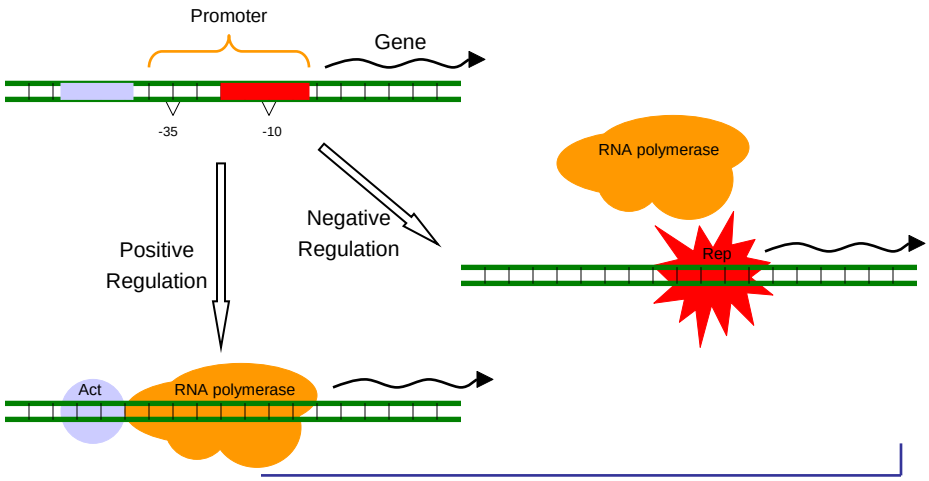
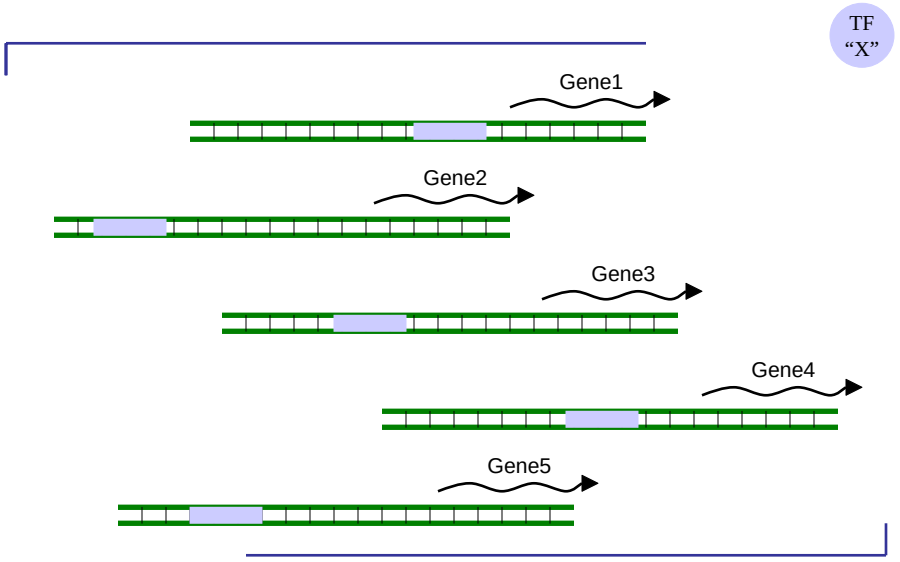
Regulatory Motifs

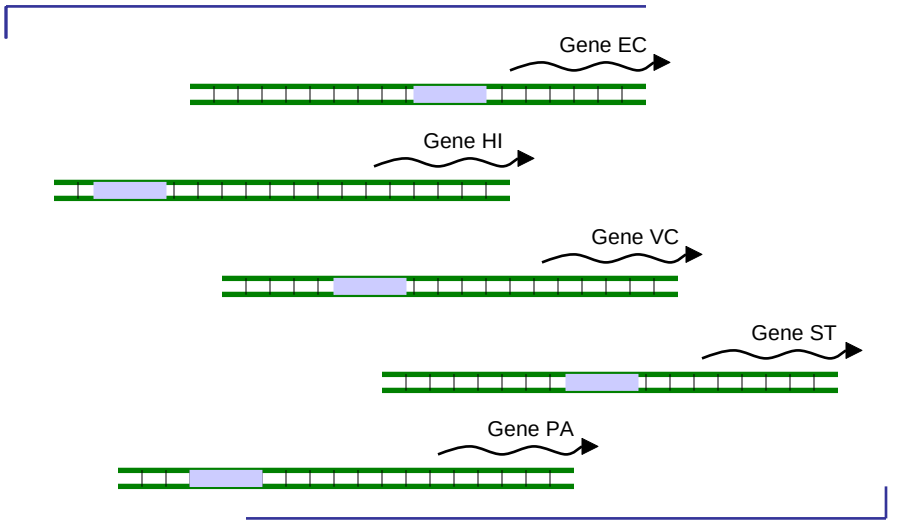
Gene Regulation



What if we believed that a number of genes were regulated by the same transcription factor?



What if we believed that a number of genes were orthologous?



How do we search upstream sequences for instances of a motif?

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAACCGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
AGTTACACTAGTGGGACACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACGAGTGTAACCGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGGCTTAGACTAGTGTGACCAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGGGCTACACTAGTTTAACCGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

If we knew *where* the motif instances were located in each sequence…

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGT**GTAACACTACTGTAAC**CGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
A**GTTACACTAGTGGGAC**ACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAAC**GTTACACGAGTGTAAC**CGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGG**CTTAGACTAGTGTGAC**CAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGG**GCTACACTAGTTTAAC**CGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

Then we could determine a motif model!

GTAACACTACTGTAAC

GTTACACTAGTGGGAC

GTTACACGAGTGTAAC

CTTAGACTAGTGTGAC

GCTACACTAGTTTAAC

A	0.0	0.0	.20	1.0	0.0	1.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	.60	1.0	0.0
C	.20	.20	0.0	0.0	.80	0.0	1.0	0.0	0.0	.20	0.0	0.0	0.0	0.0	0.0	1.0
G	.80	0.0	0.0	0.0	.20	0.0	0.0	.20	0.0	.80	0.0	.80	.20	.40	0.0	0.0
T	0.0	.80	.80	0.0	0.0	0.0	0.0	.80	0.0	0.0	1.0	.20	.80	0.0	0.0	0.0

G T T A C A C T A G T G T A A C

Consensus Sequence

But we don't know the locations of the motif instances…

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAACCGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
AGTTACACTAGTGGGACACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACGAGTGTAACCGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGGCTTAGACTAGTGTGACCAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGGGCTACACTAGTTTAACCGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

What if we knew the motif model…

A	0.0	0.0	.20	1.0	0.0	1.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	.60	1.0	0.0
C	.20	.20	0.0	0.0	.80	0.0	1.0	0.0	0.0	.20	0.0	0.0	0.0	0.0	0.0	1.0
G	.80	0.0	0.0	0.0	.20	0.0	0.0	.20	0.0	.80	0.0	.80	.20	.40	0.0	0.0
T	0.0	.80	.80	0.0	0.0	0.0	0.0	.80	0.0	0.0	1.0	.20	.80	0.0	0.0	0.0

We could determine the location of the motif instance which best matches the model…

A	0.0	0.0	.20	1.0	0.0	1.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	.60	1.0	0.0
C	.20	.20	0.0	0.0	.80	0.0	1.0	0.0	0.0	.20	0.0	0.0	0.0	0.0	0.0	1.0
G	.80	0.0	0.0	0.0	.20	0.0	0.0	.20	0.0	.80	0.0	.80	.20	.40	0.0	0.0
T	0.0	.80	.80	0.0	0.0	0.0	0.0	.80	0.0	0.0	1.0	.20	.80	0.0	0.0	0.0

Score = 0.0 * .80 * 0.0 * 1.0 * 0.0 * 0.0 * 1.0 * 0.0 * 0.0 * 0.0 * 0.0 * 0.0 * 0.0 * 0.0 * 0.0 * 1.0

Score = 0.01 * .80 * 0.01 * 1.0 * 0.01 * 0.01 * 1.0 * 0.01 * 0.01 * 0.01 * 0.01 * 0.01 * 0.01 * 0.01 * 0.01 * 1.0

Score = $8.0 * 10^{-27}$

TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAA

We could determine the location of the motif instance which best matches the model…

A	0.0	0.0	.20	1.0	0.0	1.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	.60	1.0	0.0
C	.20	.20	0.0	0.0	.80	0.0	1.0	0.0	0.0	.20	0.0	0.0	0.0	0.0	0.0	1.0
G	.80	0.0	0.0	0.0	.20	0.0	0.0	.20	0.0	.80	0.0	.80	.20	.40	0.0	0.0
T	0.0	.80	.80	0.0	0.0	0.0	0.0	.80	0.0	0.0	1.0	.20	.80	0.0	0.0	0.0

Score = 0.0 * 0.0 * .20 * 0.0 * 0.0 * 0.0 * 1.0 * 0.0 * 0.0 * .80 * 0.0 * 0.0 * .80 * .40 * 0.0 * 1.0

Score = 0.01 * 0.01 * .20 * 0.01 * 0.01 * 0.01 * 1.0 * 0.01 * 0.01 * .80 * 0.01 * 0.01 * .80 * .40 * 0.01 * 1.0

Score = $5.12 * 10^{-22}$

TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAA

We could determine the location of the motif instance which best matches the model…

A	0.0	0.0	.20	1.0	0.0	1.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	.60	1.0	0.0
C	.20	.20	0.0	0.0	.80	0.0	1.0	0.0	0.0	.20	0.0	0.0	0.0	0.0	0.0	1.0
G	.80	0.0	0.0	0.0	.20	0.0	0.0	.20	0.0	.80	0.0	.80	.20	.40	0.0	0.0
T	0.0	.80	.80	0.0	0.0	0.0	0.0	.80	0.0	0.0	1.0	.20	.80	0.0	0.0	0.0

Score = $7.16 * 10^{-28}$

TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAA

A	0.0	0.0	.20	1.0	0.0	1.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	.60	1.0	0.0
C	.20	.20	0.0	0.0	.80	0.0	1.0	0.0	0.0	.20	0.0	0.0	0.0	0.0	0.0	1.0
G	.80	0.0	0.0	0.0	.20	0.0	0.0	.20	0.0	.80	0.0	.80	.20	.40	0.0	0.0
T	0.0	.80	.80	0.0	0.0	0.0	0.0	.80	0.0	0.0	1.0	.20	.80	0.0	0.0	0.0

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGT**GTAACACTACTGTAAC**CGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
A**GTTACACTAGTGGGAC**ACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAAC**GTTACACGAGTGTAAC**CGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGG**CTTAGACTAGTGTGAC**CAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGG**GCTACACTAGTTTAAC**CGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

Expectation-Maximization (EM)

- Randomly guess the locations of each motif instance
- Repeat until convergence
  - Calculate a new motif model from the motif instances
  - Calculate new locations for the motif instances from the motif model

EM - Randomly guess the locations of each motif instance

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAACCGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAA**AATTCCG**
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
A**TCTAACGGTACGGATT**CTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
AGTTACACTAGTGGGACACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACGAGTGTAACCGCCGAA
CC**ATGTTGACACGAATTC**TG

> Salmonella typhi
GGTCGGCTTAGACTAGTGTGACCAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTAT**TGTGACTGAAAAGCGC**GTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATG**CCGGCGCCGC**
TGCTGGAACGCCTCGACCCCAGGGCTACACTAGTTTAACCGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

A	.40	.20	0.0	.20	.40	0.0	.20	.20	.40	.40	.20	.60	.20	.20	0.0	0.0
C	.20	.40	0.0	0.0	.40	.60	.20	.40	0.0	.40	.20	0.0	.20	0.0	.20	.40
G	0.0	.20	.40	.40	0.0	.40	.40	.40	.40	0.0	.20	.40	.60	.20	.40	.40
T	.40	.20	.60	.40	.20	0.0	.20	0.0	.20	.20	.40	0.0	0.0	.60	.40	.20

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAACCGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAA**AATTCCG**
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
A**TCTAACGGTACGGATT**CTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
AGTTACACTAGTGGGACACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACGAGTGTAACCGCCGAA
CC**ATGTTGACACGAATTC**TG

> Salmonella typhi
GGTCGGCTTAGACTAGTGTGACCAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTAT**TGTGACTGAAAAGCGC**GTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATG**CCGGCGCCGC**
TGCTGGAACGCCTCGACCCCAGGGCTACACTAGTTTAACCGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

A	.40	.20	0.0	.20	.40	0.0	.20	.20	.40	.40	.20	.60	.20	.20	0.0	0.0
C	.20	.40	0.0	0.0	.40	.60	.20	.40	0.0	.40	.20	0.0	.20	0.0	.20	.40
G	0.0	.20	.40	.40	0.0	.40	.40	.40	.40	0.0	.20	.40	.60	.20	.40	.40
T	.40	.20	.60	.40	.20	0.0	.20	0.0	.20	.20	.40	0.0	0.0	.60	.40	.20

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAACCGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCAC**AAAGGTTAGCAATAAC**TGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCG**GCATAAGTAGTAAGTG**CCGTGCCTCCGCCATT
AGTTACACTAGTGGGACACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACG**AGTGTAACCGCCGAA**
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGGCTTAGACTAGTGTGACCAAAAAGCTTTTGCTGAA**GTTTCAGGGTAAGAAG**AACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGGGCTACACTA**GTTTAACCGGAACGCC**GCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

A	.40	.20	.40	0.0	.40	.80	.20	.20	.20	0.0	.60	.80	.20	.60	.60	0.0
C	0.0	.20	0.0	0.0	.20	0.0	.20	.40	.20	.20	.20	.20	.20	0.0	.20	.60
G	.60	.20	0.0	.40	.20	0.0	.40	.20	.60	.60	0.0	0.0	.40	.20	0.0	.40
T	0.0	.40	.60	.60	.20	.20	.20	.20	0.0	.20	.20	0.0	.20	0.0	.20	0.0

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAACCGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCAC**AAAGGTTAGCAATAAC**TGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCG**GCATAAGTAGTAAGTG**CCGTGCCTCCGCCATT
AGTTACACTAGTGGGACACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACG**AGTGTAACCGCCGAA**
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGGCTTAGACTAGTGTGACCAAAAAGCTTTTGCTGAA**GTTTCAGGGTAAGAAG**AACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGGGCTACACTA**GTTTAACCGGAACGCC**GCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

A	.40	.20	.40	0.0	.40	.80	.20	.20	.20	0.0	.60	.80	.20	.60	.60	0.0
C	0.0	.20	0.0	0.0	.20	0.0	.20	.40	.20	.20	.20	.20	.20	0.0	.20	.60
G	.60	.20	0.0	.40	.20	0.0	.40	.20	.60	.60	0.0	0.0	.40	.20	0.0	.40
T	0.0	.40	.60	.60	.20	.20	.20	.20	0.0	.20	.20	0.0	.20	0.0	.20	0.0

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAACCGGCATTTTCTGCTTTTCC
TGCCGAT**ATTTTTTCTTATCTAC**CTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
A**GTTACACTAGTGGGAC**ACC

> Vibrio cholerae
ATTTGTGGCG**GTTTTCAAATGCTTGG**AGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACGAGTGTAACCGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGG**CTTAGACTAGTGTGAC**CAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGGGCTACACTA**GTTTAACCGGAACGCC**GCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

A	.20	0.0	0.0	.40	.20	.60	.20	.20	.60	0.0	.40	0.0	.20	0.0	.60	0.0
C	.20	0.0	0.0	0.0	.20	.20	.60	.40	0.0	0.0	0.0	.40	.20	.40	.20	.80
G	.60	0.0	0.0	0.0	.20	0.0	0.0	0.0	.20	.60	.20	.20	.40	.20	.20	.20
T	0.0	1.0	1.0	.60	.40	.20	.20	.40	.20	.40	.40	.40	.20	.40	0.0	0.0

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGTGTAACACTACTGTAACCGGCATTTTCTGCTTTTCC
TGCCGAT**ATTTTTTCTTATCTAC**CTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
A**GTTACACTAGTGGGAC**ACC

> Vibrio cholerae
ATTTGTGGCG**GTTTTCAAATGCTTGG**AGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACGAGTGTAACCGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGG**CTTAGACTAGTGTGAC**CAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGGGCTACACTA**GTTTAACCGGAACGCC**GCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

A	.20	0.0	0.0	.40	.20	.60	.20	.20	.60	0.0	.40	0.0	.20	0.0	.60	0.0
C	.20	0.0	0.0	0.0	.20	.20	.60	.40	0.0	0.0	0.0	.40	.20	.40	.20	.80
G	.60	0.0	0.0	0.0	.20	0.0	0.0	0.0	.20	.60	.20	.20	.40	.20	.20	.20
T	0.0	1.0	1.0	.60	.40	.20	.20	.40	.20	.40	.40	.40	.20	.40	0.0	0.0

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGT**GTAACACTACTGTAAC**CGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
A**GTTACACTAGTGGGAC**ACC

> Vibrio cholerae
ATTTGTGGCG**GTTTTCAAATGCTTGG**AGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACGAGTGTAACCGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGG**CTTAGACTAGTGTGAC**CAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGG**GCTACACTAGTTTAAC**CGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

A	0.0	0.0	.20	.80	0.0	.80	.20	.20	1.0	0.0	0.0	0.0	0.0	.40	.80	0.0
C	.20	0.0	0.0	0.0	.60	.20	.80	0.0	0.0	.20	0.0	.20	0.0	0.0	0.0	.80
G	.80	0.0	0.0	0.0	.20	0.0	0.0	0.0	0.0	.60	.20	.60	.20	.40	.20	.20
T	0.0	1.0	.80	.20	.20	0.0	0.0	.80	0.0	.20	.80	.20	.80	.20	0.0	0.0

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGT**GTAACACTACTGTAAC**CGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
A**GTTACACTAGTGGGAC**ACC

> Vibrio cholerae
ATTTGTGGCG**GTTTTCAAATGCTTGG**AGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAACGTTACACGAGTGTAACCGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGG**CTTAGACTAGTGTGAC**CAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGG**GCTACACTAGTTTAAC**CGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

A	0.0	0.0	.20	.80	0.0	.80	.20	.20	1.0	0.0	0.0	0.0	0.0	.40	.80	0.0
C	.20	0.0	0.0	0.0	.60	.20	.80	0.0	0.0	.20	0.0	.20	0.0	0.0	0.0	.80
G	.80	0.0	0.0	0.0	.20	0.0	0.0	0.0	0.0	.60	.20	.60	.20	.40	.20	.20
T	0.0	1.0	.80	.20	.20	0.0	0.0	.80	0.0	.20	.80	.20	.80	.20	0.0	0.0

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGT**GTAACACTACTGTAAC**CGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
A**GTTACACTAGTGGGAC**ACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAAC**GTTACACGAGTGTAAC**CGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGG**CTTAGACTAGTGTGAC**CAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGG**GCTACACTAGTTTAAC**CGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

A	0.0	0.0	.20	1.0	0.0	1.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	.60	1.0	0.0
C	.20	.20	0.0	0.0	.80	0.0	1.0	0.0	0.0	.20	0.0	0.0	0.0	0.0	0.0	1.0
G	.80	0.0	0.0	0.0	.20	0.0	0.0	.20	0.0	.80	0.0	.80	.20	.40	0.0	0.0
T	0.0	.80	.80	0.0	0.0	0.0	0.0	.80	0.0	0.0	1.0	.20	.80	0.0	0.0	0.0

> Escherichia coli
TTGATTCCCTGAATGCCCGCTTAGT**GTAACACTACTGTAAC**CGGCATTTTCTGCTTTTCC
TGCCGATATTTTTTCTTATCTACCTCACAAAGGTTAGCAATAACTGCTGGGAAAATTCCG
AGTTAGTCGTTATATTCTAT

> Haemophilus influenzae
ATCTAACGGTACGGATTCTCCAAAGGCCTATGGAATCTTGTAGAATATGAAACGTTCTAA
TAAATCATAAAGTTGGAGCAAACGCTCGGCATAAGTAGTAAGTGCCGTGCCTCCGCCATT
A**GTTACACTAGTGGGAC**ACC

> Vibrio cholerae
ATTTGTGGCGGTTTTCAAATGCTTGGAGAATGGGTACATGATCCGCTTGGCATTGAAGGT
GAGGCTGGCAGCAGCGAAGGTCTGGGGCTGTTTGAAC**GTTACACGAGTGTAAC**CGCCGAA
CCATGTTGACACGAATTCTG

> Salmonella typhi
GGTCGG**CTTAGACTAGTGTGAC**CAAAAAGCTTTTGCTGAAGTTTCAGGGTAAGAAGAACC
AGCTCCTAGTAAAAAGACTATTGTGACTGAAAAGCGCGTCAGCGCAAAGCCGACCGCACA
AAACGCACAAGGAGTTACAG

> Pseudomonas aeruginosa
ACGCGGCCAGGGTCTTCTCCTGCGAGATCATGCGCGGCGCGCCGCGCATGCCGGCGCCGC
TGCTGGAACGCCTCGACCCCAGG**GCTACACTAGTTTAAC**CGGAACGCCGCCAGTGGATCG
GCCTGCCCCAGCTATTGCTC

Expectation-Maximization (EM)

- Randomly guess the locations of each motif instance
- Repeat until convergence
  - Calculate a new motif model from the motif instances
  - Calculate new locations for the motif instances from the motif model

Each motif instance is *best scoring* match to motif model

Gibbs Sampling

- Randomly guess the locations of each motif instance
- Repeat until convergence
  - Calculate a new motif model from the motif instances
  - Calculate new locations for the motif instances from the motif model

Each motif instance is *sampled* from scores of matches to motif model