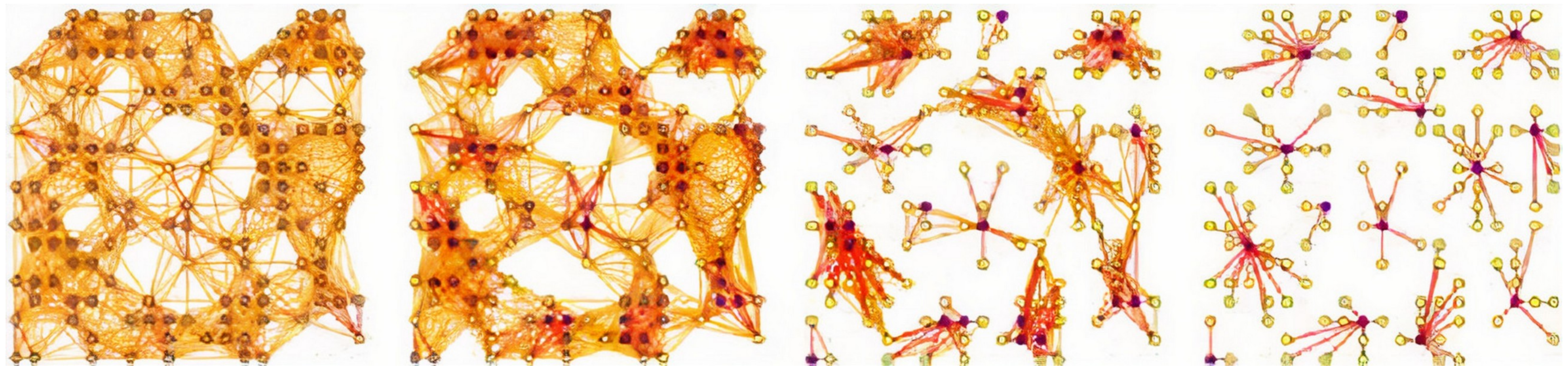


Network clustering

- There are several algorithms to find clusters in a network
- Modularity can be used to measure the validity of the clusters
- Hierarchical clustering: Merge nodes until modularity stops increasing.
- Markov clustering: Number of clusters automatically detected

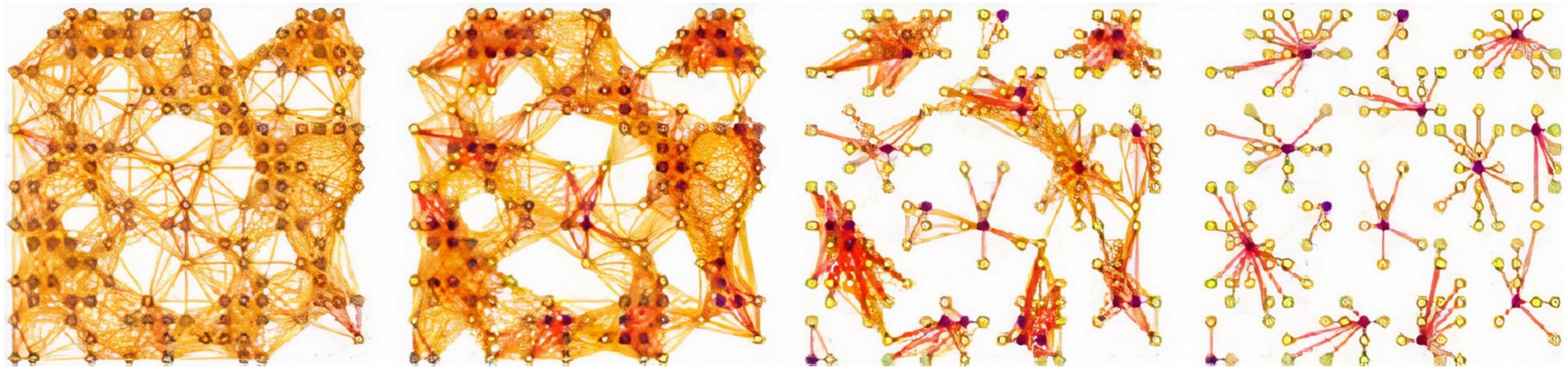
Markov clustering

- Consider the network as a markov process
- Nodes as states, edges as transition probabilities
- Random walks on the graph will infrequently go from one natural cluster to another



Markov clustering

- 3 operations repeated until convergence:
  - Expansion: Simulate random walk on the graph
  - Pruning: Remove the least frequented (low probability) paths
  - Inflation: Increase contrast between probabilities



Markov clustering

Convert to transition probabilities

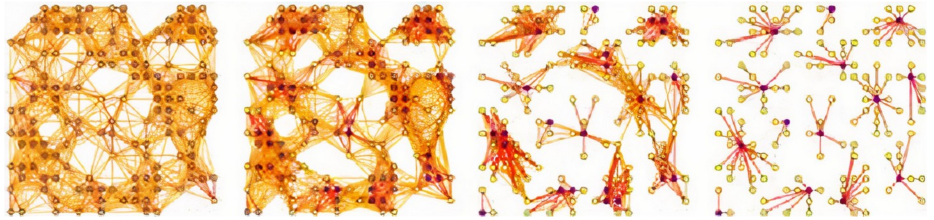
$$\begin{tikzcd}
A \arrow[r] & \boxed{A \text{ -> } W} \arrow[d] \\
& \boxed{W \text{ -> } W^2} \arrow[d] \\
& \boxed{(W^2)_{ij} \text{-> } [(W^2)_{ij}]^r} \arrow[d] \\
& \boxed{M[M<p] = 0} \arrow[uuu, bend right=60]
\end{tikzcd}$$

Expansion: Enhance flow to well connected nodes

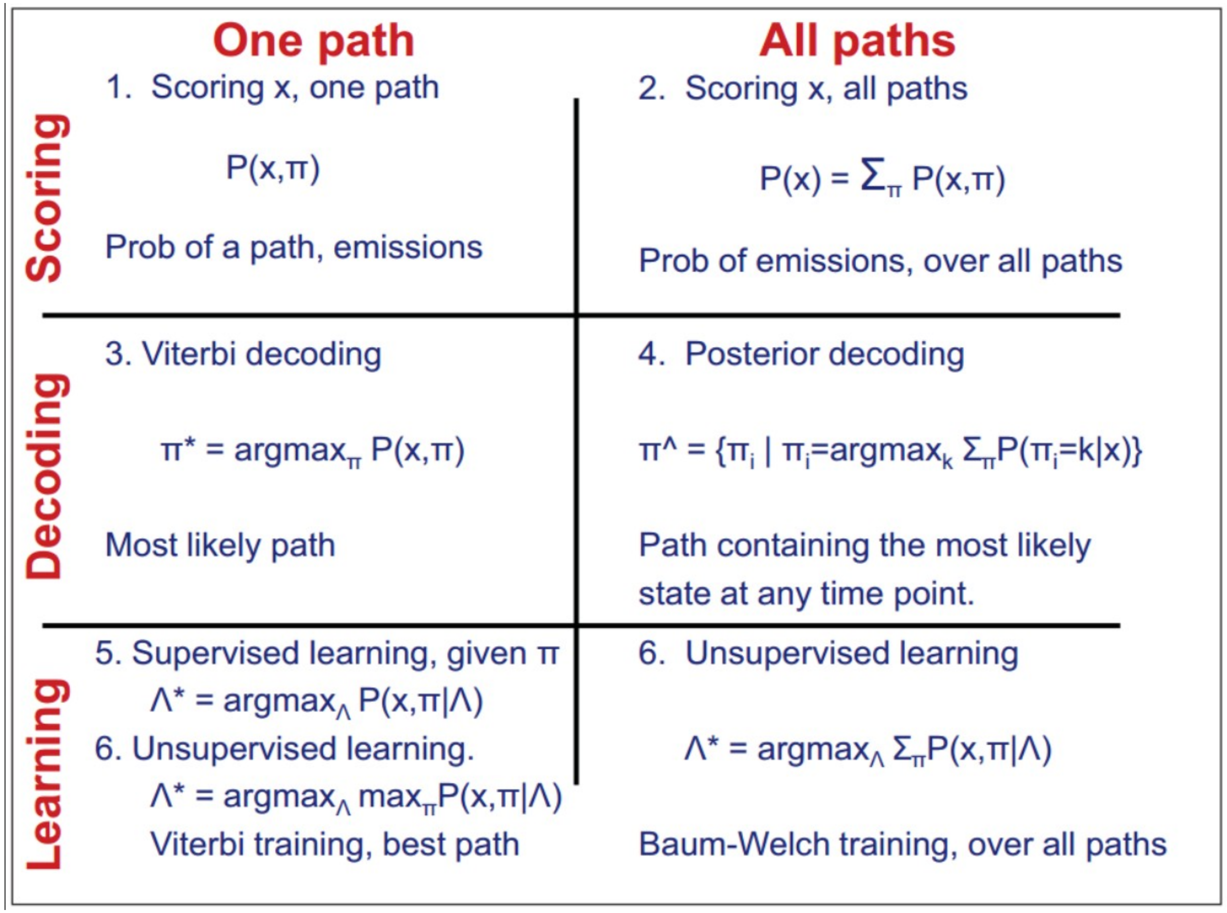
Inflation: Increase inequalities among nodes

Pruning: Remove near-0 values to accelerate convergence

Repeat until convergence: matrix values change very little



If you want to learn more about HMM



	One path	All paths
Scoring	1. Scoring x, one path $P(x,\pi)$ Prob of a path, emissions	2. Scoring x, all paths $P(x) = \Sigma_\pi P(x,\pi)$ Prob of emissions, over all paths
Decoding	3. Viterbi decoding $\pi^* = \text{argmax}_\pi P(x,\pi)$ Most likely path	4. Posterior decoding $\pi\hat{} = \{\pi_i \mid \pi_i=\text{argmax}_k \Sigma_\pi P(\pi_i=k \mid x)\}$ Path containing the most likely state at any time point.
Learning	5. Supervised learning, given π $\Lambda^* = \text{argmax}_\Lambda P(x,\pi \mid \Lambda)$ 6. Unsupervised learning. $\Lambda^* = \text{argmax}_\Lambda \max_\pi P(x,\pi \mid \Lambda)$ Viterbi training, best path	6. Unsupervised learning $\Lambda^* = \text{argmax}_\Lambda \Sigma_\pi P(x,\pi \mid \Lambda)$ Baum-Welch training, over all paths

6.047/6.878 Computational Biology: Genomes, Networks, Evolution (Fall 2012) Lecture 07 - HMMs II (2012-09-29): `link

The main questions on HMMs

1. Scoring x, one path = Joint probability of a sequence and a path, given the model

- GIVEN a HMM M, a path π, and a sequence x,
- FIND Prob[x, π | M]

➔ "Running the model", simply multiply emission and transition probabilities

➔ Application: "all promoter" vs. "all backgorund" comparisons

2. Scoring x, all paths = total probability of a sequence, summed across all paths

- GIVEN a HMM M, a sequence x
- FIND the total probability P[x | M] summed across all paths

➔ Forward algorithm, sum score over all paths (same result as backward)

SCORING

3. Viterbi decoding = parsing a sequence into the optimal series of hidden states

- GIVEN a HMM M, and a sequence x,
- FIND the sequence π^* of states that maximizes P[x, π | M]

➔ Viterbi algorithm, dynamic programming, max score over all paths, trace pointers find path

4. Posterior decoding = total prob that emission x_i came from state k, across all paths

- GIVEN a HMM M, a sequence x
- FIND the total probability P[π_i = k | x, M)

➔ Posterior decoding: run forward & backward algorithms to & from state π_I =k

PARSING

5. Supervised learning = optimize parameters of a model given training data

- GIVEN a HMM M, with unspecified transition/emission probs., labeled sequence x,
- FIND parameters $\theta = (e_i, a_{ij})$ that maximize P[x | θ]

➔ Simply count frequency of each emission and transition observed in the training data

6. Unsupervised learning = optimize parameters of a model given training data

- GIVEN a HMM M, with unspecified transition/emission probs., unlabeled sequence x,
- FIND parameters $\theta = (e_i, a_{ij})$ that maximize P[x | θ]

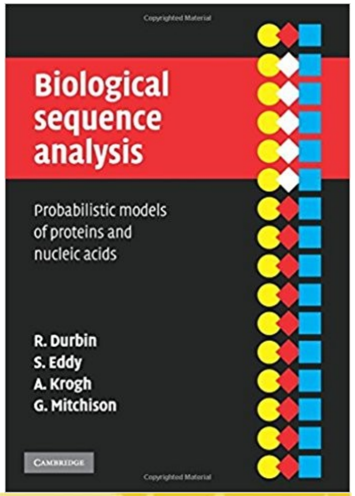
➔ Viterbi training: guess parameters, find optimal Viterbi path (#2), update parameters (#5), iterate

➔ Baum-Welch training: guess, sum over all emissions/transitions (#4), update (#5), iterate

LEARNING

Additional Resources

- Yoon, 2009, Curr. Genomics: Review on the applications of HMM in genomics: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2766791/
- Blog post on Markov clustering: https://medium.com/analytics-vidhya/demystifying-markov-clustering-aeb6cdabbfc7
- Book on graph theory: Graphs, Networks and Algorithms, Dieter Jungnickel, 2013
- Book on probabilitic models in genomics: Biological Sequence Analysis Probabilistic Models of Proteins and Nucleic Acids by Richard Durbin, Sean R. Eddy, Anders Krogh, Graeme Mitchison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Biological sequence analysis

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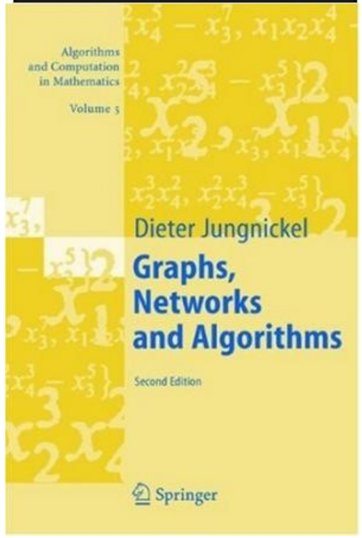
Algorithms and Computation in Mathematics
Volume 5

Dieter Jungnickel

Graphs, Networks and Algorithms

Second Edition

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