Bio334
Phylogenetic reconstruction
Part I: Distance-based methods

Janko Tackmann & Nicolas Näpflin
For questions, feel free to contact us on Slack or via:
janko.tackmann@mls.uzh.ch or
nicolas.naepflin@mls.uzh.ch

Setup for today

- Exercises: `Bio334/04_njtrees/exercises`
- If you haven't cloned the repository yet:
  - Open the terminal, `cd` to a directory of your choice, then type `` `git clone https://github.com/meringlab/Bio334` ``
- If you cloned it yesterday:
  - make sure to type `git pull` within the Bio334 folder to get the latest updates

Exercise 1 – Questions

- Complexity

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- Complexity

$$\binom{n}{2} = \frac{n!}{2!\,(n-2)!} = \frac{n\,(n-1)}{2} \sim O(n^2)$$

Time: 1000 proteins -> 1 s

10.000 proteins -> 100 s

100.000 proteins -> 10.000s (~ 3 hours)

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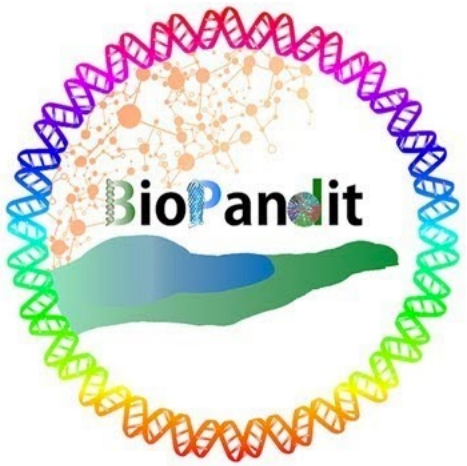
  - All amino acid transitions have equal probability: unrealistic
    - Use explicit substitution matrices (BLOSUM, PAM)

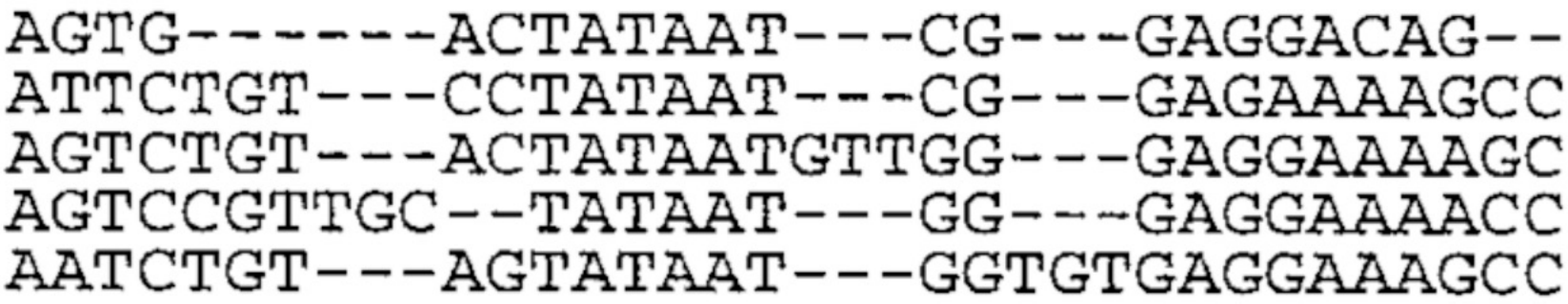
PAM Substitution Matrix

	A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V
A	4	-3	-1	-1	-3	-2	0	1	-3	-2	-3	-3	-2	-5	1	1	1	-7	-4	0
R	-3	7	-2	-4	-5	1	-3	-5	1	-3	-5	2	-1	-6	-1	-1	-3	1	-6	-4
N	-1	-2	5	3	-5	-1	1	-1	2	-3	-4	1	-4	-5	-2	1	0	-5	-2	-3
D	-1	-4	3	5	-7	0	4	-1	-1	-4	-6	-1	-5	-8	-3	-1	-2	-9	-6	-4
C	-3	-5	-5	-7	9	-8	-8	-5	-4	-3	-8	-8	-7	-7	-4	-1	-4	-9	-1	-3
Q	-2	1	-1	0	-8	6	2	-3	3	-4	-2	0	-2	-7	-1	-2	-2	-7	-6	-3
E	0	-3	1	4	-8	2	5	-1	-1	-3	-5	-1	-4	-8	-2	-1	-2	-9	-5	-3
G	1	-5	-1	-1	-5	-3	-1	5	-4	-5	-6	-3	-4	-6	-2	0	-2	-9	-7	-3
H	-3	1	2	-1	-4	3	-1	-4	7	-4	-3	-2	-4	-3	-1	-2	-3	-4	-1	-3
I	-2	-3	-3	-4	-3	-4	-3	-5	-4	6	1	-3	1	0	-4	-3	0	-7	-3	3
L	-3	-5	-4	-6	-8	-2	-5	-6	-3	1	6	-4	3	0	-4	-4	-3	-3	-3	0
K	-3	2	1	-1	-8	0	-1	-3	-2	-3	-4	5	0	-7	-3	-1	-1	-6	-6	-4
M	-2	-1	-4	-5	-7	-2	-4	-4	-4	1	3	0	9	-1	-4	-3	-1	-6	-5	1
F	-5	-6	-5	-8	-7	-7	-8	-6	-3	0	0	-7	-1	8	-6	-4	-5	-1	4	-3
P	1	-1	-2	-3	-4	-1	-2	-2	-1	-4	-4	-3	-4	-6	7	0	-1	-7	-7	-3
S	1	-1	1	-1	-1	-2	-1	0	-2	-3	-4	-1	-3	-4	0	4	2	-3	-4	-2
T	1	-3	0	-2	-4	-2	-2	-2	-3	0	-3	-1	-1	-5	-1	2	5	-7	-4	0
W	-7	1	-5	-9	-9	-7	-9	-9	-4	-7	-3	-6	-6	-1	-7	-3	-7	12	-2	-9
Y	-4	-6	-2	-6	-1	-6	-5	-7	-1	-3	-3	-6	-5	4	-7	-4	-4	-2	9	-4
V	0	-4	-3	-4	-3	-3	-3	-3	-3	3	0	-4	1	-3	-3	-2	0	-9	-4	5



Exercise 1 – Questions

- Shortcomings of naïve Jaccard
  - All amino acid transitions have equal probability: unrealistic
    - Use explicit substitution matrices (BLOSUM, PAM)
  - Dependencies between neighboring sites (e.g. indels) are not considered
    - Smaller gap penalties, explicit modeling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ATTCTGT---CCTATAAT---CG---GAGAAAAGCC
AGTCTGT---ACTATAATGTTGG---GAGGAAAAGC
AGTCCGTTGC--TATAAT---GG---GAGGAAAACC
AATCTGT---AGTATAAT---GGTGTGAGGAAAGCC

Exercise 1 – Questions

- Nucleotides vs Amino acids

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  - Nucleotides
    - High resolution: small differences can be detected
    - More neutrally evolving regions: less biased similarity estimates
    - Distinction between synonymous and non-synonymous mutations

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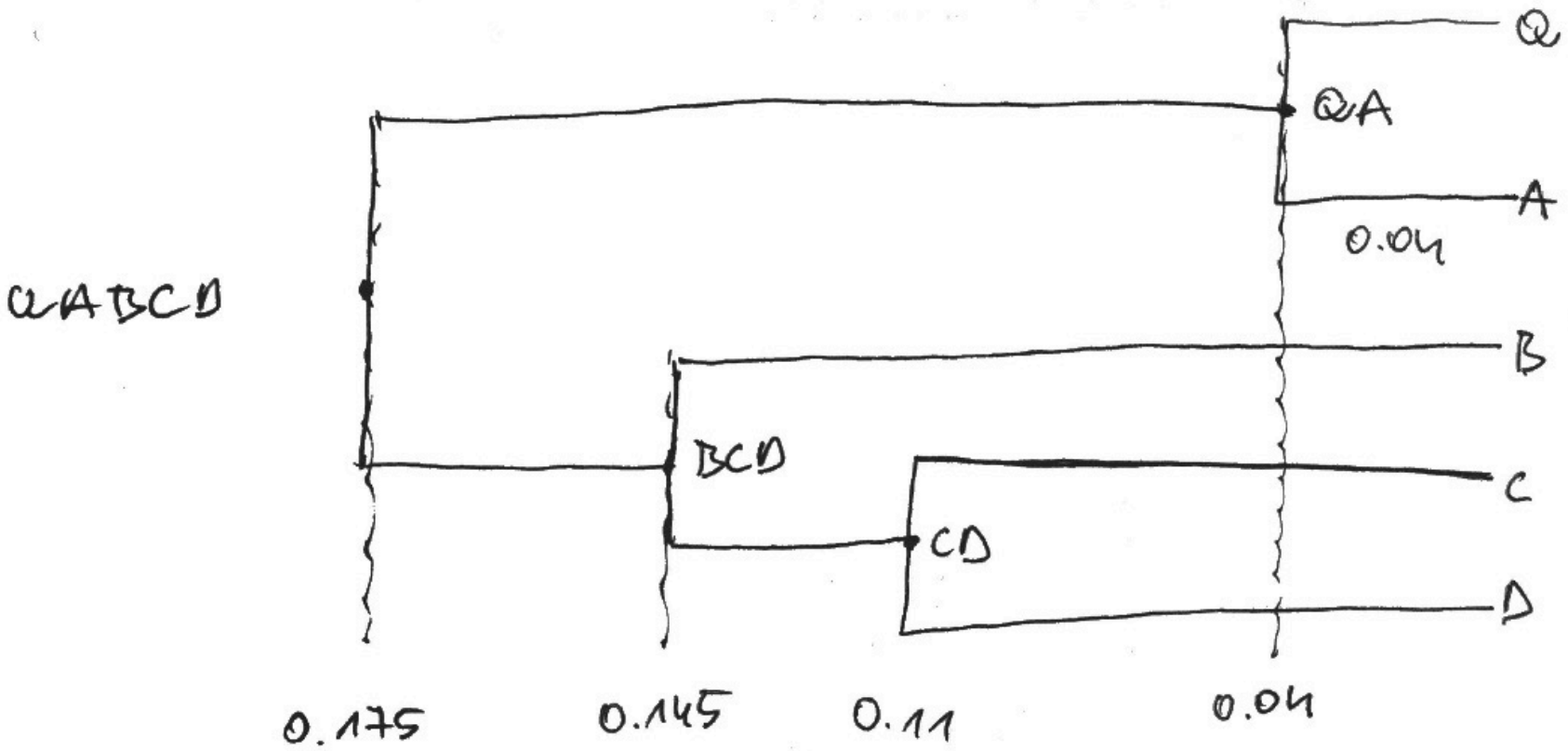
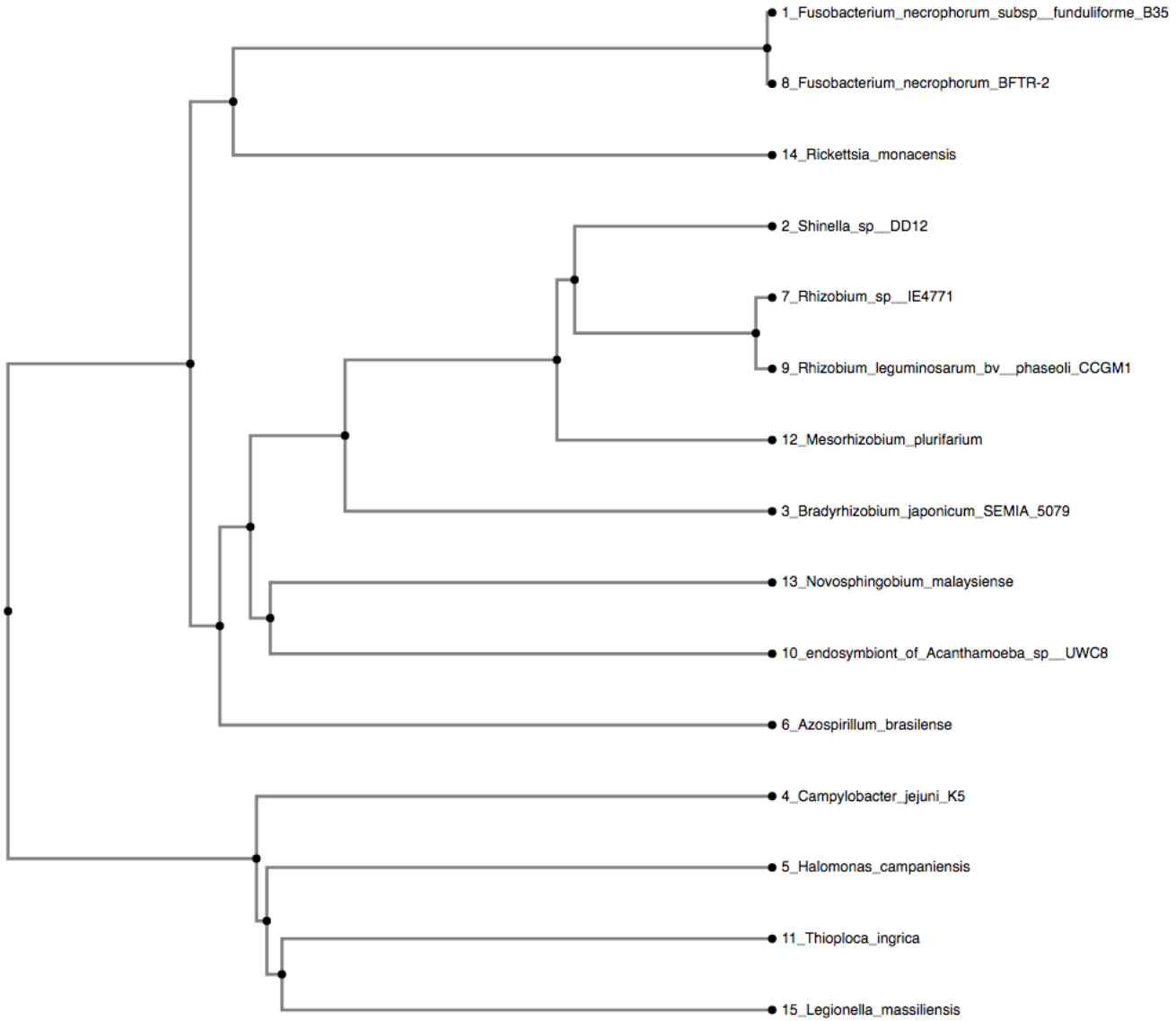
- Nucleotides vs Amino acids
  - Nucleotides
    - High resolution: small differences can be detected
    - More neutrally evolving regions: less biased similarity estimates
    - Distinction between synonymous and non-synonymous mutations
  - Amino acids
    - Stable over longer evolutionary time frames, used to address questions on non-recent evolution

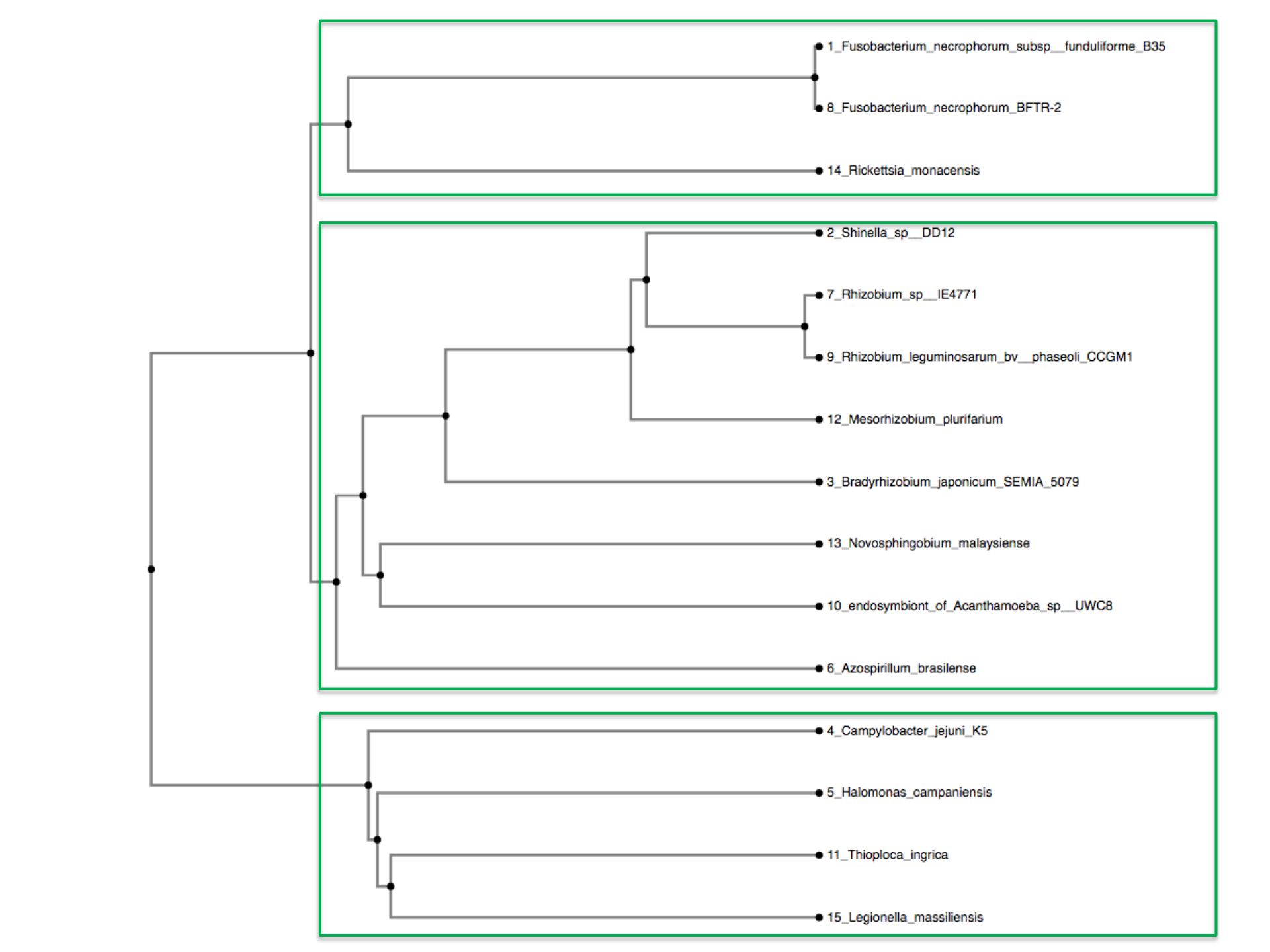
Exercise 2 – Questions

	Q	A	B	C	D		
Q	0	0.08	0.36	0.36	0.38		
A	0.08	0	0.32	0.34	0.36		
B	0.36	0.32	0	0.32	0.26		
C	0.36	0.34	0.32	0	0.22		
D	0.38	0.36	0.26	0.22	0		
	QA	B	C	D			
QA	0	0.34	0.35	0.37			
B	0.34	0	0.32	0.26			
C	0.35	0.32	0	0.22			
D	0.37	0.26	0.22	0			
	QA	B	CD				
QA	0	0.34	0.36				
B	0.34	0	0.29				
CD	0.36	0.29	0				
	QA	BCD					
QA	0	0.35333333					
BCD	0.35333333	0					


QABCD
Q
QA
A
0.04
B
BCD
C
CD
D
0.175
0.145
0.11
0.04

Exercise 3 – Questions

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8_Fusobacterium_necrophorum_BFTR-2
14_Rickettsia_monacensis
2_Shinella_sp__DD12
7_Rhizobium_sp__IE4771
9_Rhizobium_leguminosarum_bv__phaseoli_CCGM1
12_Mesorhizobium_plurifarium
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13_Novosphingobium_malaysiense
10_endosymbiont_of_Acanthamoeba_sp__UWC8
6_Azospirillum_brasilense
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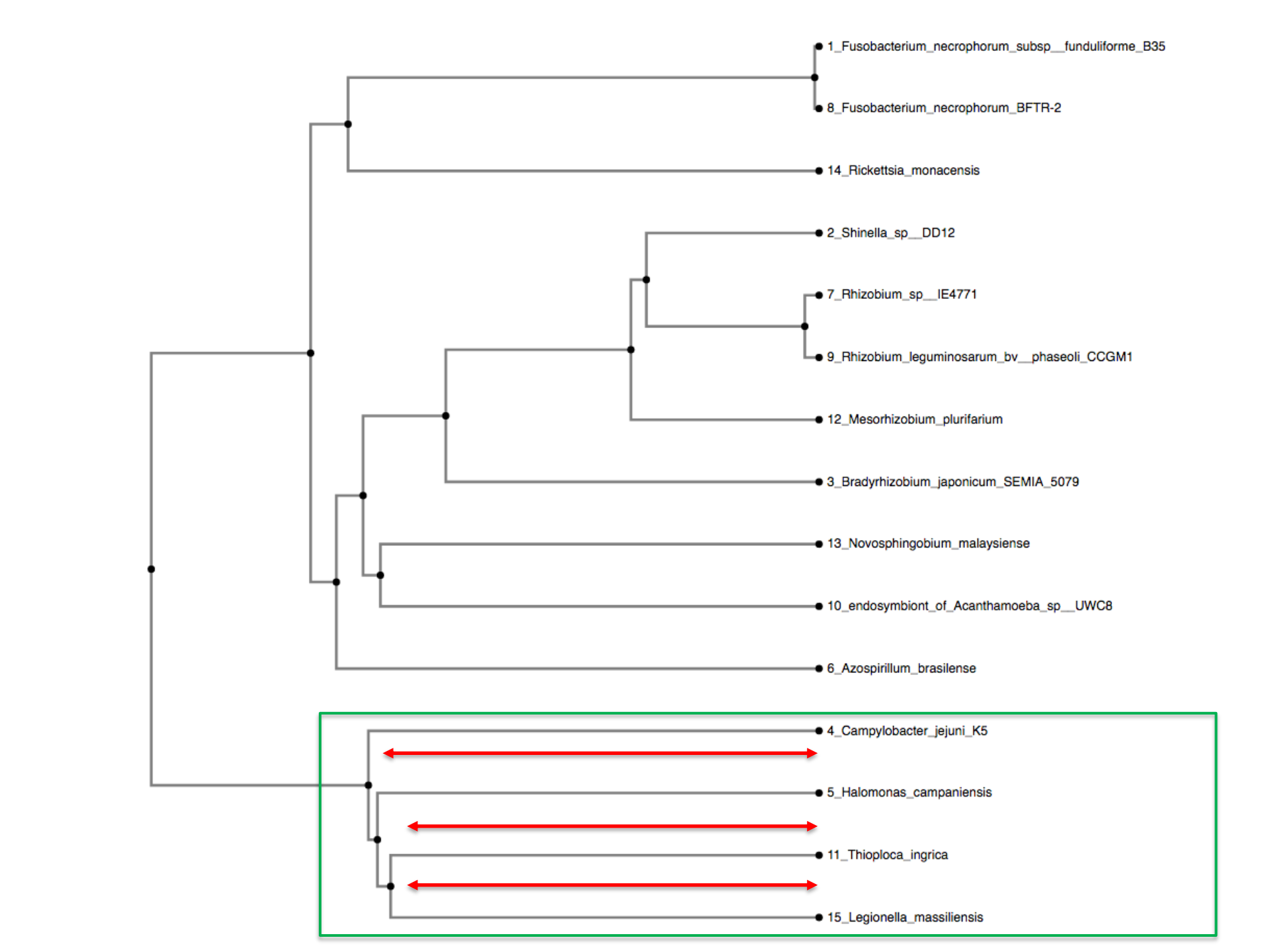
5_Halomonas_campaniensis
11_Thioploca_ingrica
15_Legionella_massiliensis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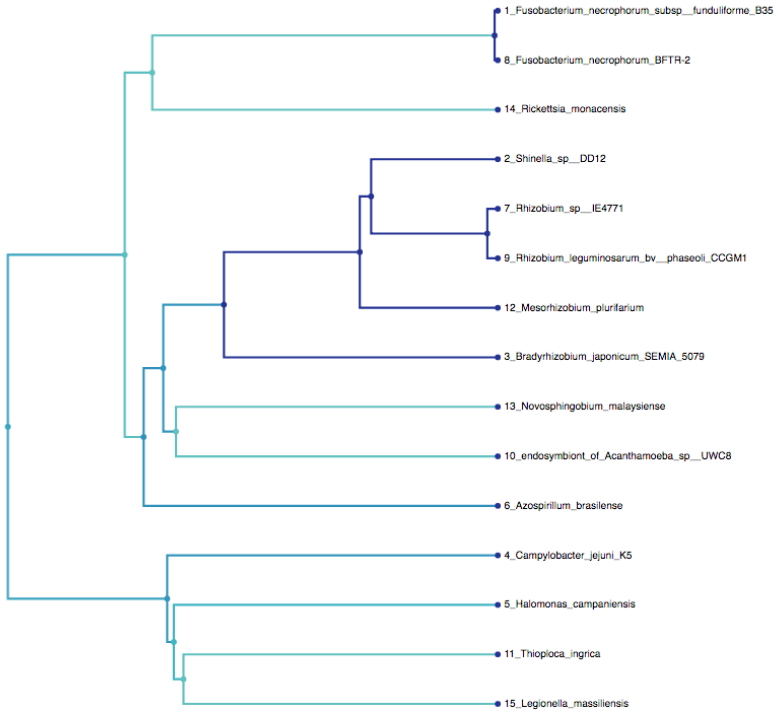
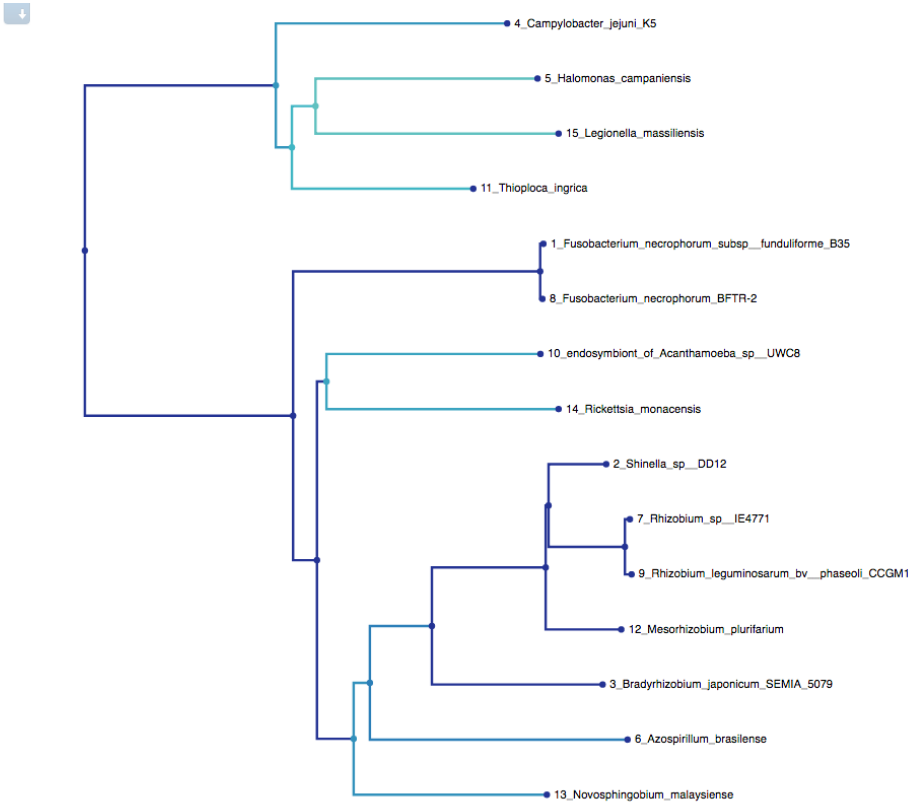
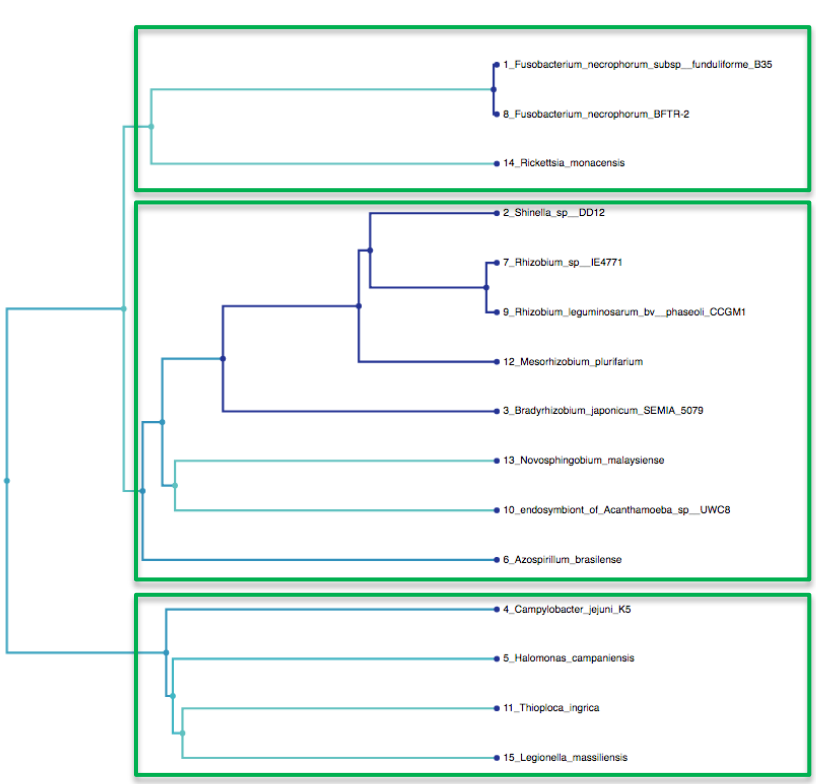
Fusobacterium necrophorum subsp. funduliforme B35

Fusobacterium	**necrophorum**	**subsp. funduliforme**	**B35**
Genus	Species	Subspecies	Type strain

Exercise 4 – Questions



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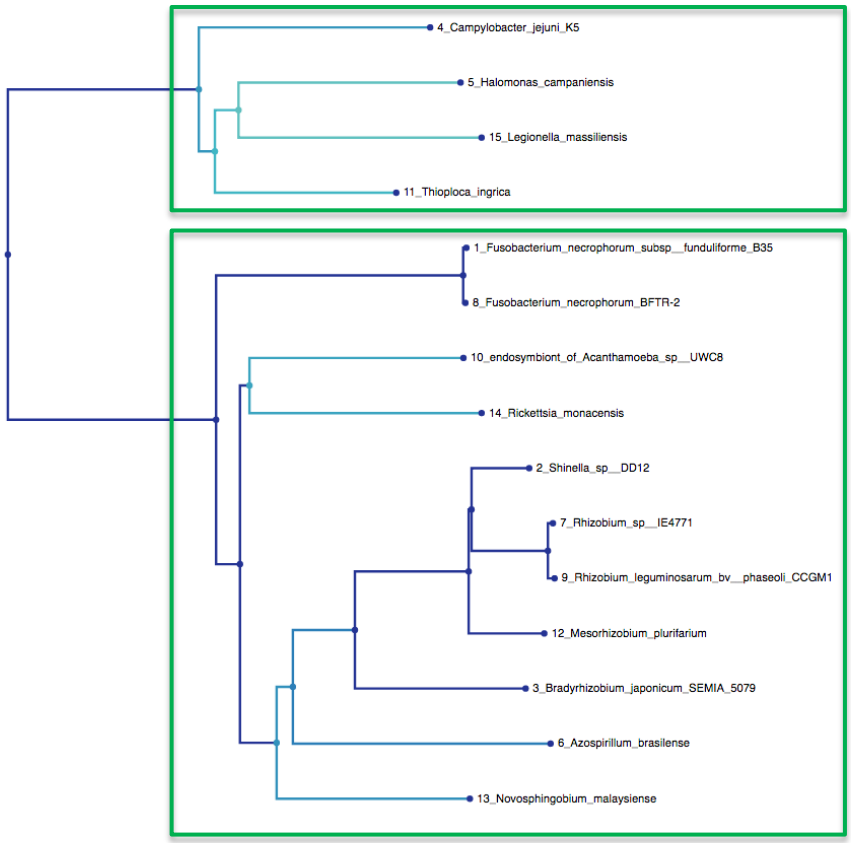
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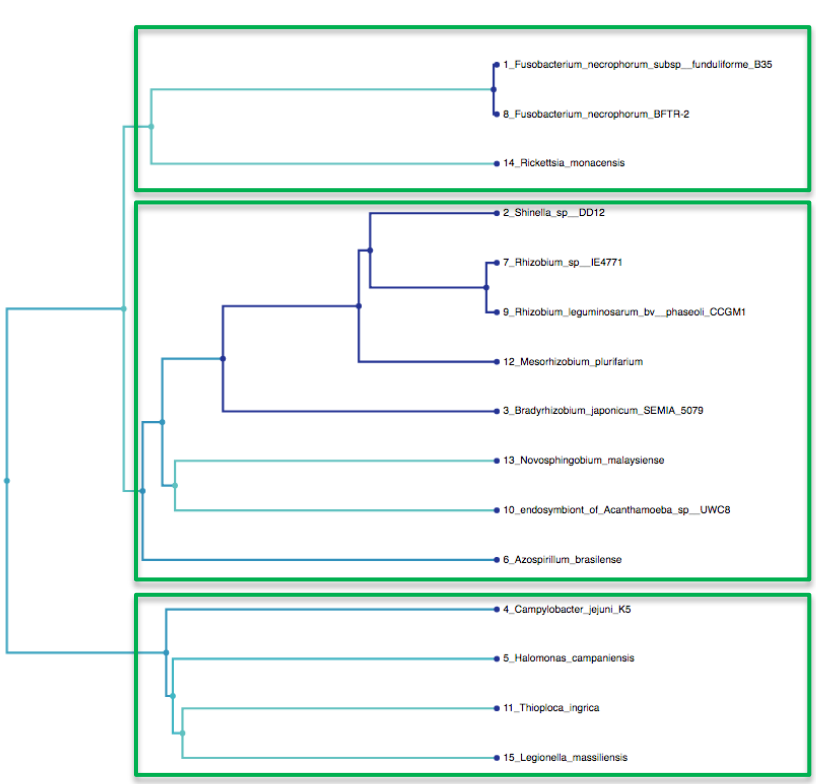
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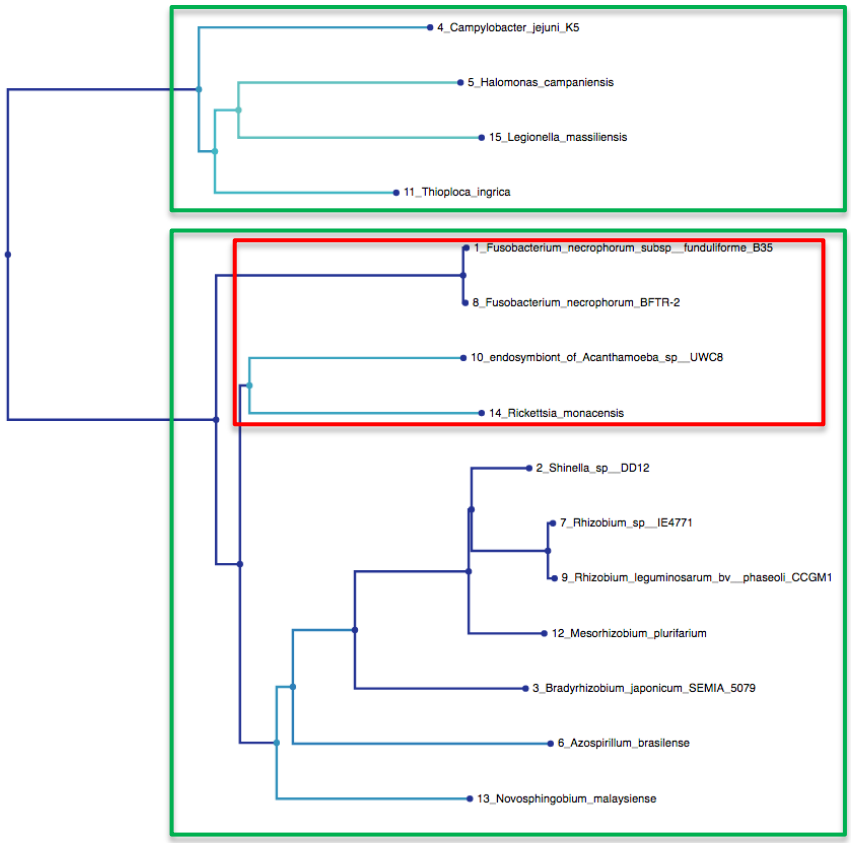
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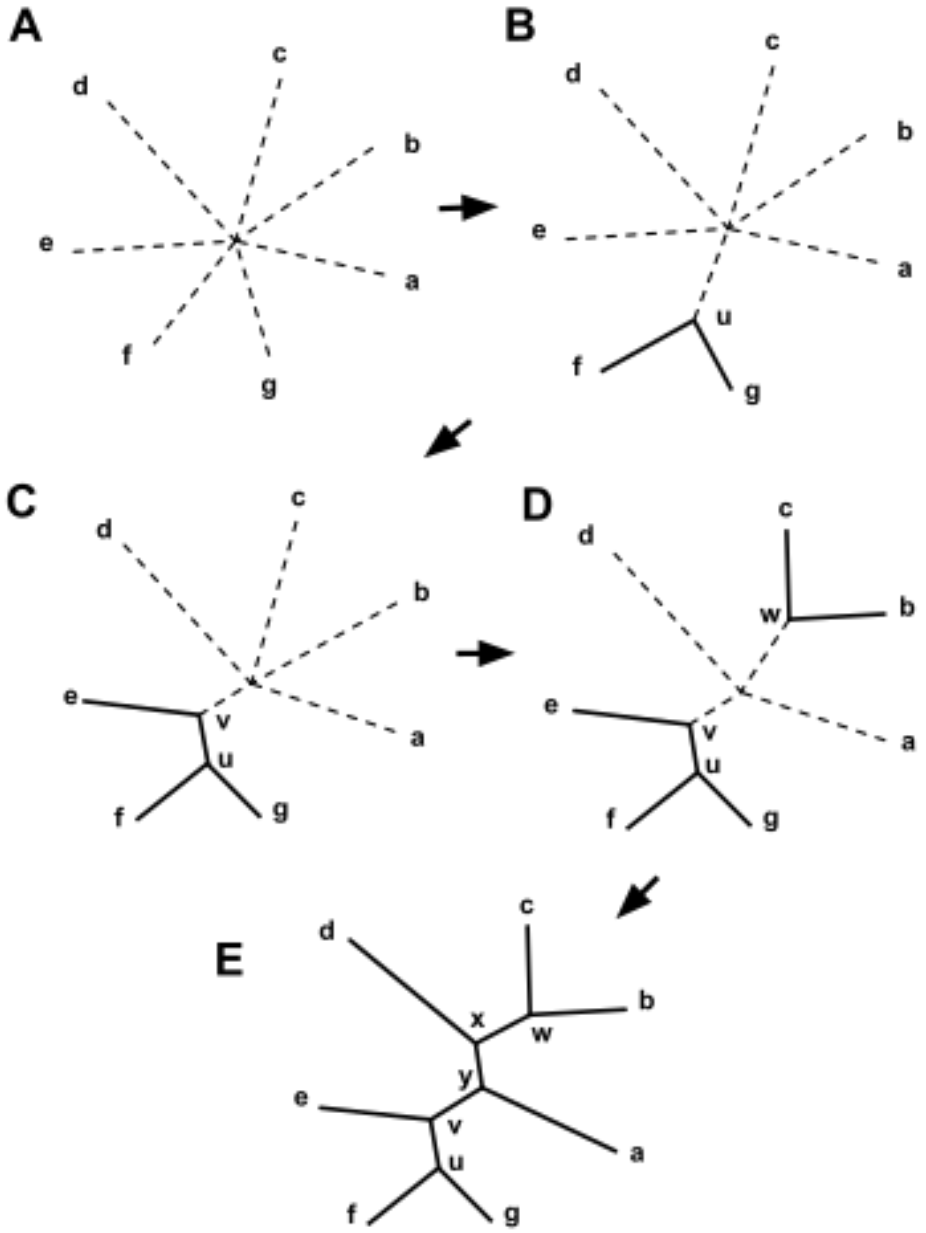

$$Q(i,j) =$$

$$(n-2)d(i,j) - \sum_{k=1}^{n} d(i,k) - \sum_{k=1}^{n} d(j,k)$$