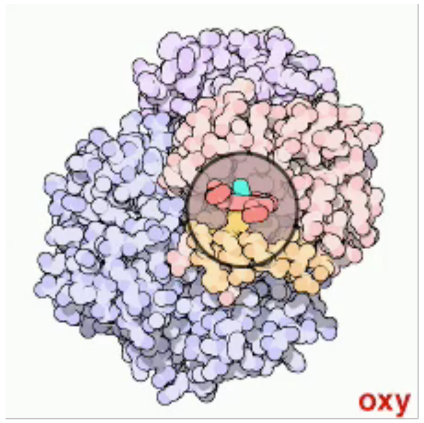
```
$ wget http://ssolo.web.elte.hu/lab_slides.pdf
```

```
$ cd ~/workshop_materials
$ wget http://ssolo.web.elte.hu/lab_data.tgz
$ tar xzf lab  data.tgz
$ cd lab_data
```

The stories of gene families can be complicated

The story of each gene family consist of a unique series of evolutionary events that often results in a change of copy number and shifts in function.

Human hemolglobin is composed of

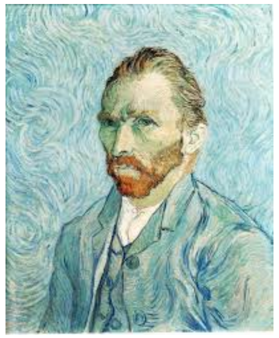


molecular machine

$2\alpha + 2\beta$ **chains.**

$2\alpha+$

Human



adult

$+2\beta$ (97%)

$+2\delta$ (3%)

fetus

$+2\gamma$

Cow

adult

$+2\{\beta\delta\}$

fetus

$+2\gamma$

Horse

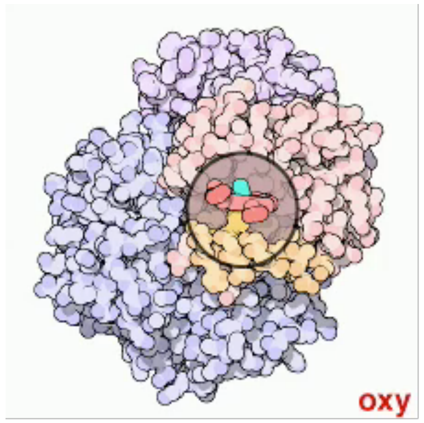
adult and fetus

$+2\{\beta\delta\}$

The stories of gene families can be complicated

The story of each gene family consist of a unique series of evolutionary events that often results in a change of copy number and shifts in function.

Human hemolglobin is composed of



molecular machine

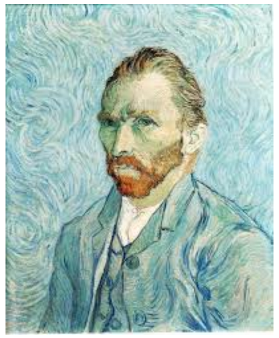
$2\alpha + 2\beta$ **chains.**

Human

Cow

Horse

$2\alpha+$



adult

$+2\beta$ (97%)

$+2\delta$ (3%)

fetus

$+2\gamma$

adult

$+2\{\beta\delta\}$

fetus

$+2\gamma$

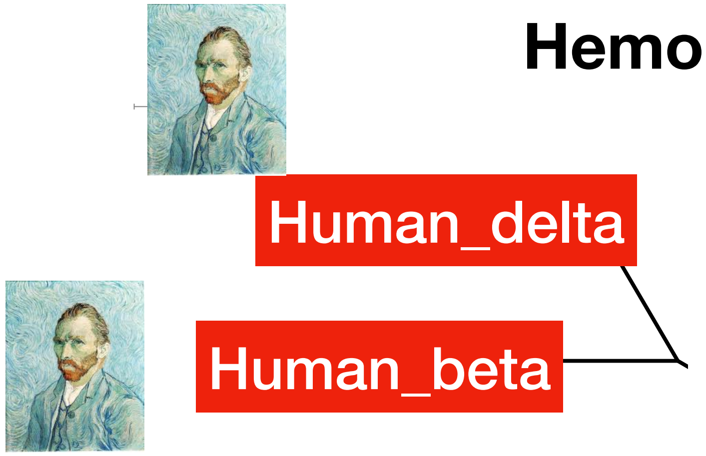
adult and fetus

$+2\{\beta\delta\}$

`Hemoglobin/`

```
$ cd ~/workshop_materials/lab_data/Hemoglobin
```

Hemoglobin gene tree



Human_delta

Human_beta

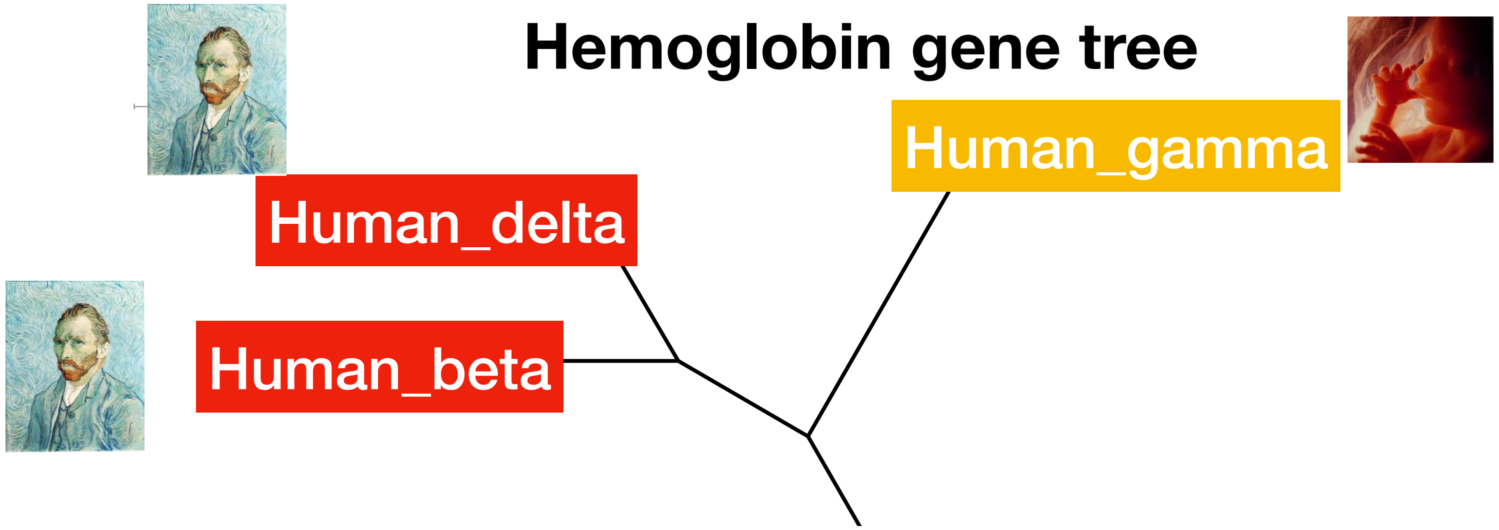
Hemoglobin.tree

```
(Human_beta:1,Human_delta:1):1,
```

`Hemoglobin/`

```
$ cd ~/workshop_materials/lab_data/Hemoglobin
```

Hemoglobin gene tree



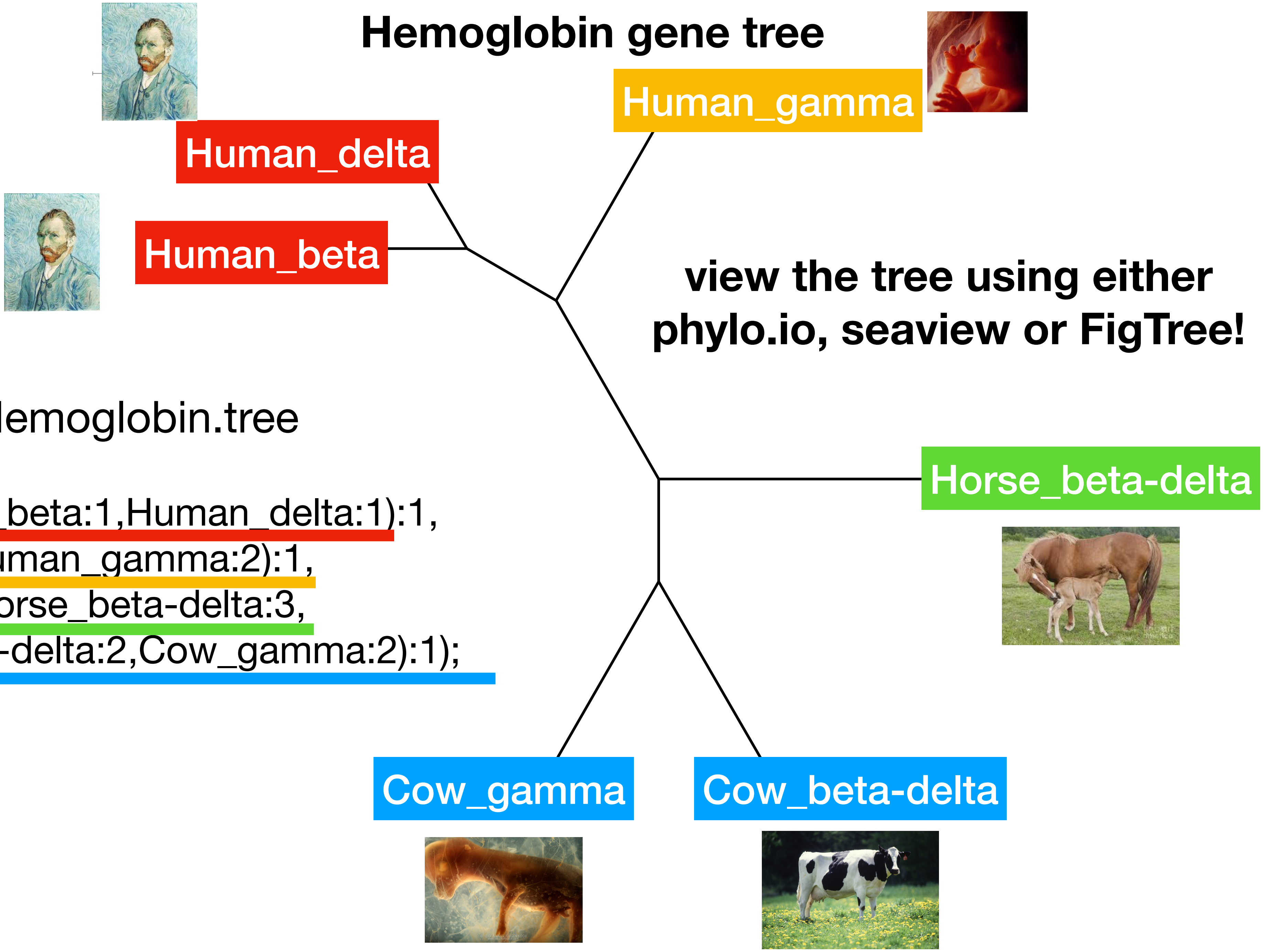
Hemoglobin.tree

```
((Human_beta:1,Human_delta:1):1,
Human_gamma:2):1,
```

`Hemoglobin/`

```
$ cd ~/workshop_materials/lab_data/Hemoglobin
```

Hemoglobin gene tree



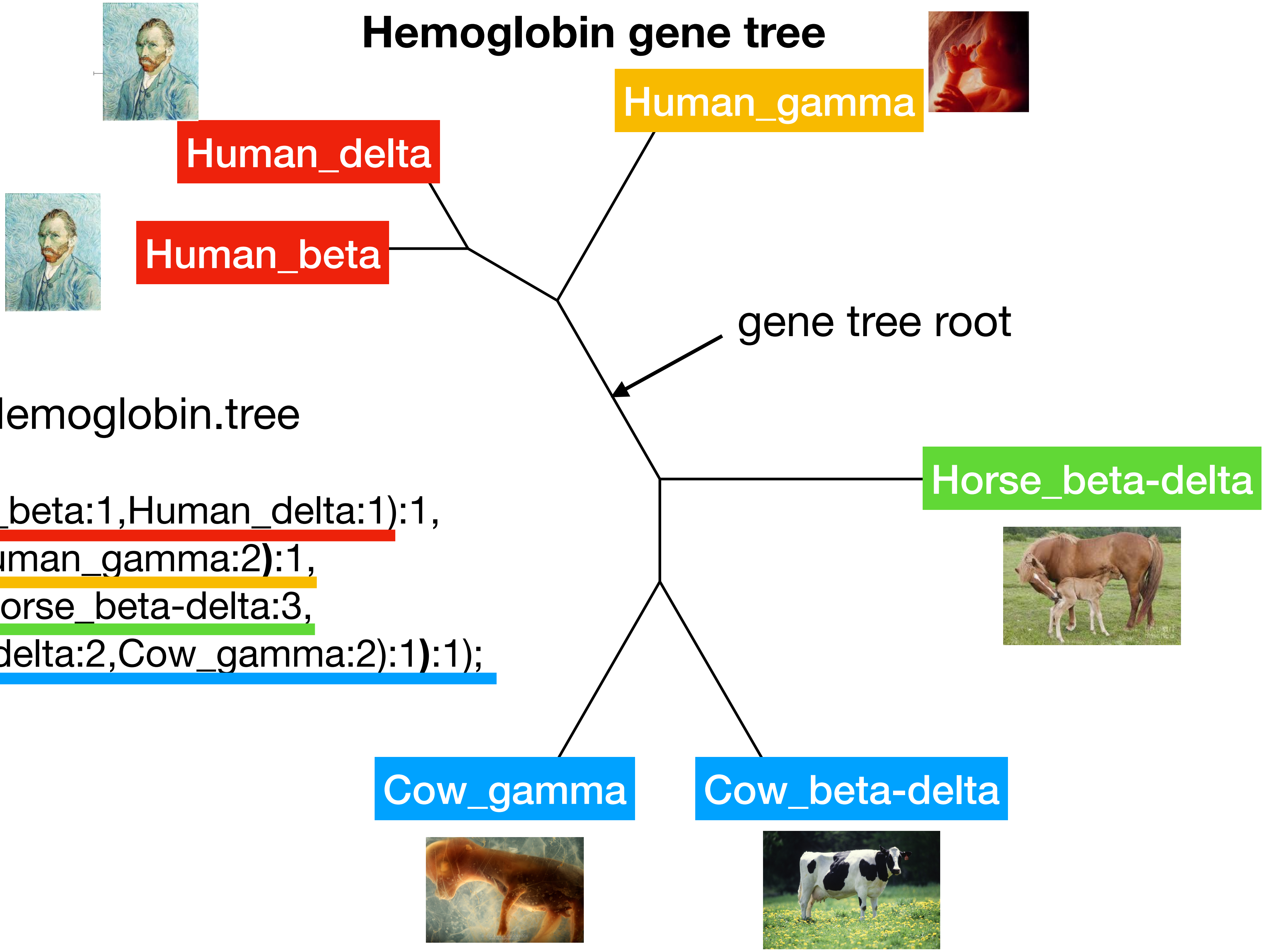
view the tree using either phylo.io, seaview or FigTree!

Hemoglobin.tree

```
(((Human_beta:1,Human_delta:1):1,
Human_gamma:2):1,
Horse_beta-delta:3,
(Cow_beta-delta:2,Cow_gamma:2):1);
```

Hemoglobin/

```
$ cd ~/workshop_materials/lab_data/Hemoglobin
```



Hemoglobin gene tree

Hemoglobin.tree

```
(((Human_beta:1,Human_delta:1):1,
Human_gamma:2):1,
(Horse_beta-delta:3,
(Cow_beta-delta:2,Cow_gamma:2):1):1);
```

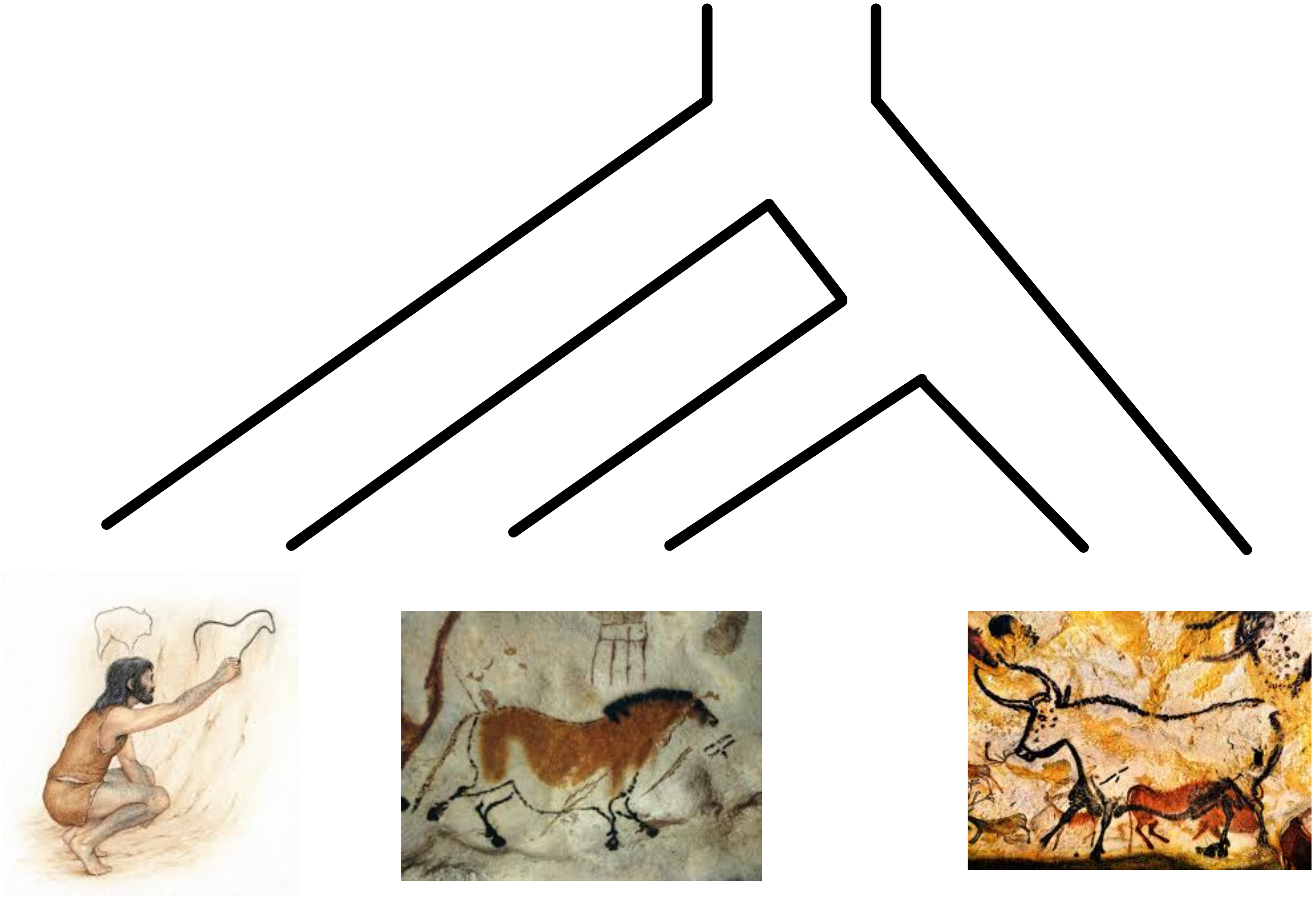
`Hemoglobin/`

Species tree

HuHoCo.tree

(Human:2,(Horse:1,Cow:1):1);

species tree root



Human

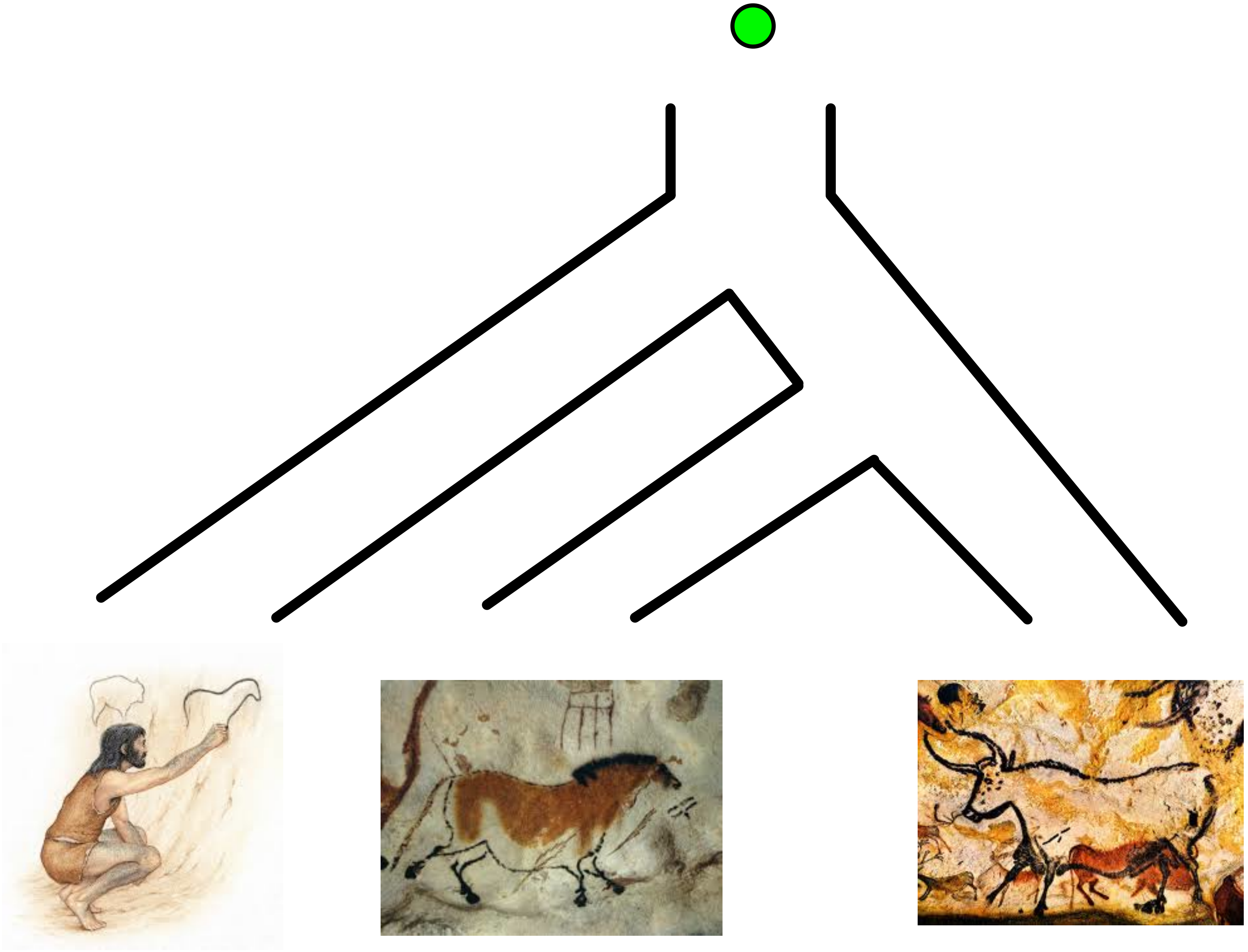
Horse

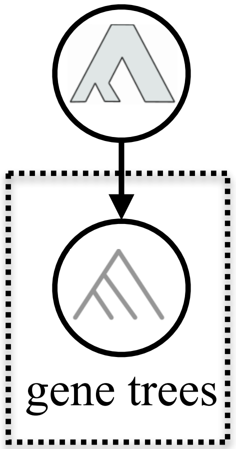
Cow

species

Hemoglobin/

DL along S





DL

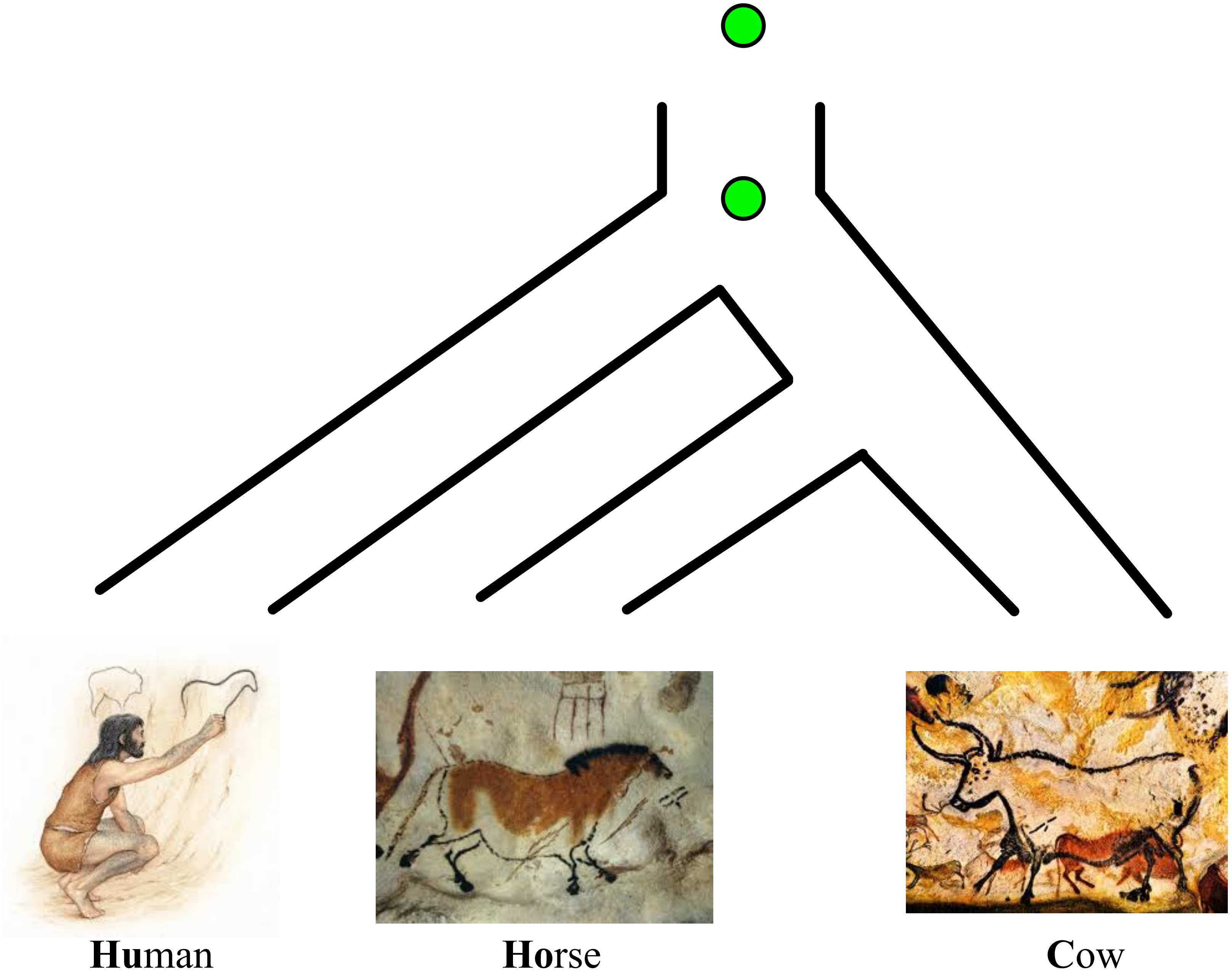
species tree

gene trees

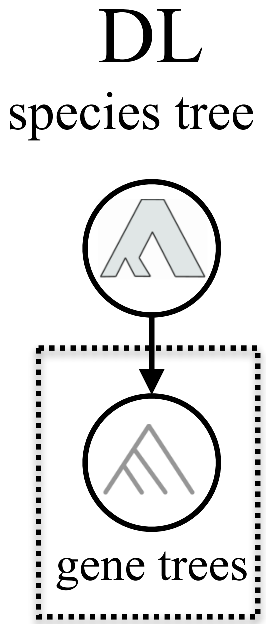
species

Hemoglobin/

DL along S

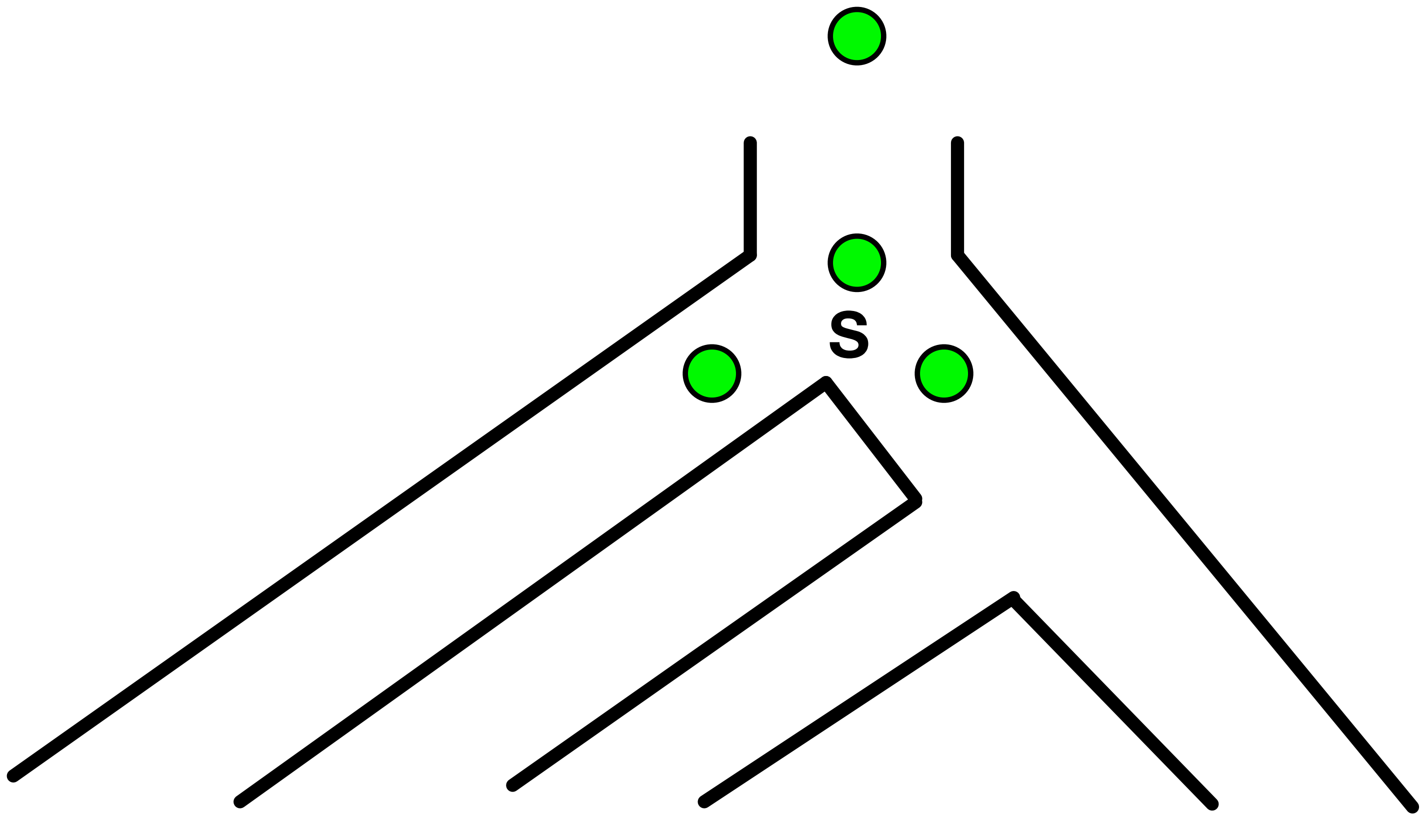


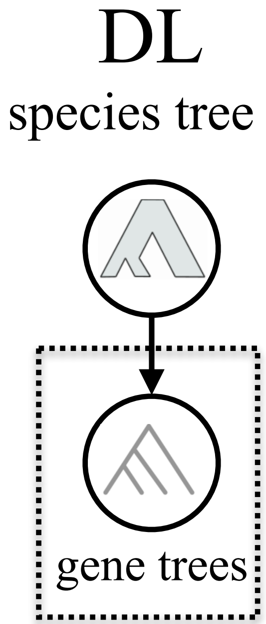
species



Hemoglobin/

DL along S




DL

species tree

gene trees


Human

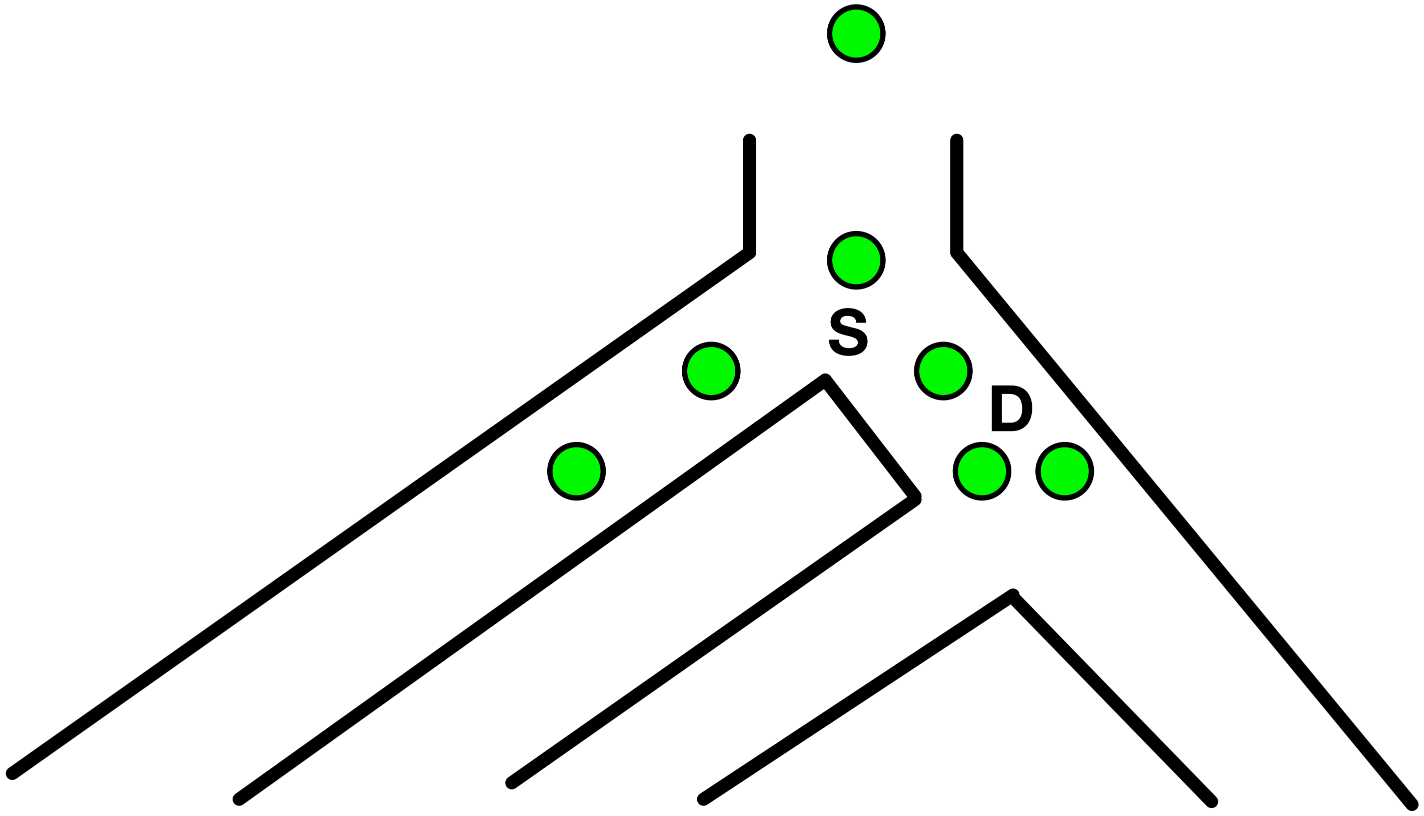

Horse

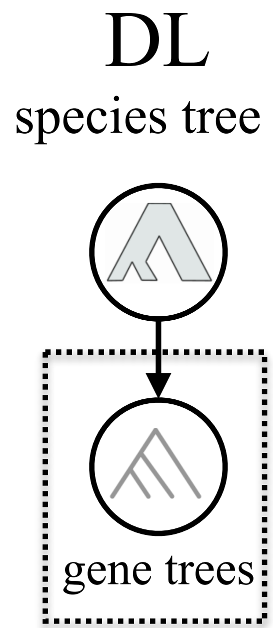

Cow

species

Hemoglobin/

DL along S





DL

species tree

gene trees

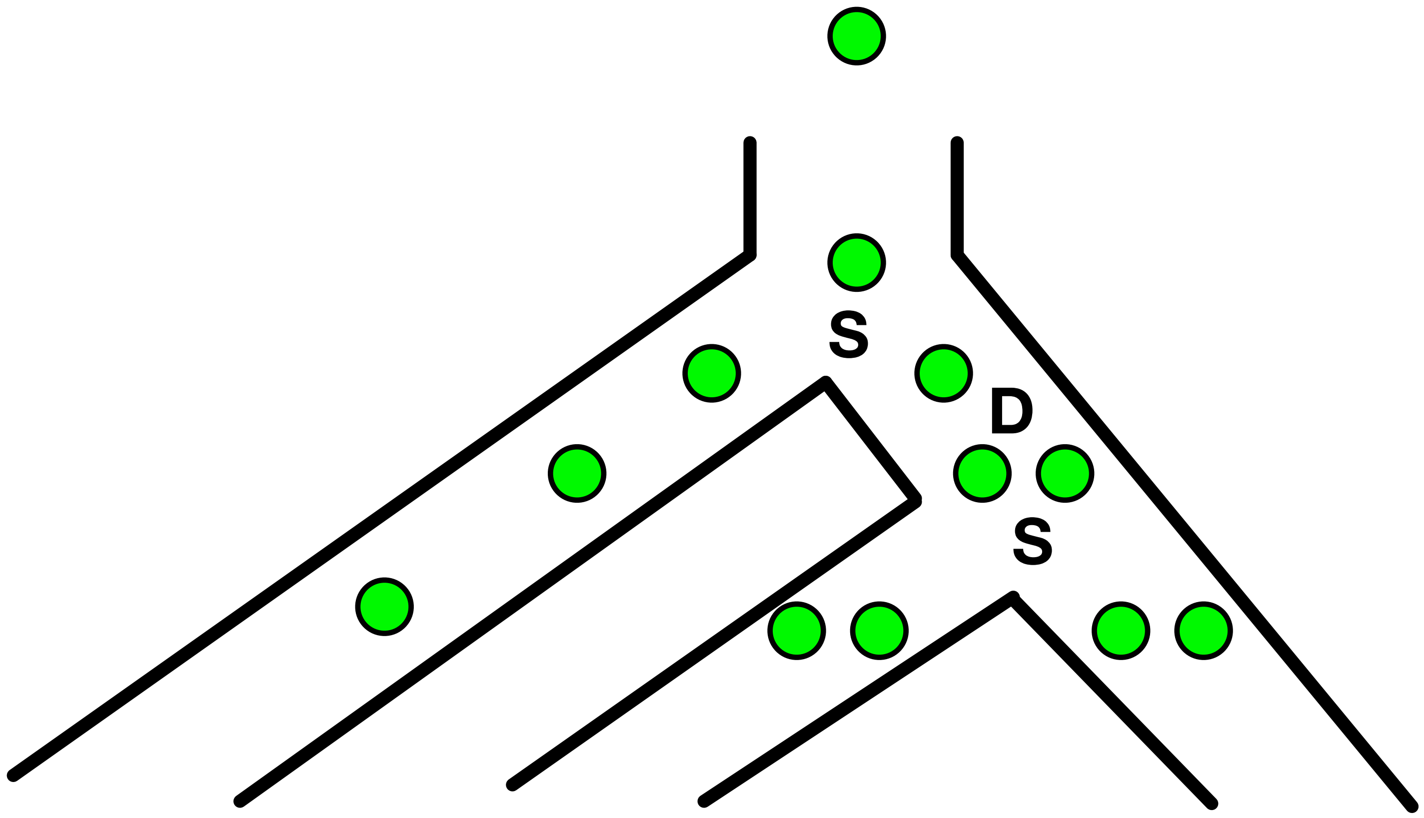
Human

Horse

Cow

species

DL along S

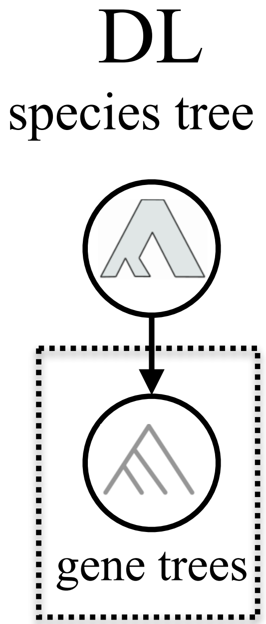



Human


Horse


Cow

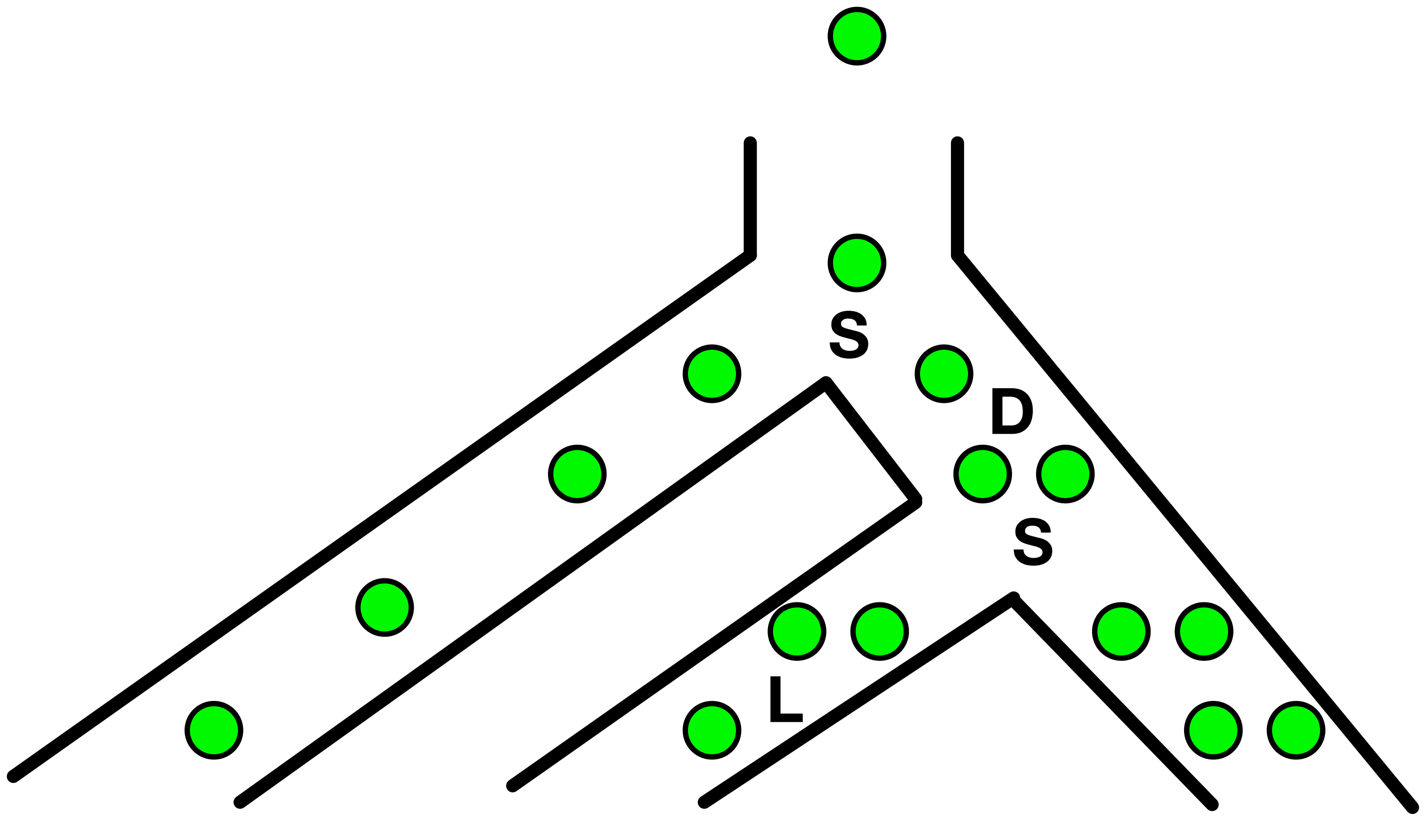
species

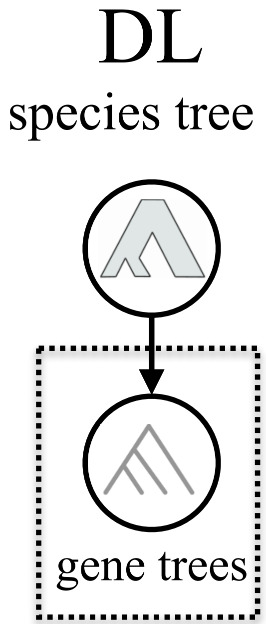

DL

species tree

gene trees

DL along S





Human

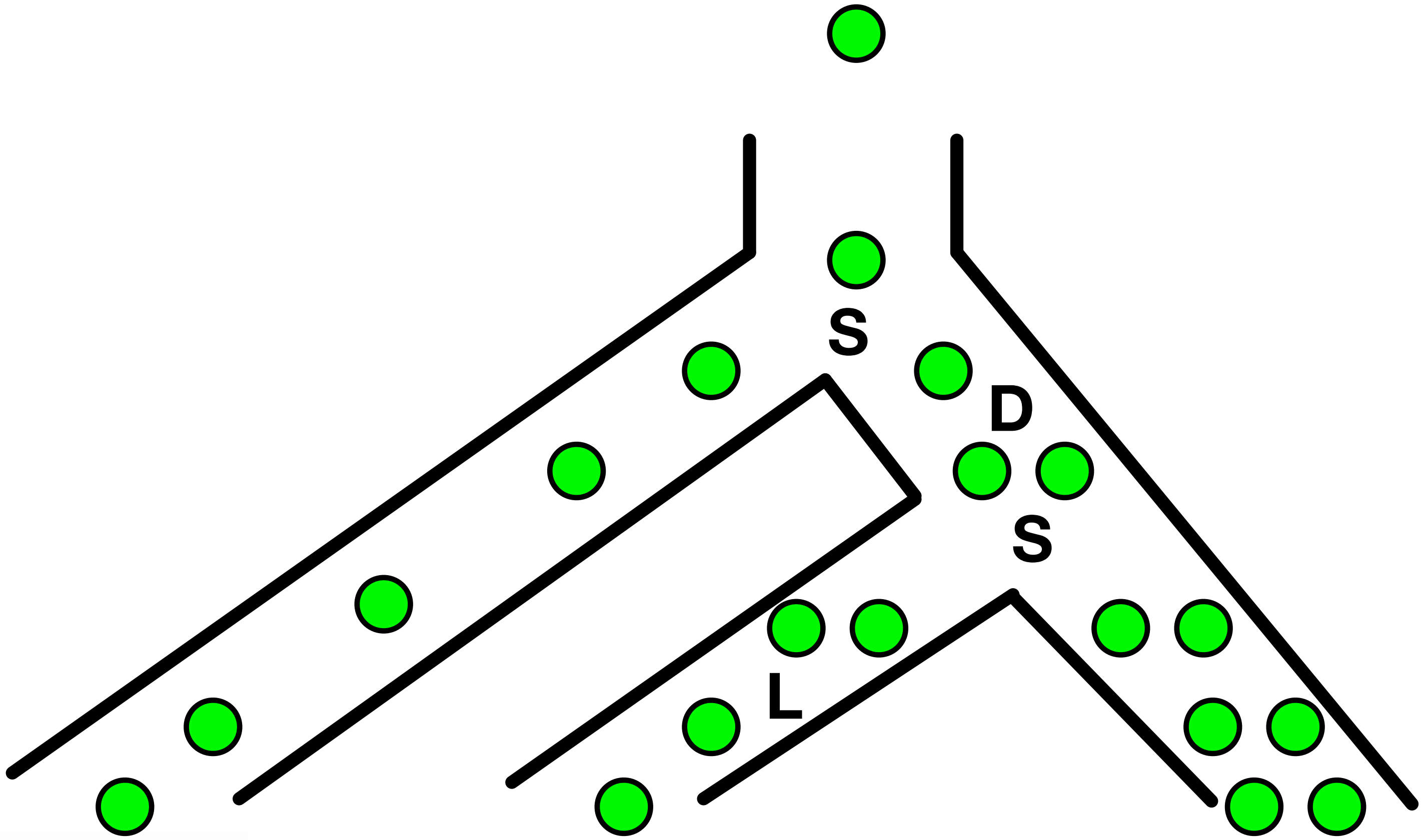
Horse

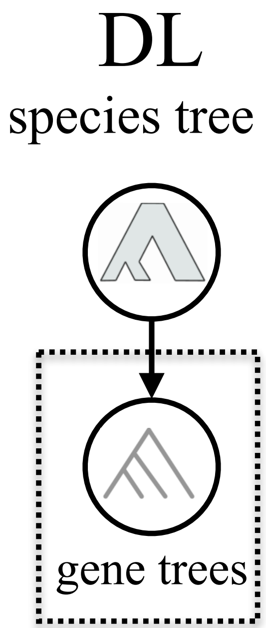
Cow

species

Hemoglobin/

DL along S





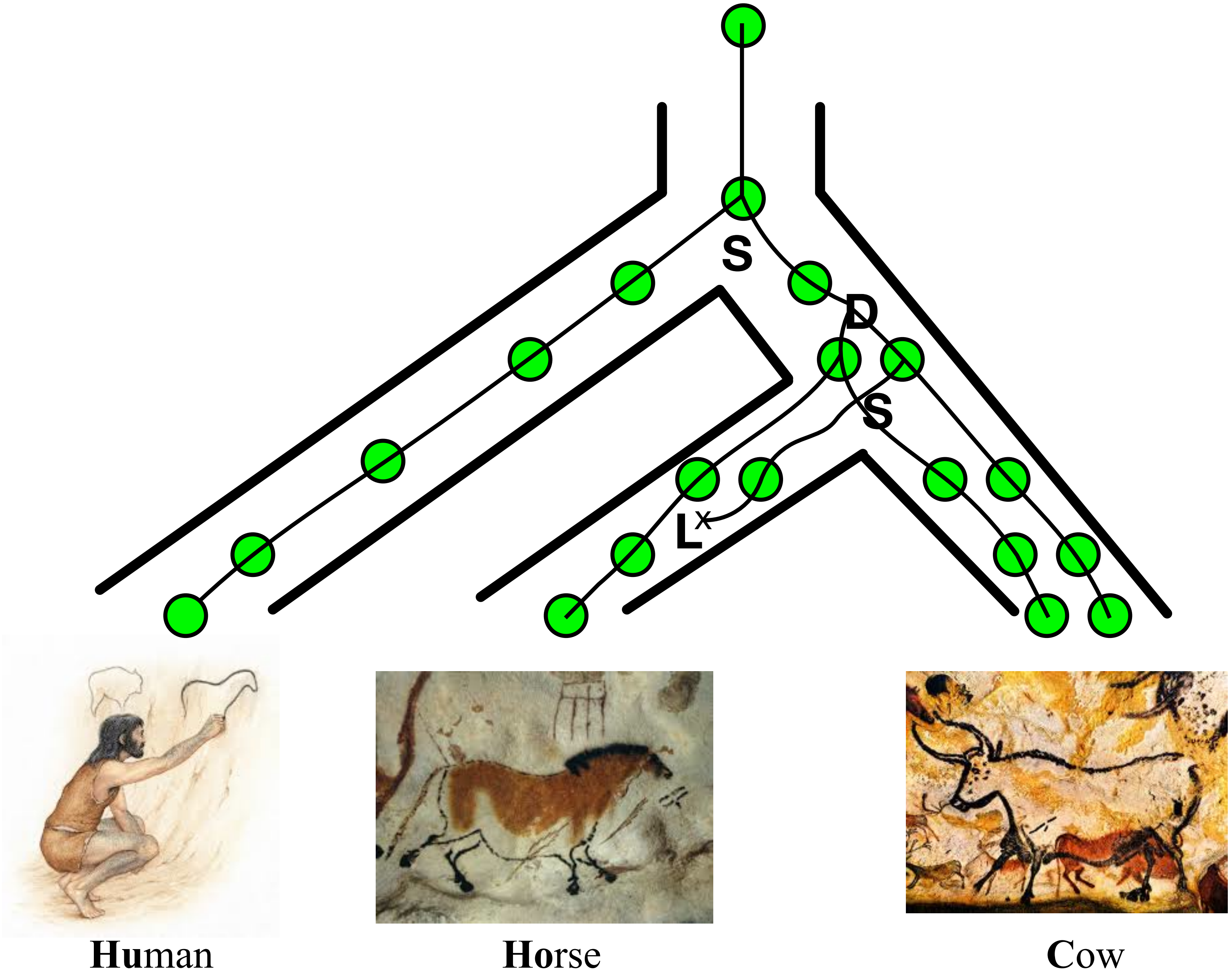
Human

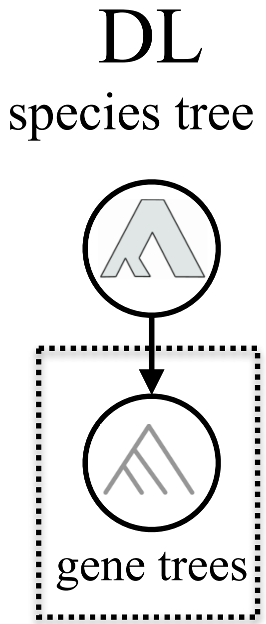
Horse

Cow

species

DL along S



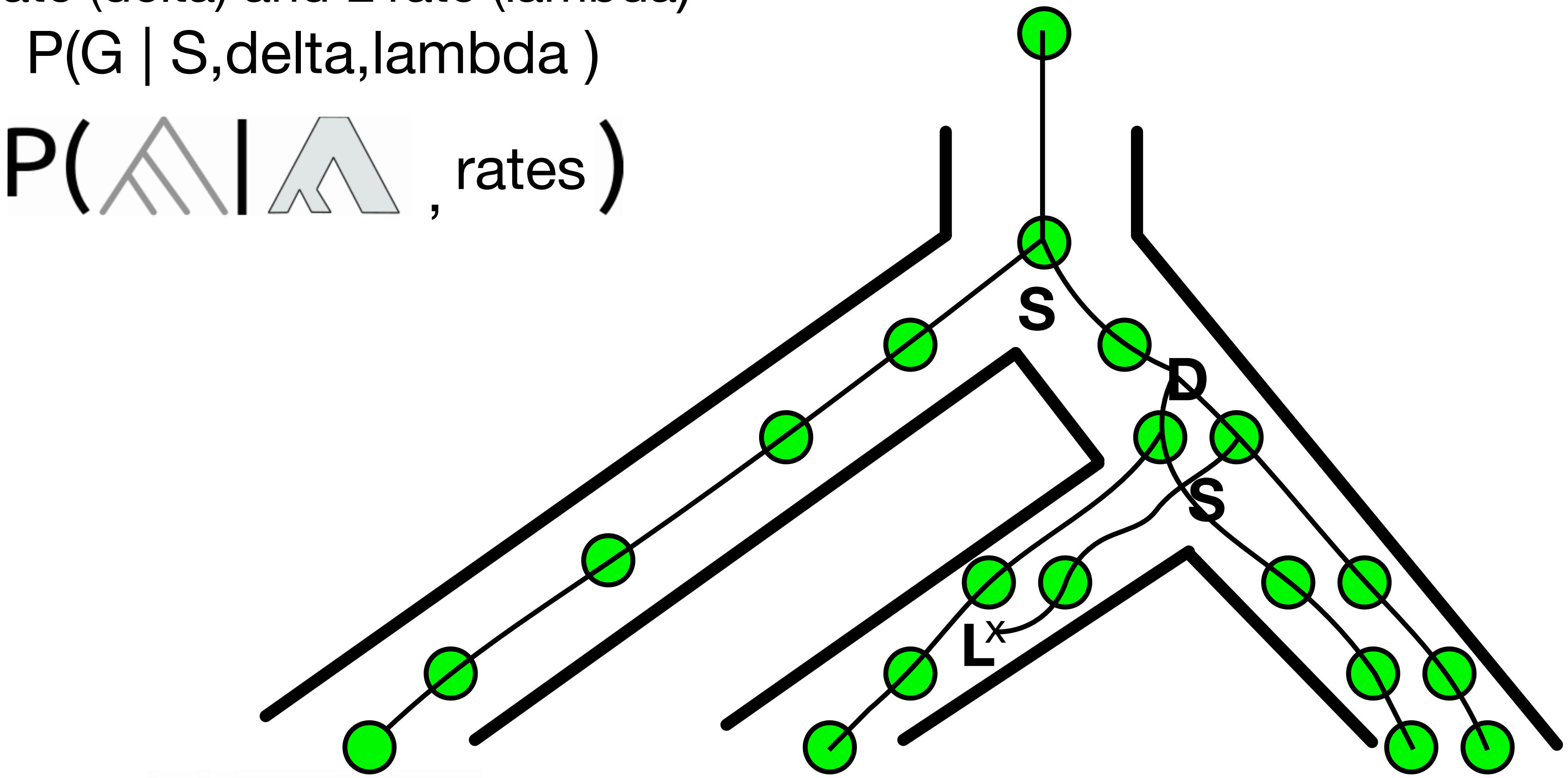


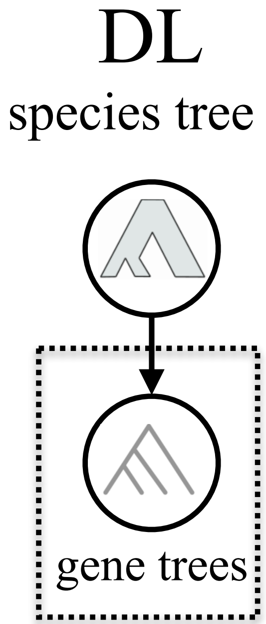
species

DL along S

Given G and S we want to calculate:

1. D rate (delta) and L rate (lambda)
2. P(G | S,delta,lambda)





Human

Horse

Cow

species

```
Hemoglobin/
```

```
ALEobserve Hemoglobin.tree
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
less HuHoCo.tree_Hemoglobin.tree.ale.ml_rec
```

```
#ALEml using ALE v0.5 by Szollosi GJ et al.; ssolo@elte.hu; CC BY-SA 3.0;

S:        (Human:1,(Horse:0.5,Cow:0.5)1:0.5)2;


Input ale from: Hemoglobin.tree.ale
>logl: -4.45543
rate of  Duplications       Transfers         Losses
ML        0.76128 0         1e-10

10 reconciled G-s:

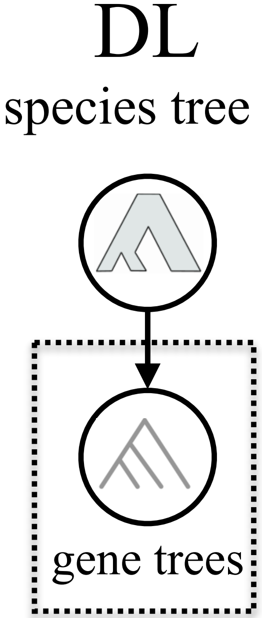
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@1|0.5|Human:1)D@1|0.55|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.2|Cow:1).1:2).2:0;
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.1|Human:1)D@0|0.4|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.4|Cow:1).1:2).2:0;
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.15|Human:1)D@0|0.25|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.2|Cow:1).1:2).2:0;
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.25|Human:1)D@1|0.75|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.4|Cow:1).1:2).2:0;
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.1|Human:1)D@0|0.25|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.2|Cow:1).1:2).2:0;
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1)D@0|0.3|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.05|Cow:1).1:2).2:0;
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.2|Human:1)D@1|0.55|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.2|Cow:1).1:2).2:0;
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.35|Human:1)D@1|0.5|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.05|Cow:1).1:2).2:0;
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.15|Human:1)D@0|0.3|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.15|Cow:1).1:2).2:0;
# of     Duplications       Transfers         Losses    Speciations
Total     3         0         0         2

# of     Duplications       Transfers         Losses    copies
S_terminal_branch             Cow       1         0         0         2
S_terminal_branch             Horse     0         0         0         1
S_terminal_branch             Human     2         0         0         3
S_internal_branch             1         0         0         0         1
S_internal_branch             2         0         0         0         1
HuHoCo.tree_Hemoglobin.tree.ale.ml_rec (END)
```

species tree

ML log-likelihood (tau=0)

ML rates (tau=0)



10 random reconciled gene trees
sampled according to joint likelihood

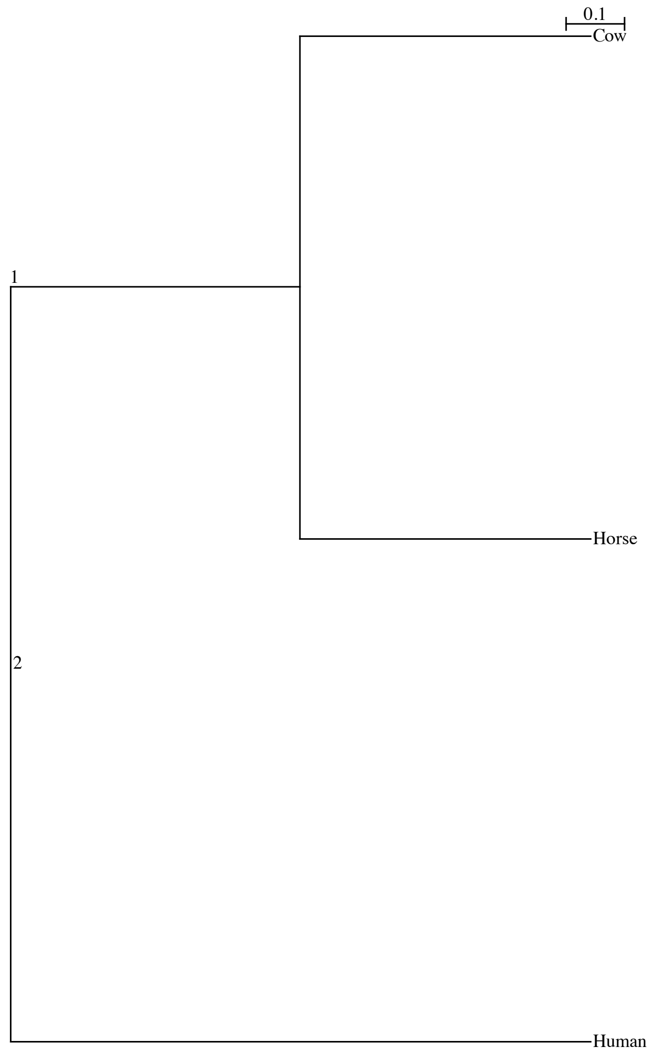
mean number of events
per branch in sampled
reconciliations

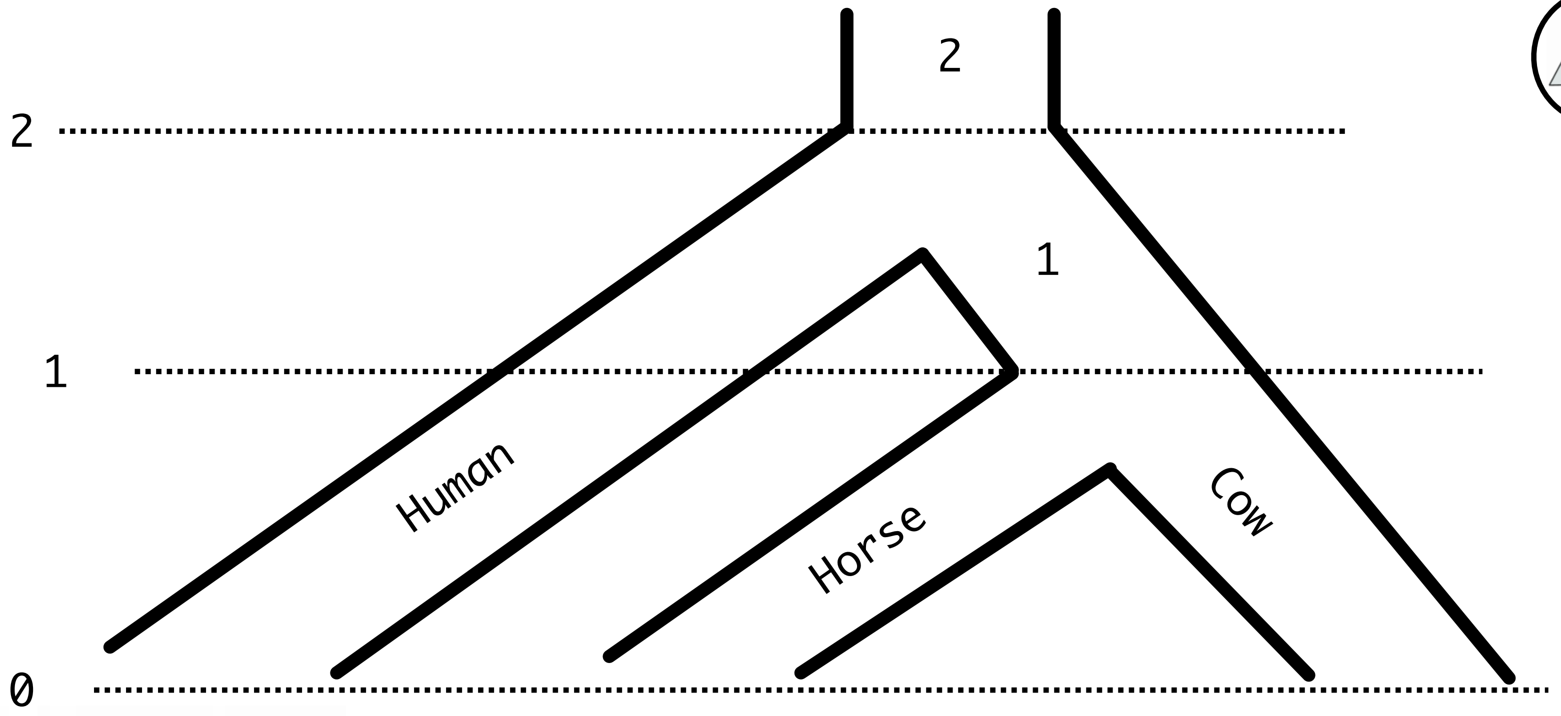
sum over reconciled
gene trees

Hemoglobin/

```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

```
S:      (Human:1,(Horse:0.5,Cow:0.5)1:0.5)2;
```





Human

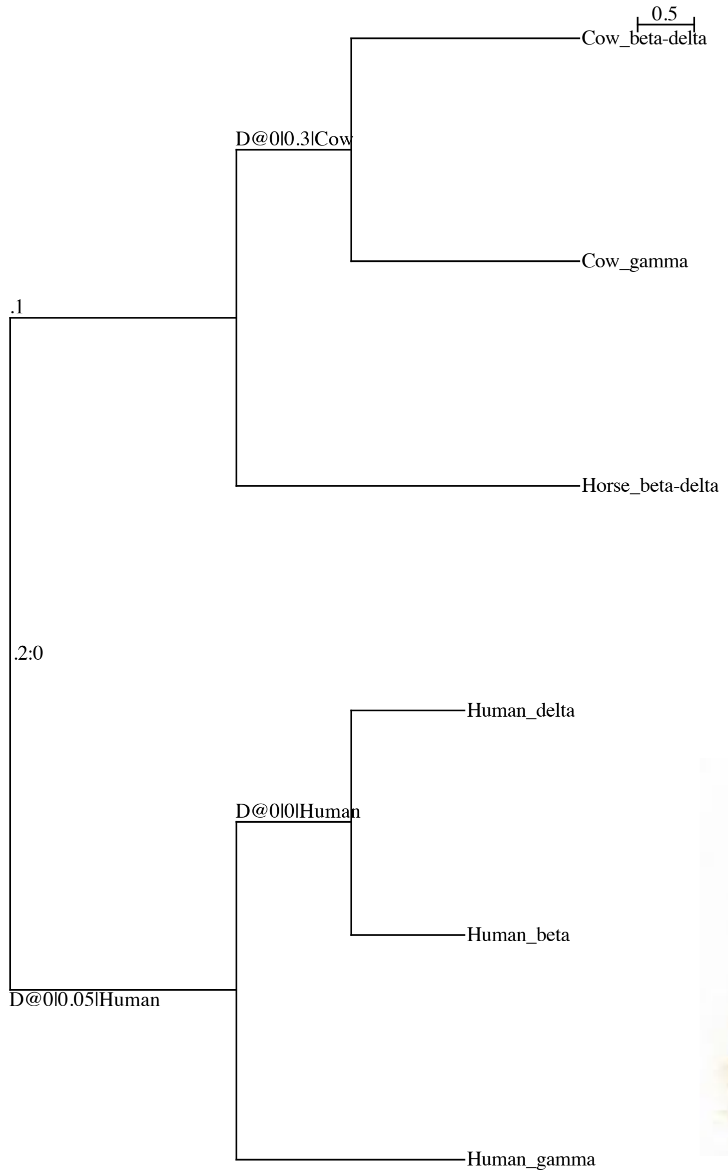
Horse

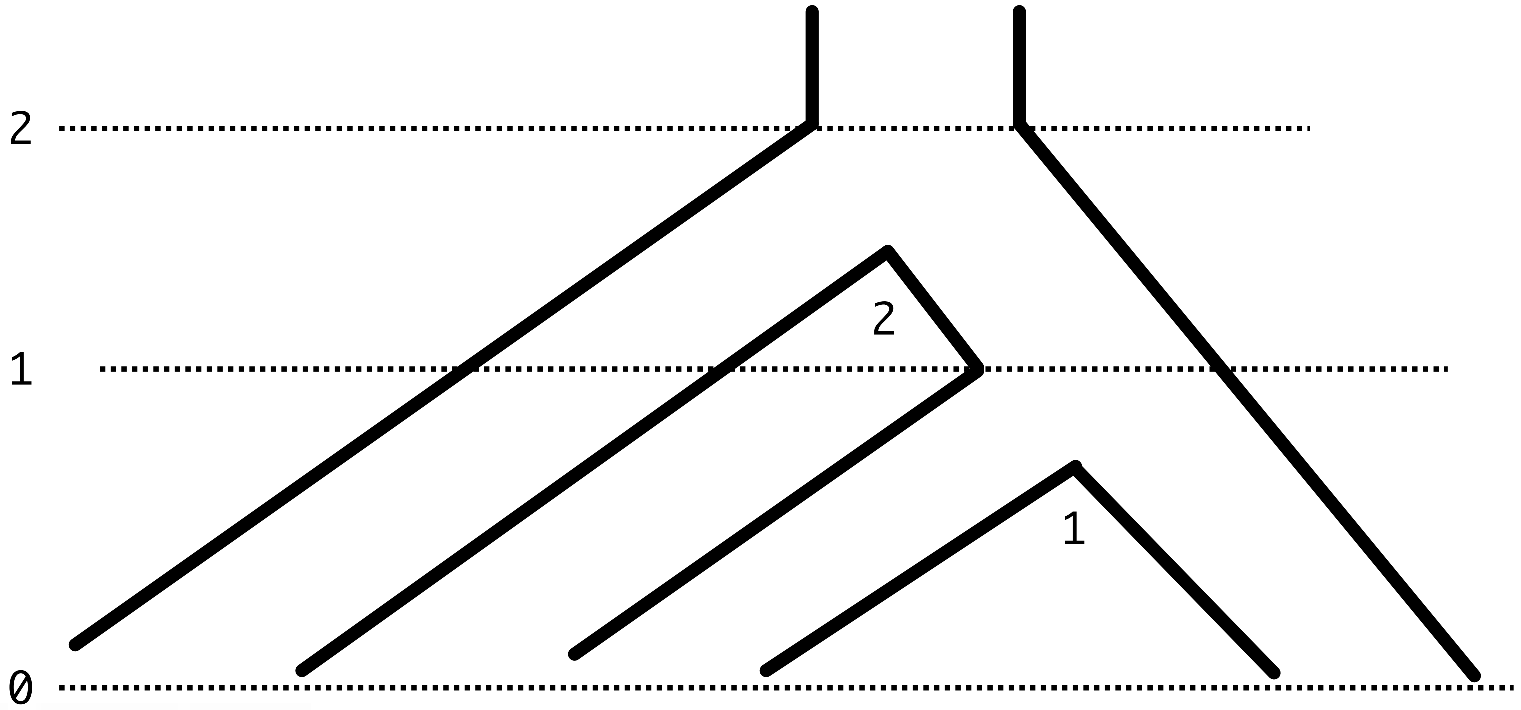
Cow

Hemoglobin/

```
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;
```

```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```





Human

Horse

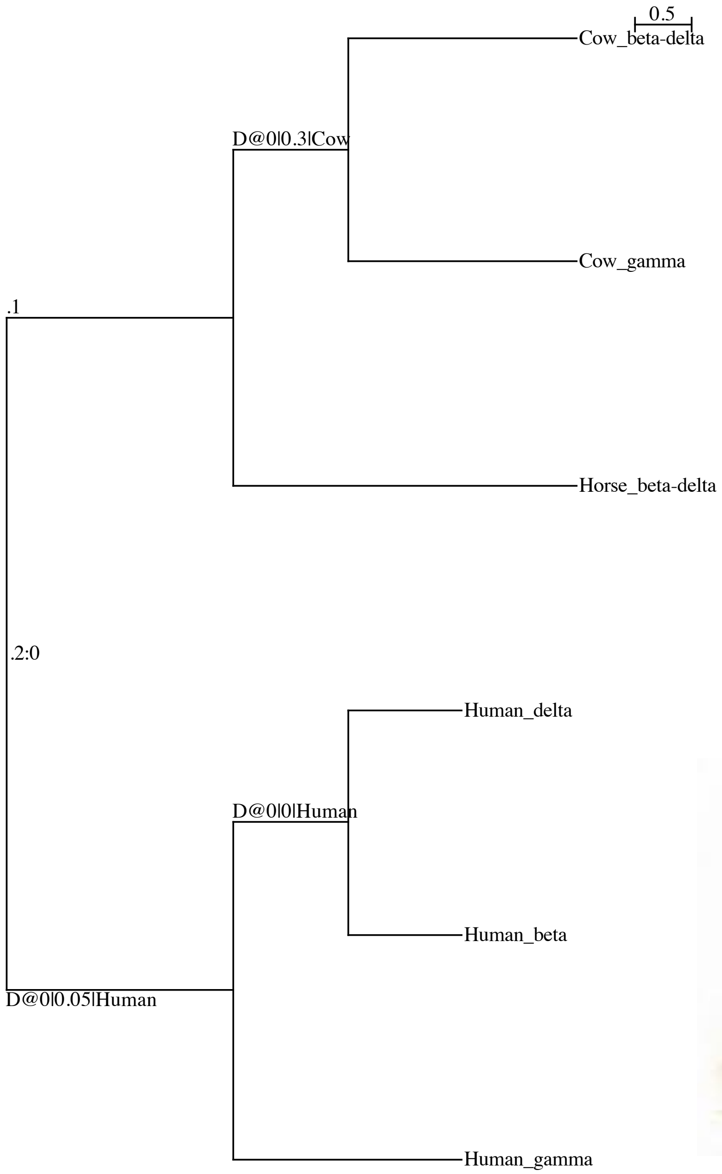
Cow

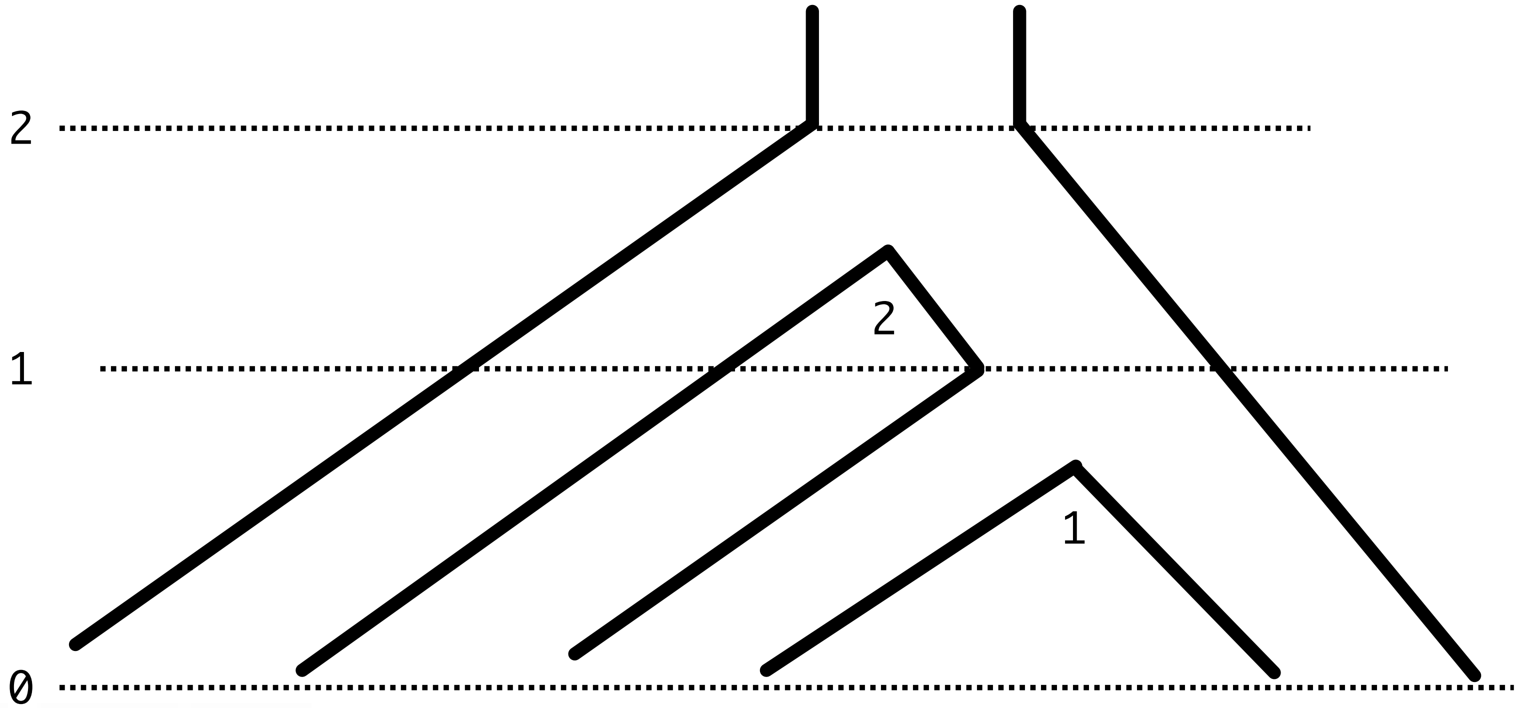
Hemoglobin/

```
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;
```

```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

```
(..).2:0;
```





Human

Horse

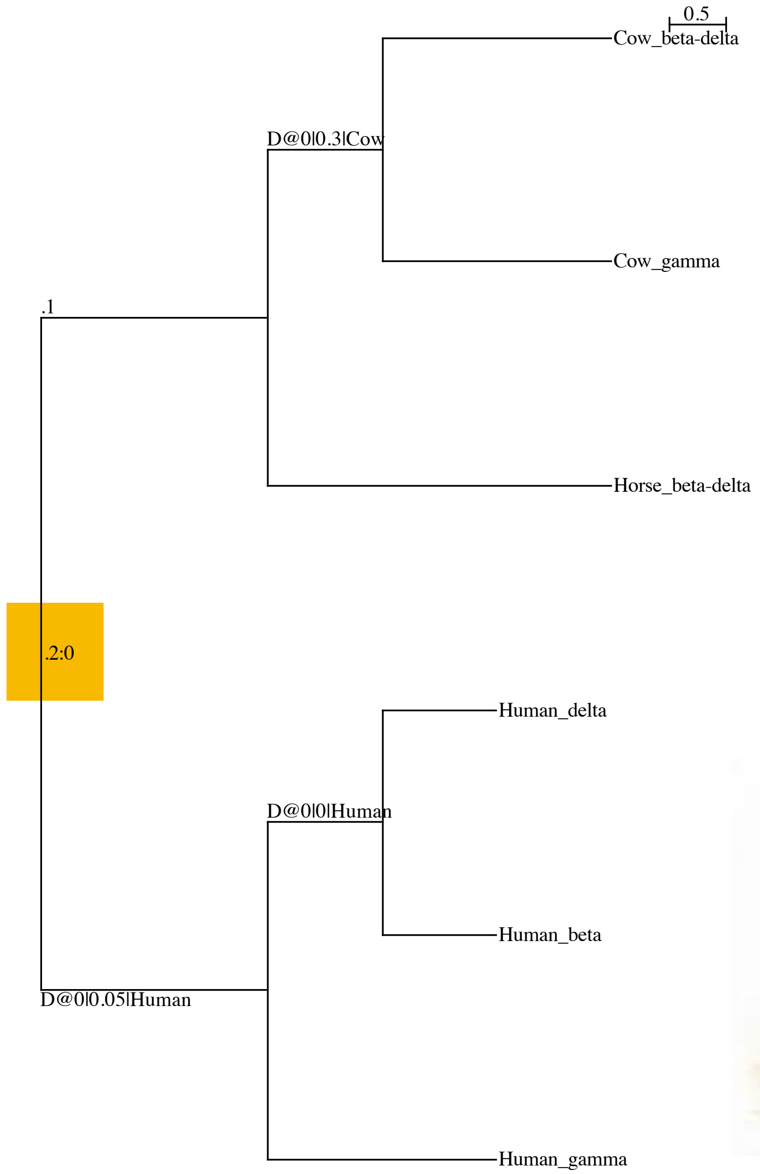
Cow

Hemoglobin/

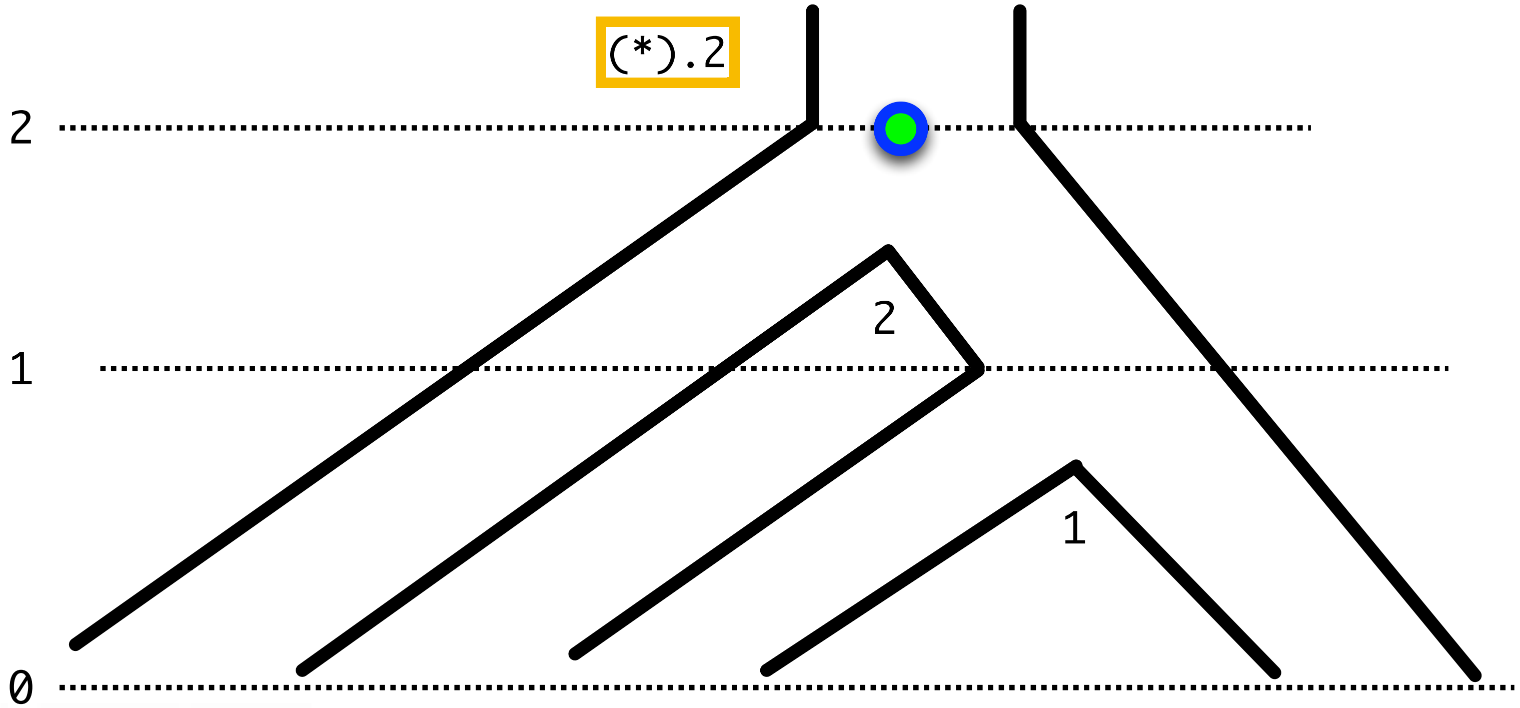
```
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;
```

```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

(..).2:0;



(*).2



Human

Horse

Cow

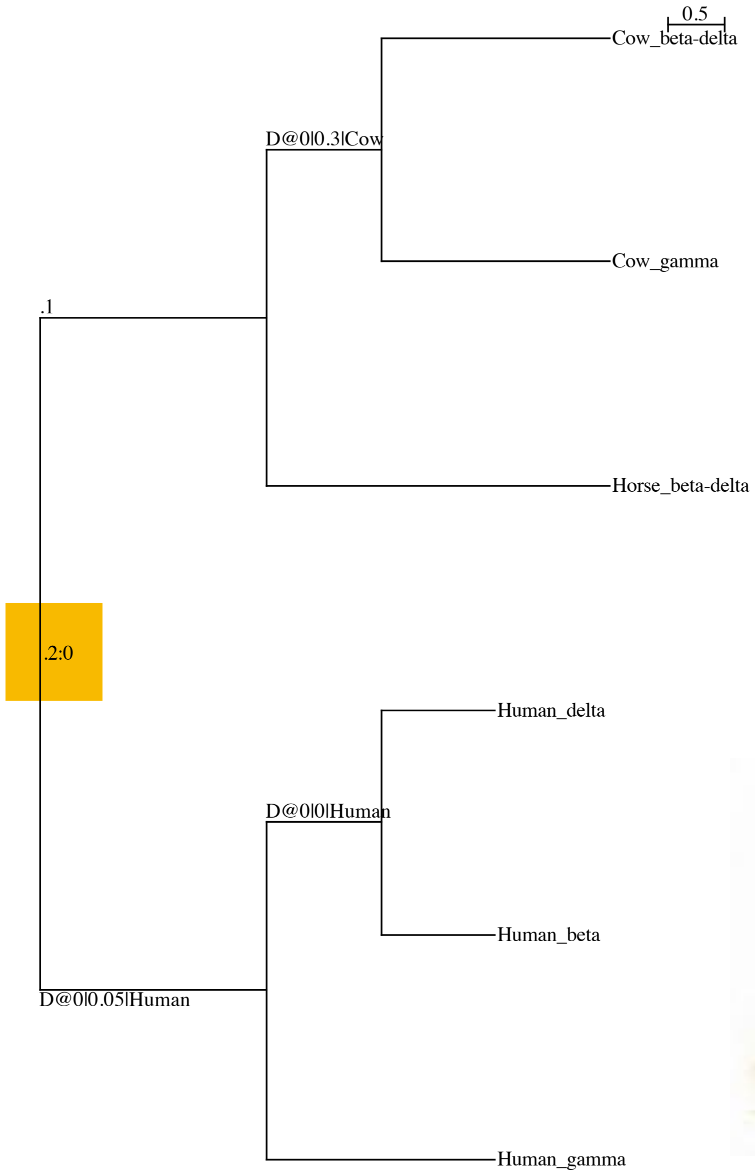
Hemoglobin/

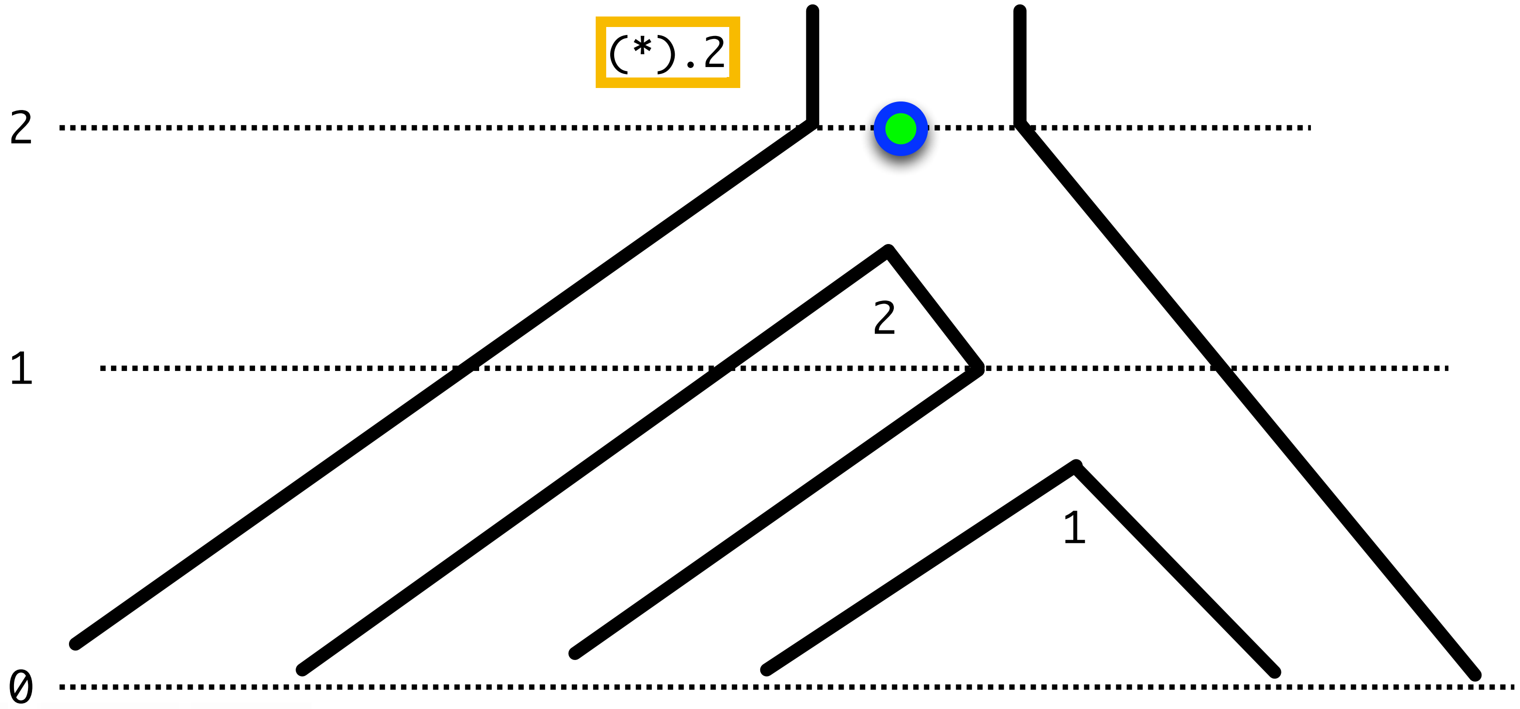
```
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;
```

```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

```
(..).2:0;
```

```
( (..)D@0|0.05|Human:2 , (..).1:2 ).2:0; ).2:0;
```





Human

Horse

Cow

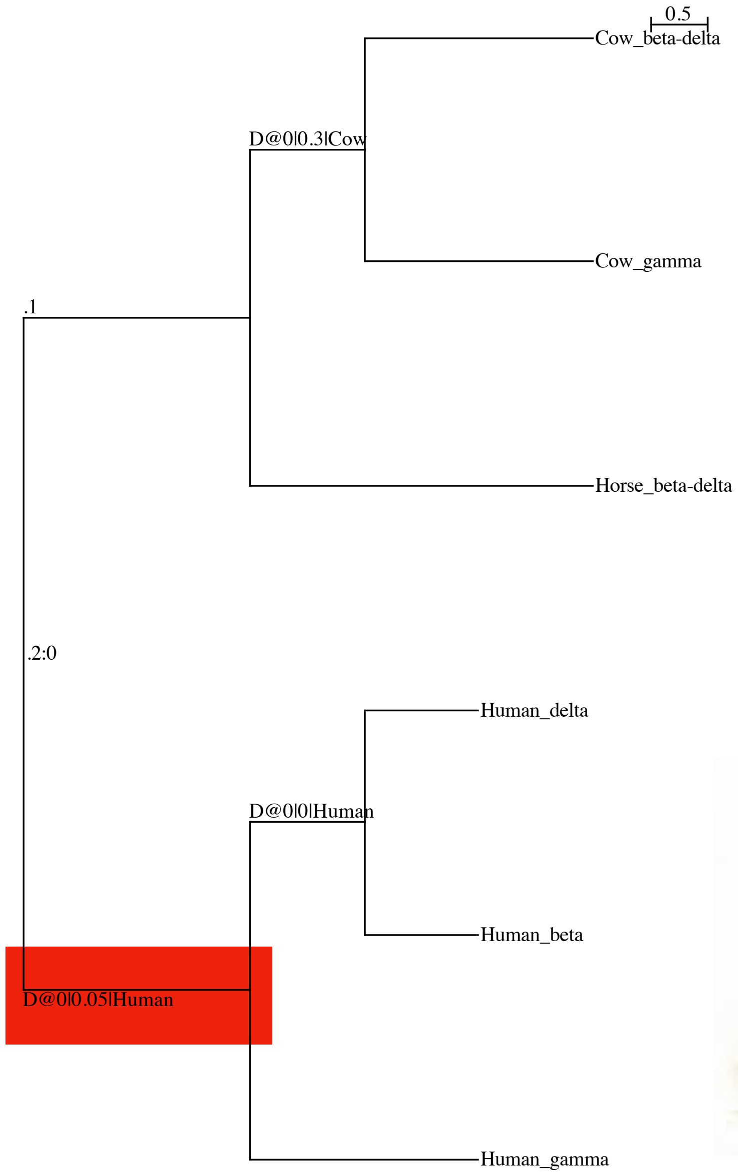
Hemoglobin/

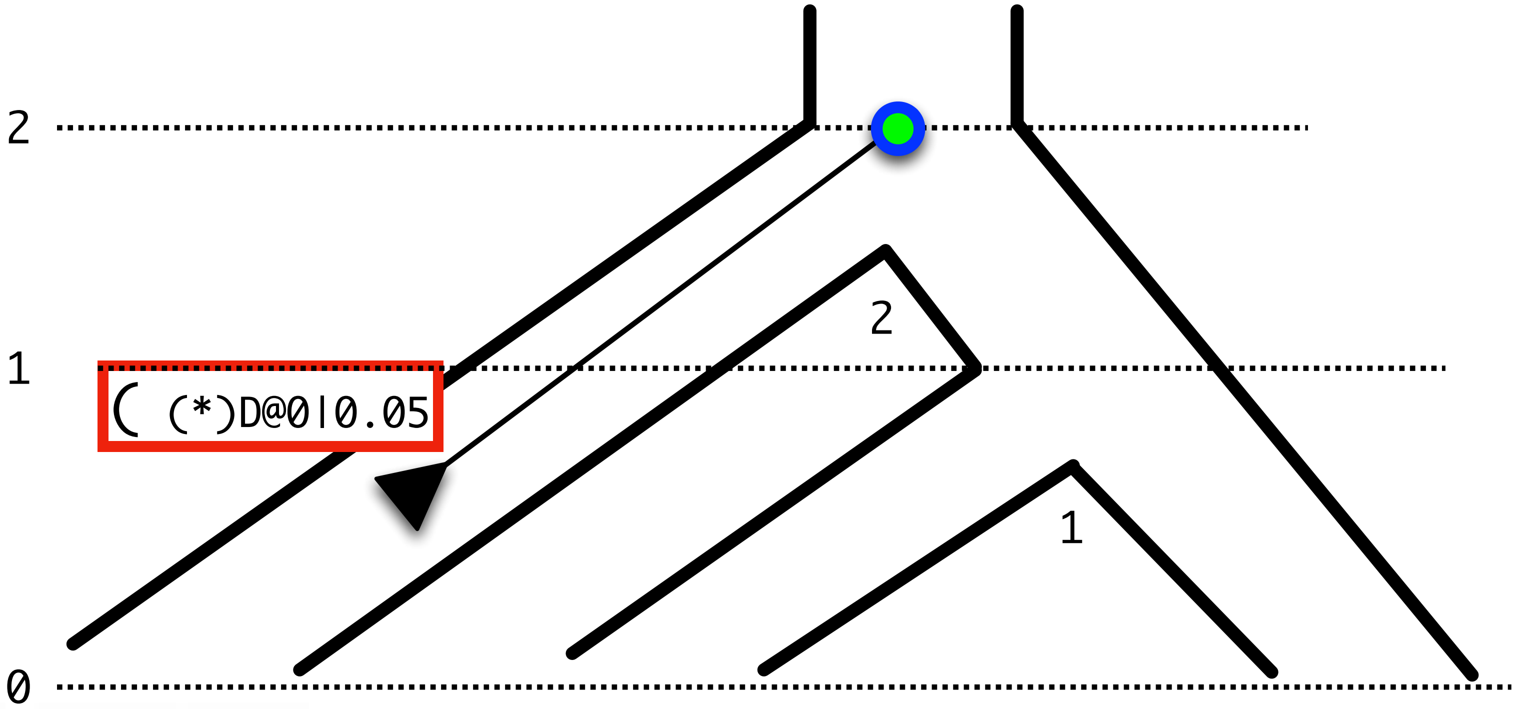
```
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;
```

```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

(..).2:0;

((..)D@0|0.05|Human:2 , (..).1:2).2:0;).2:0;





Human

Horse

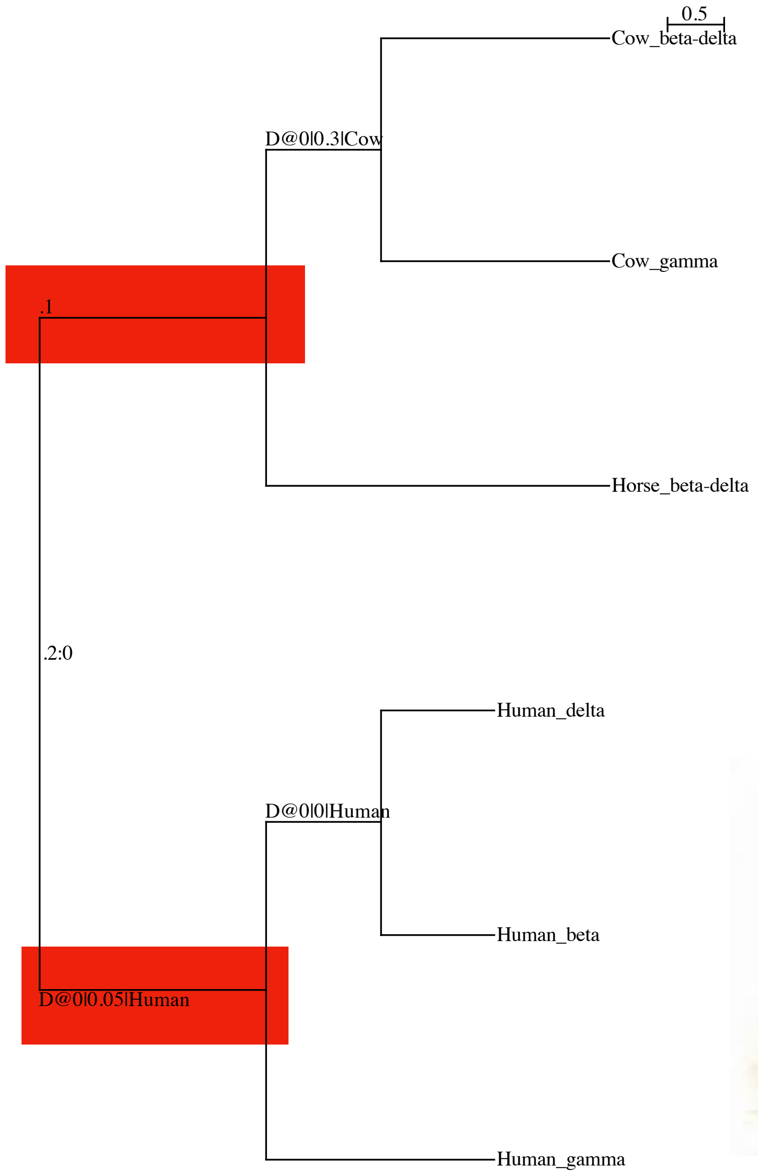
Cow

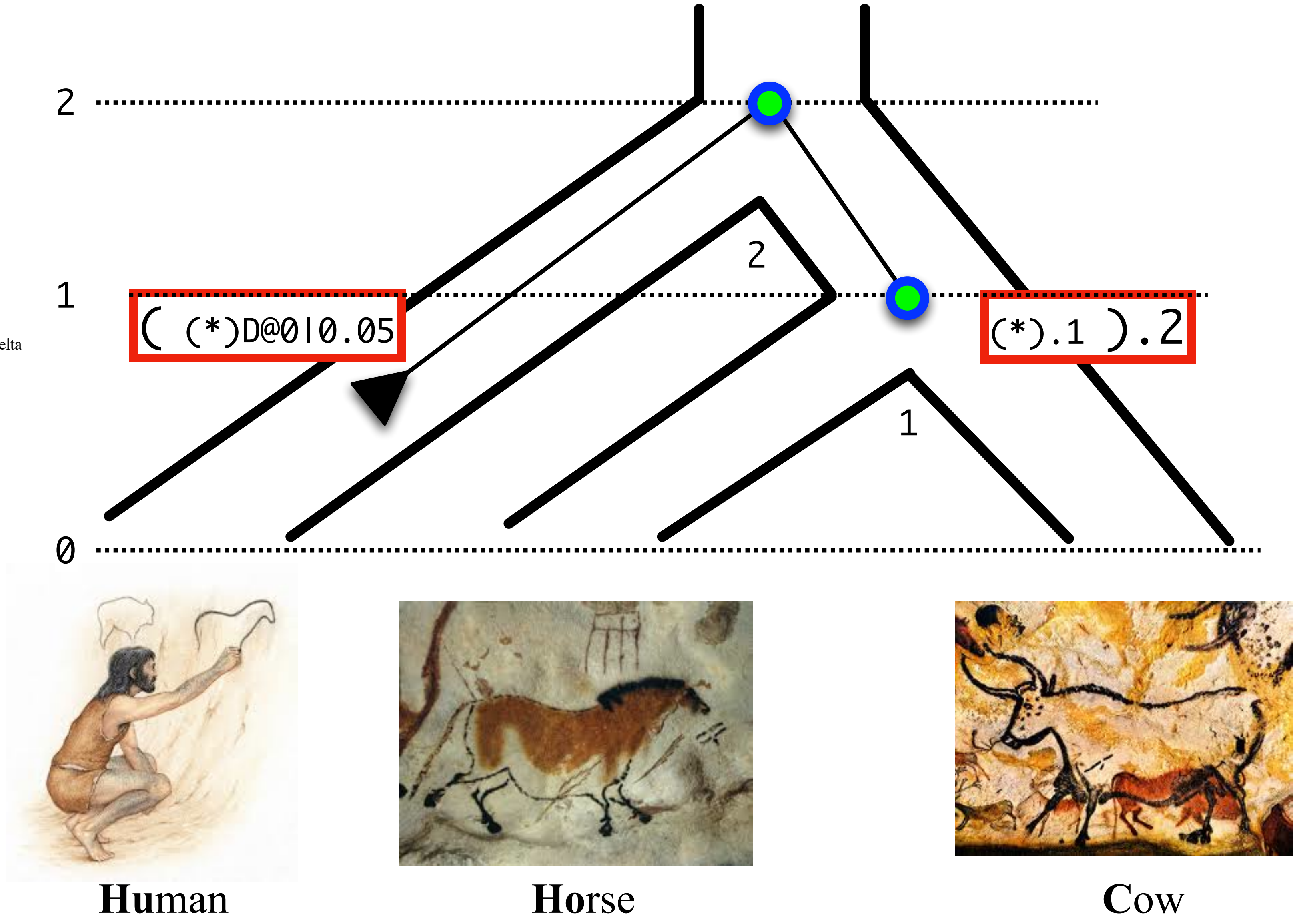
Hemoglobin/

```
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;
```

```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

```
(..).2:0;    ( (..)D@0|0.05|Human:2 , (..).1:2 ).2:0; ).2:0;
```





Hemoglobin/

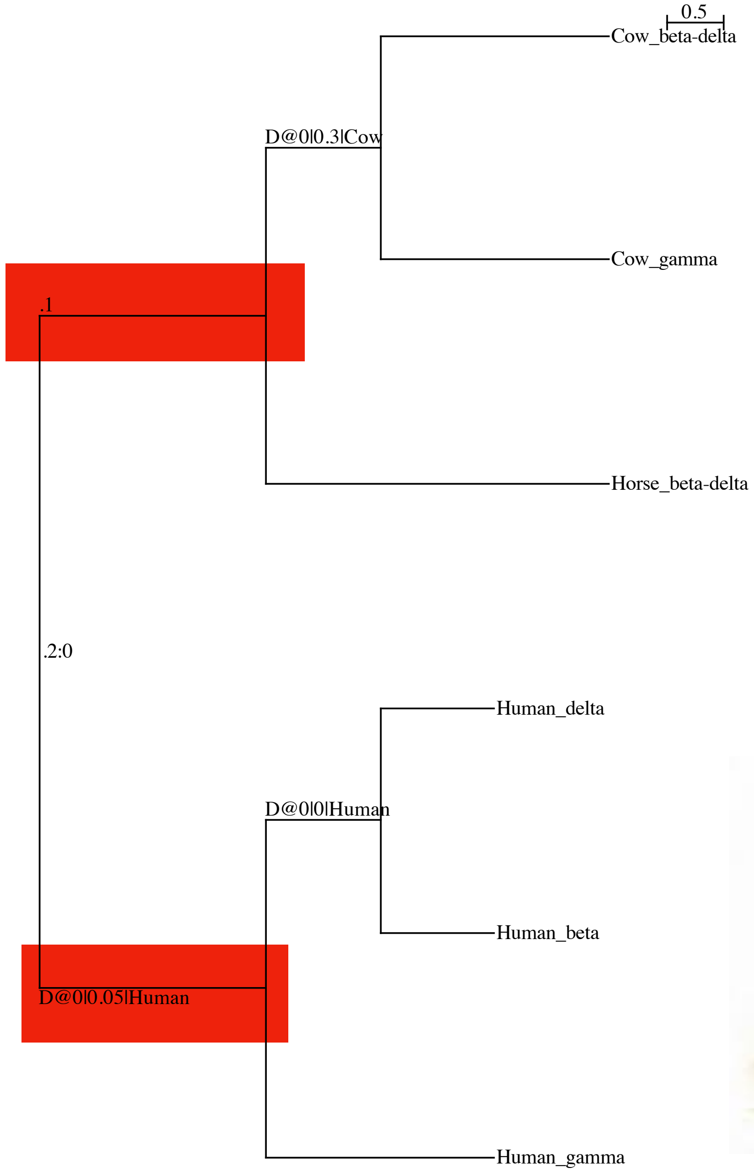
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;

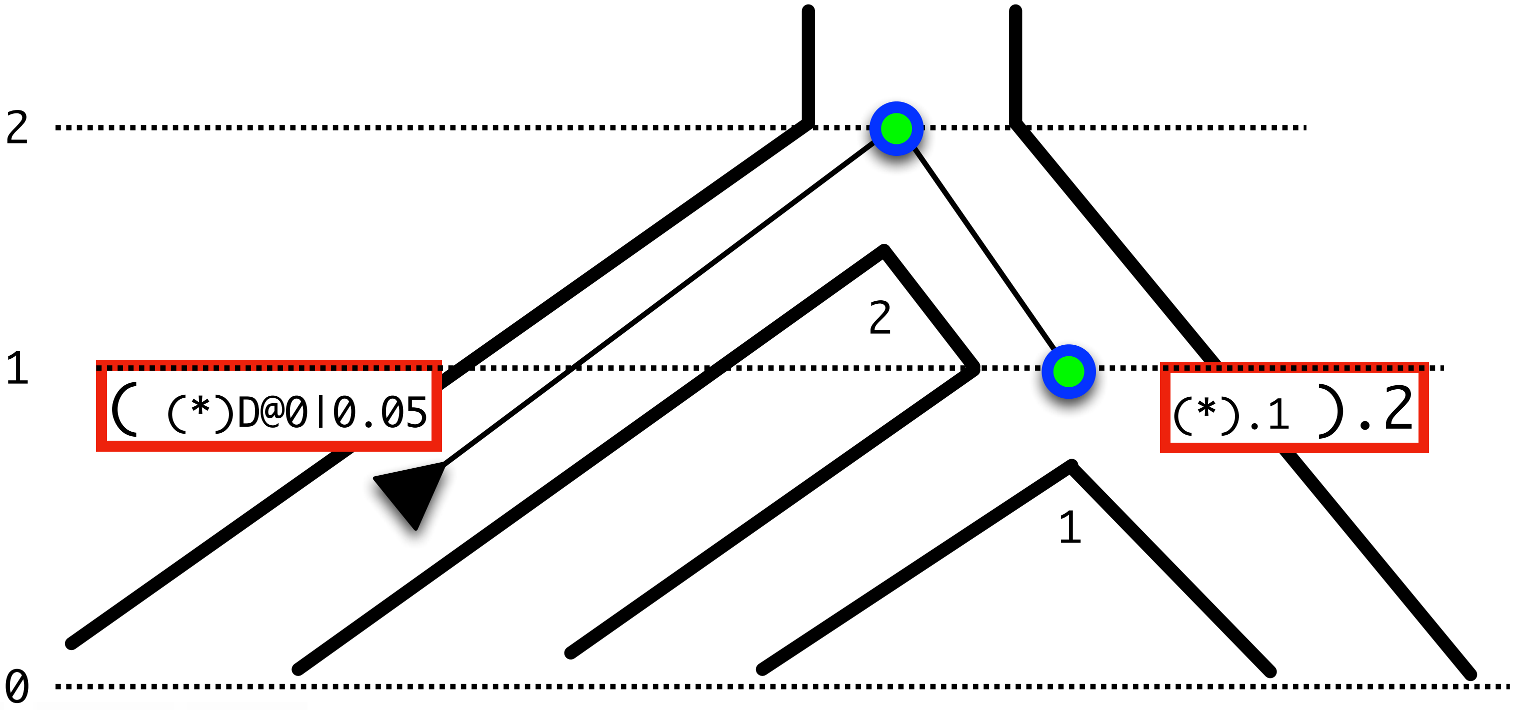
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10

(..).2:0;

((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2 ,

, (Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;).2:0;





Human

Horse

Cow

Hemoglobin/

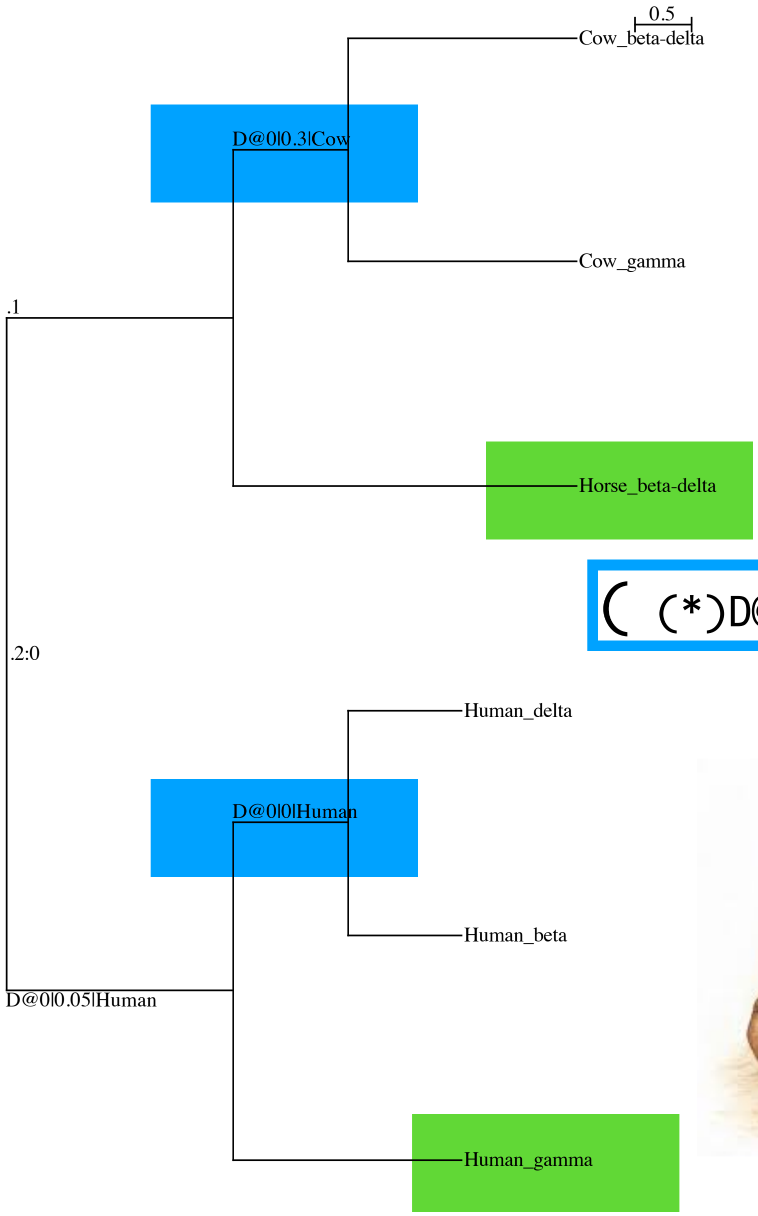
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;

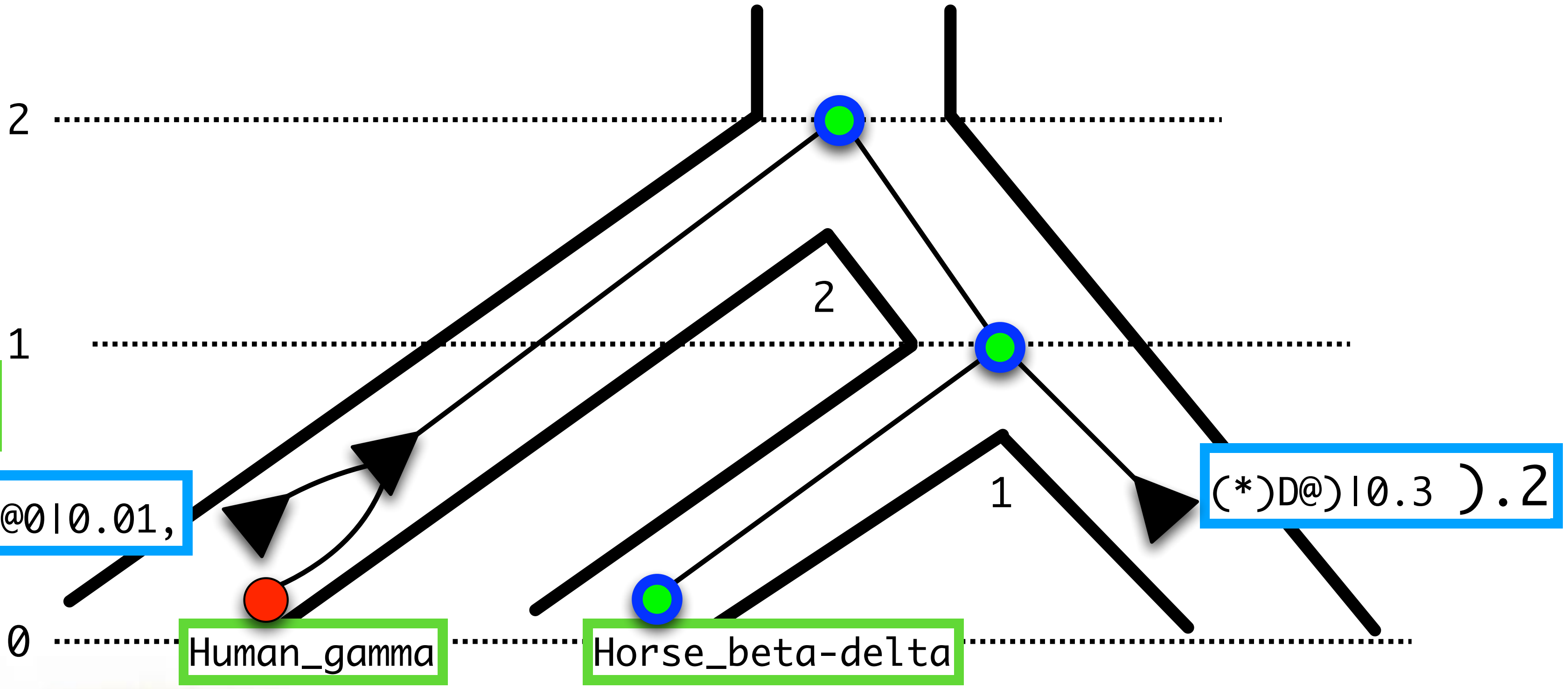
```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

(..).2:0;

((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2 ,

, (Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;).2:0;





Human

Horse

Cow

Hemoglobin/

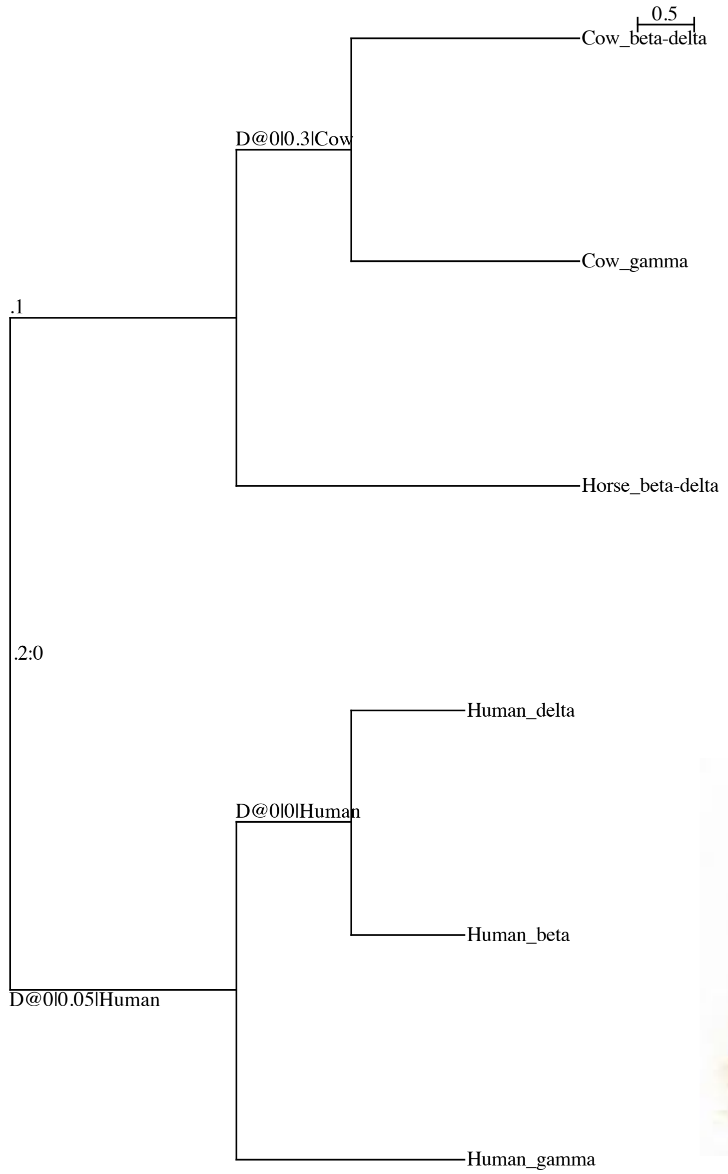
```
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;
```

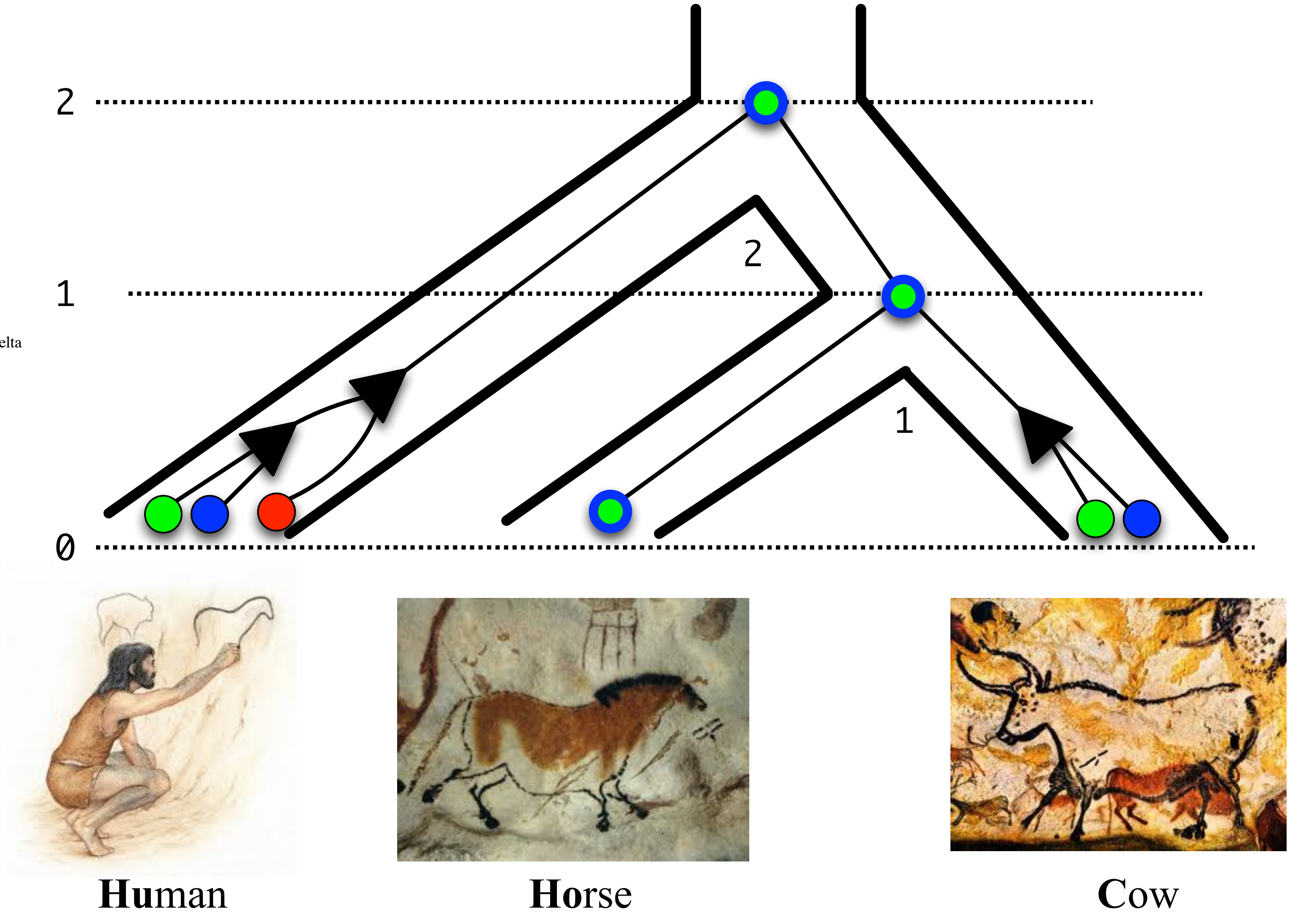
```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

```
(..).2:0;

((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2 ,

, (Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2 ).2:0; ).2:0;
```





Hemoglobin/

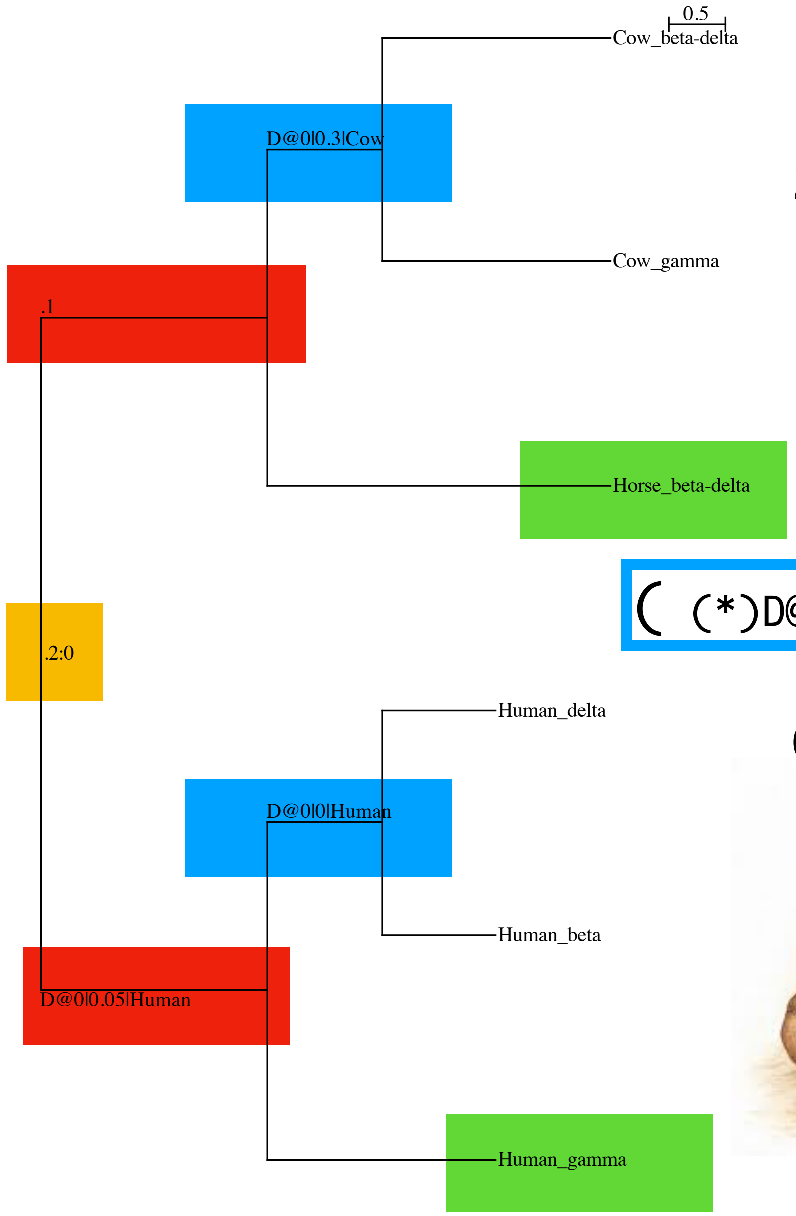
```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

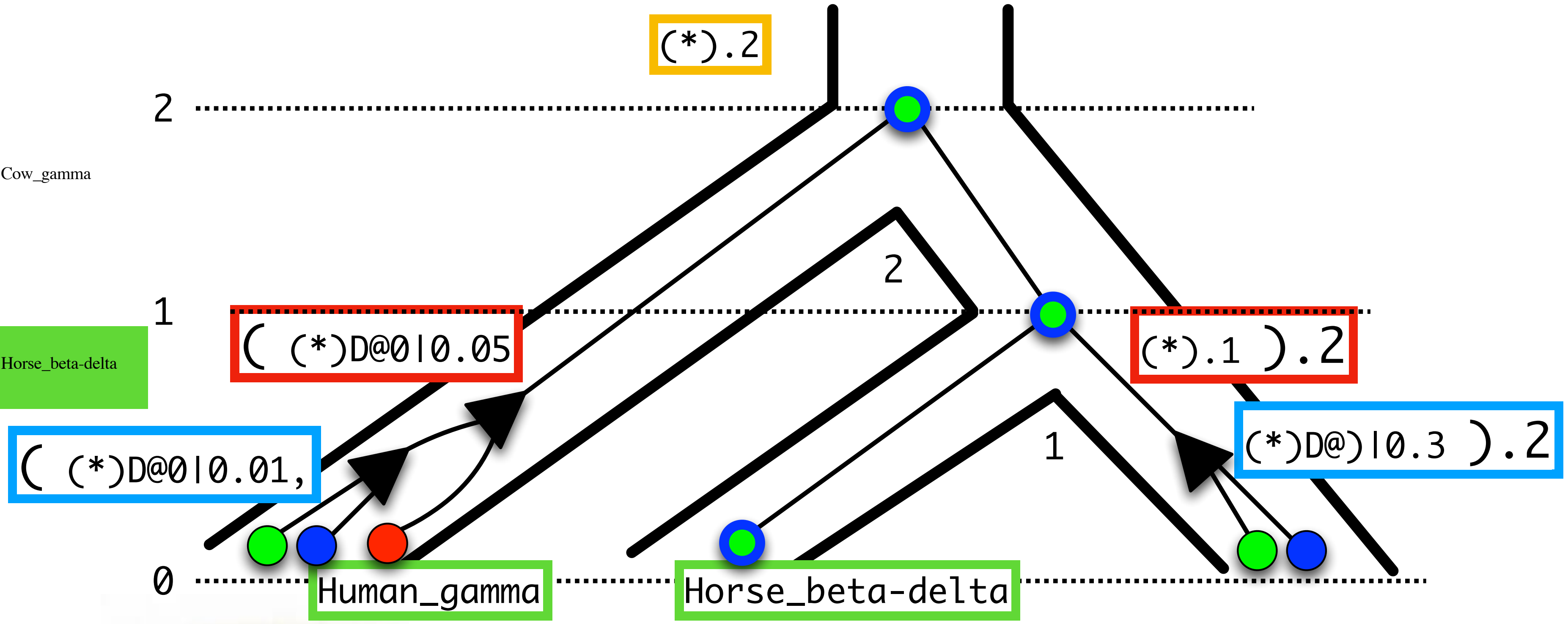
```
((Human_gamma:2,(Human_beta:1,Human_delta:1)D@0|0.01|Human:1)D@0|0.05|Human:2,(Horse_beta-delta:3,(Cow_gamma:2,Cow_beta-delta:2)D@0|0.3|Cow:1).1:2).2:0;
```

```
# of      Duplications    Transfers       Losses   Speciations
Total   3        0        0        2

# of      Duplications    Transfers       Losses   copies
S_terminal_branch         Cow     1       0        0        2
S_terminal_branch         Horse   0       0        0        1
S_terminal_branch         Human   2       0        0        3
S_internal_branch         1       0       0        0        1
S_internal_branch         2       0       0        0        1
```

← mean number of events per branch in sampled reconciliations





Human

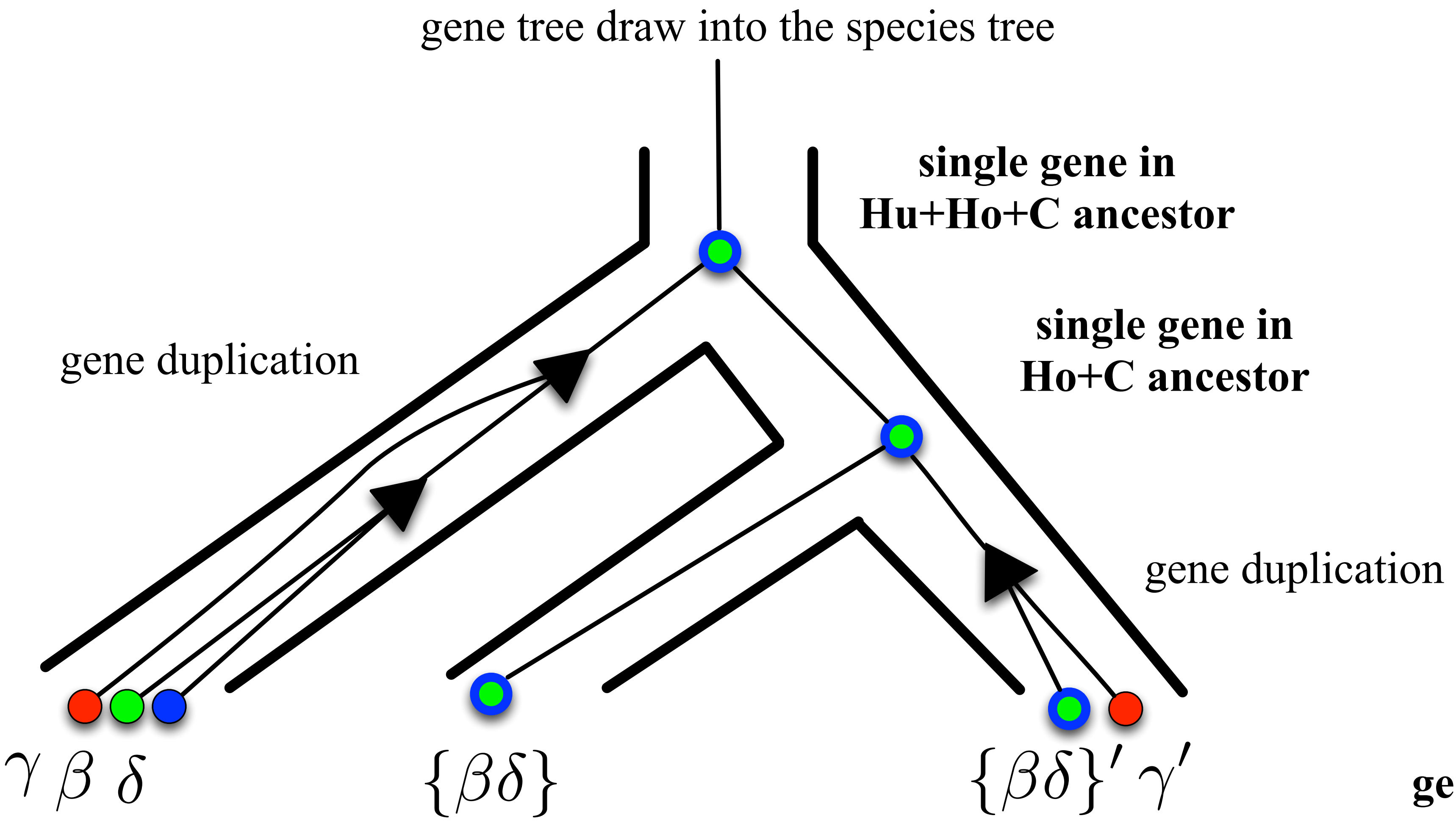
Horse

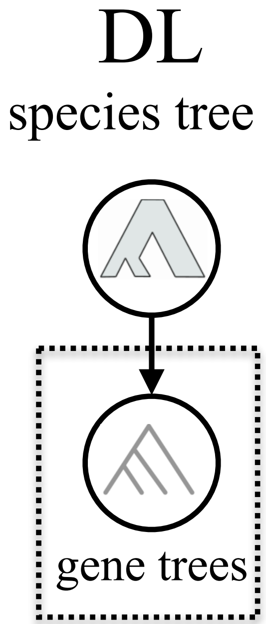
Cow

view the tree using either phylo.io, seaview or FigTree!

The stories gene families can be complicated

The story of each gene family consist of a unique series of evolutionary events that often results in a change of copy number and shifts in function.





genes

Human

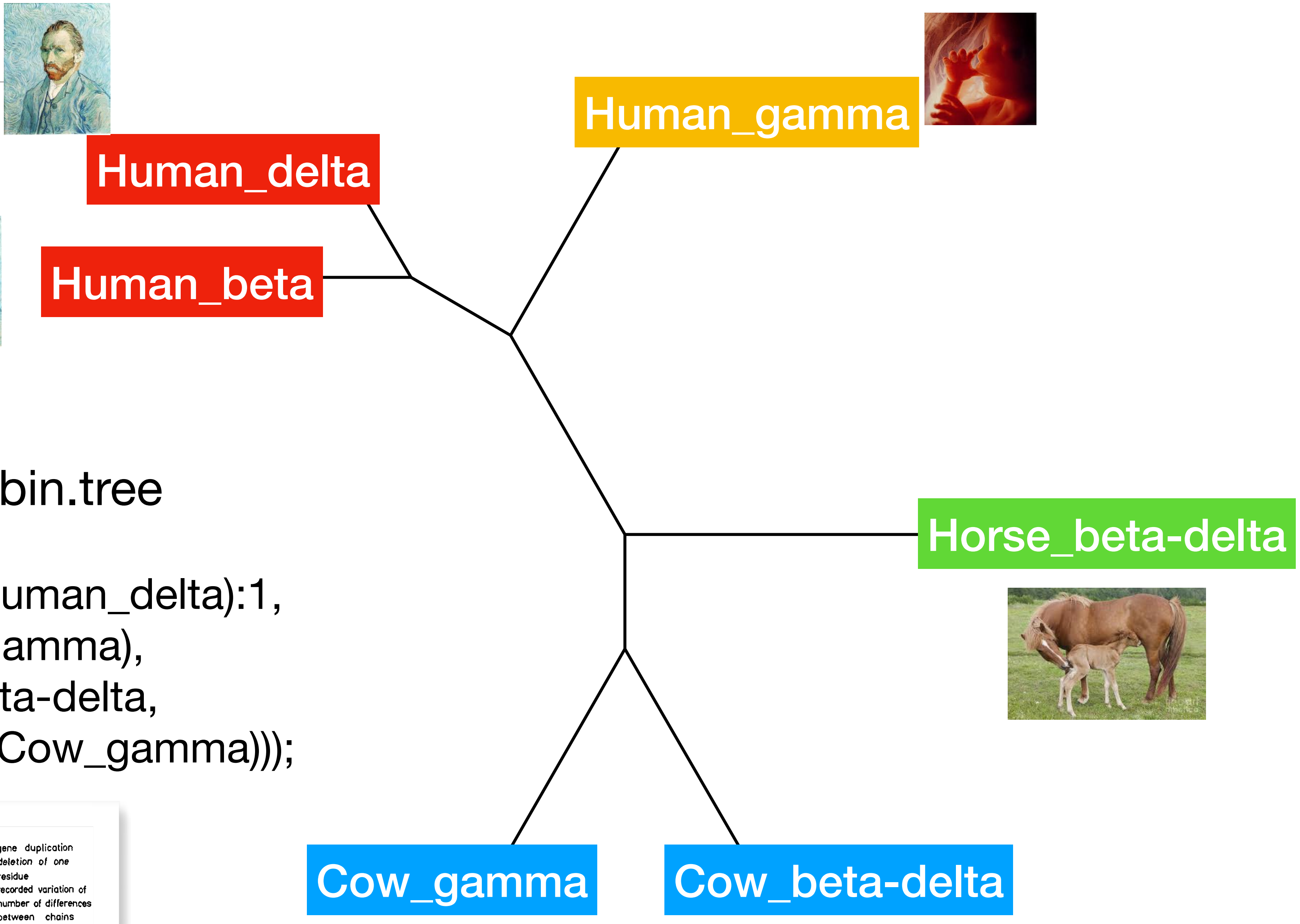
Horse

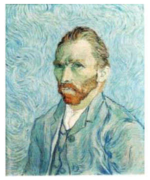
Cow

speices

`Hemoglobin/`

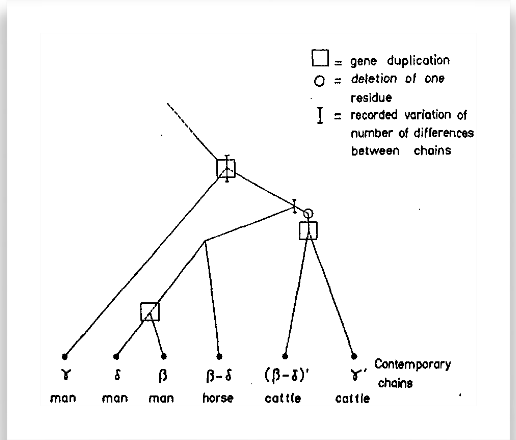
Hemoglobin gene tree





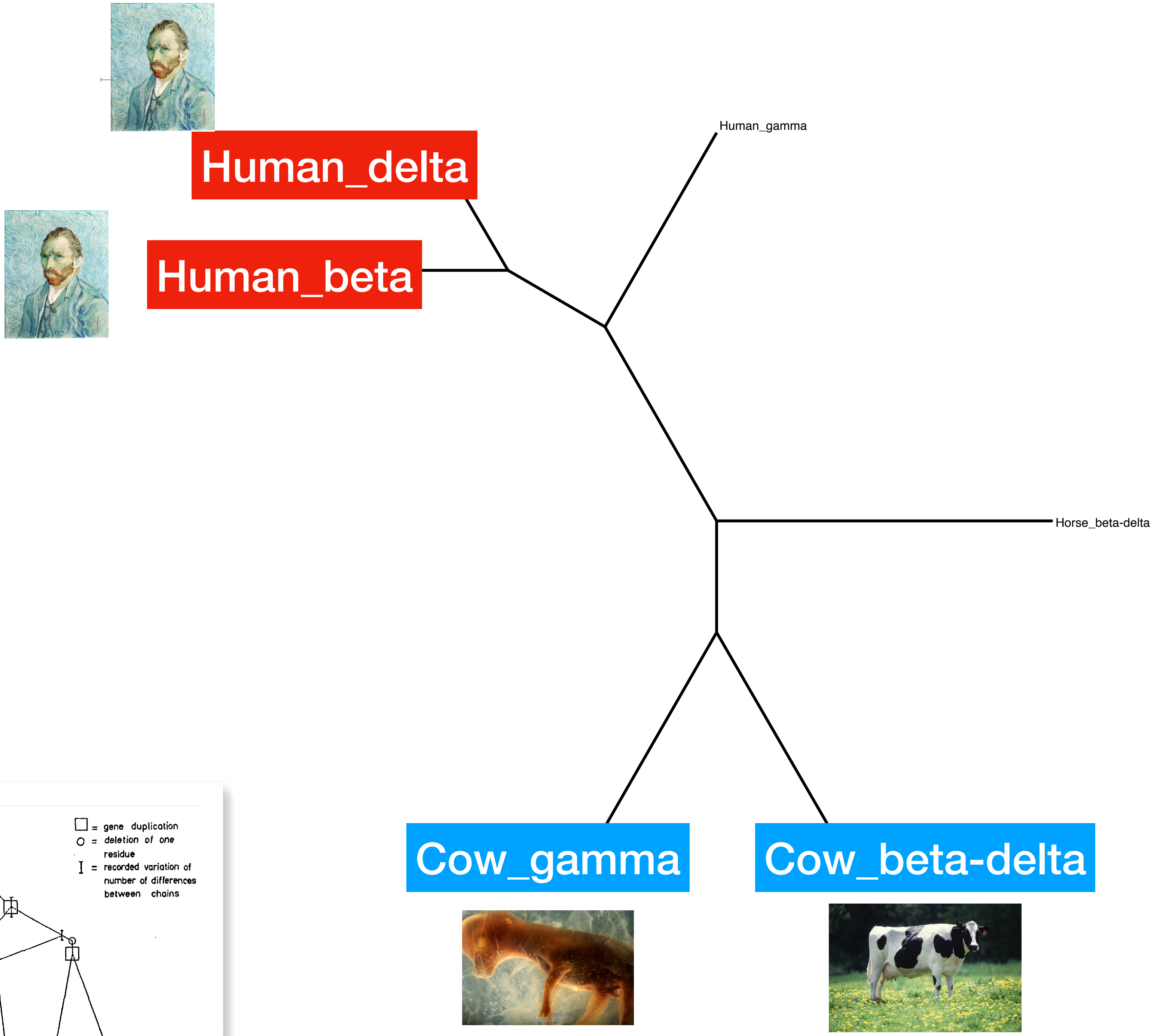
Hemoglobin.tree

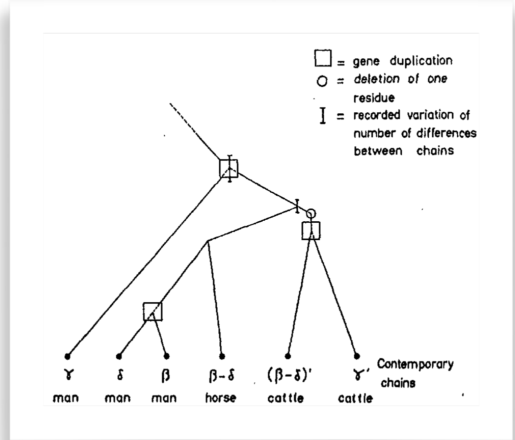
(((Human_beta,Human_delta):1,
Human_gamma),
(Horse_beta-delta,
(Cow_beta-delta,Cow_gamma)));



Zukerkandl & Pauling 1965

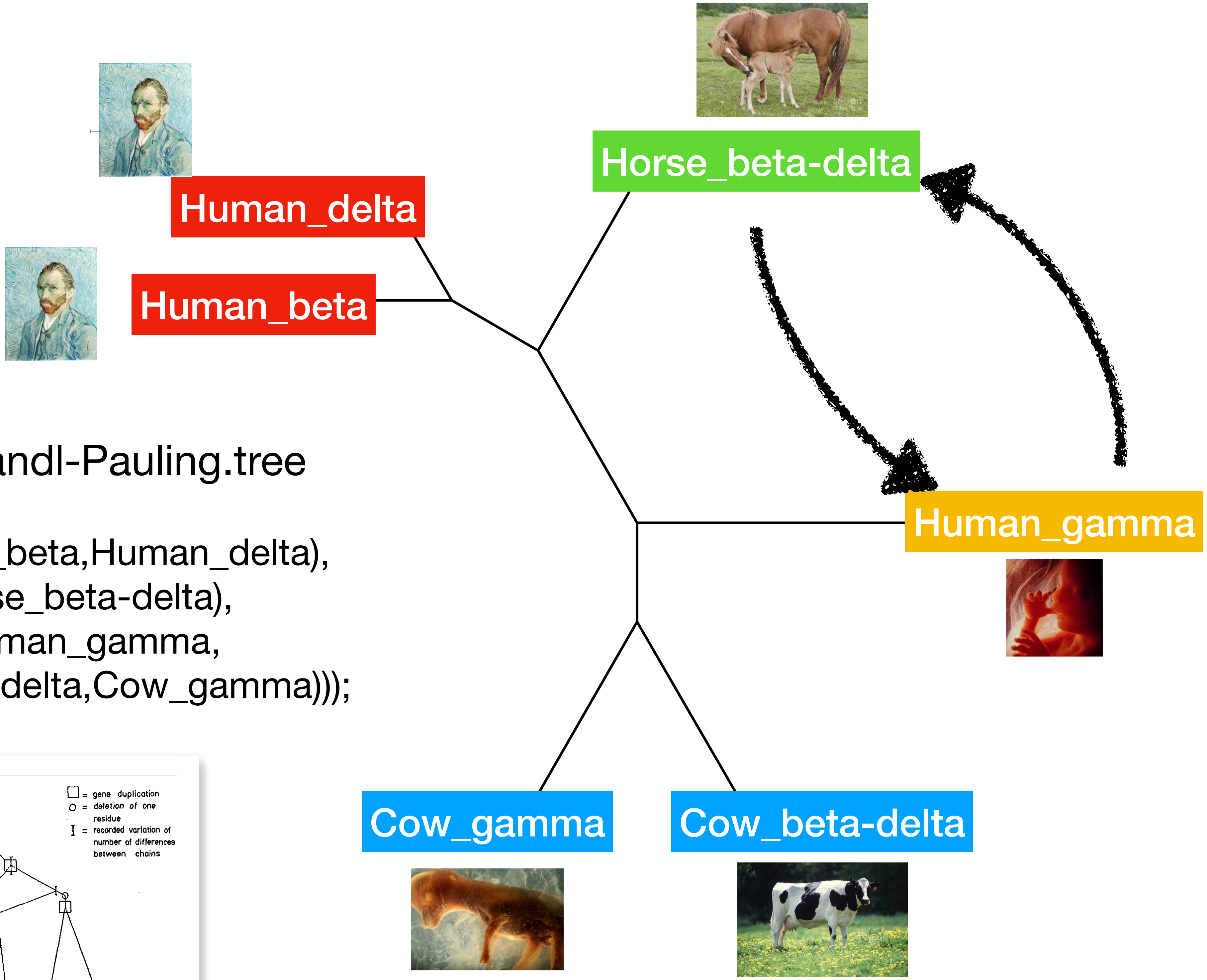
Hemoglobin/





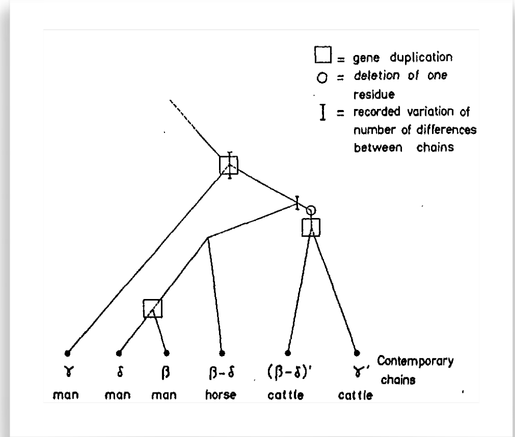
Zukerkandl & Pauling 1965

The first ever gene tree



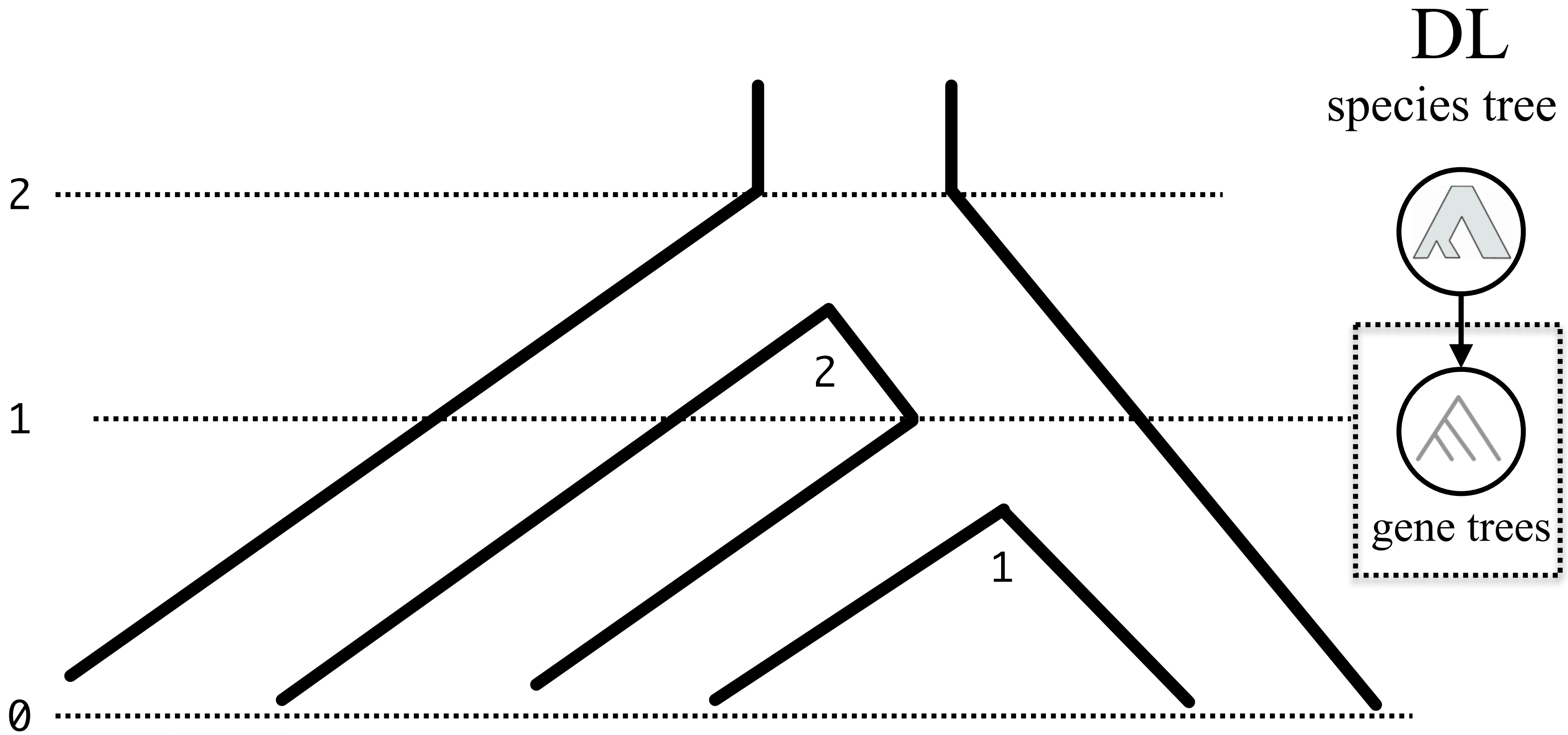
Zukerkandl-Pauling.tree

((((Human_beta,Human_delta),
Horse_beta-delta),
(Human_gamma,
(Cow_beta-delta,Cow_gamma)));



Zukerkandl & Pauling 1965

```
Hemoglobin/
        ALEobserve Zukerkandl-Pauling.tree
        ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale tau=0 sample=10
```



Human

Horse

Cow

`Hemoglobin/`

```
ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale tau=0 sample=10
```

```
#ALEml using ALE v0.5 by Szollosi GJ et al.; ssolo@elte.hu; CC BY-SA 3.0;

S:      (Human:1,(Horse:0.5,Cow:0.5)1:0.5)2;


Input ale from: HuHoCo.tree_Zukerkandl-Pauling.tree.ale
>logl: -10.0385
rate of  Duplications   Transfers       Losses
ML      0.721451        0       0.699903

10 reconciled G-s:

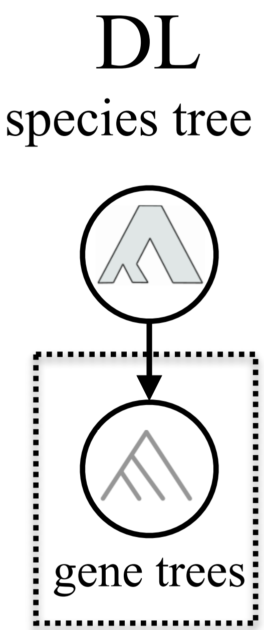
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.2|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@1|0.55|Human:1).2:1)D@2|1.05|2:0;
(Horse_beta-delta.2.1:2,((Human_beta:1,Human_delta:1).2D@1|0.55|Human:1,(Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.1|Cow:2).2:1)D@2|1|2:2)D@2|1.35|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.45|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.2|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.4|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.15|Human:1).2:1)D@2|1.45|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.3|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0|Human:1).2:1)D@2|1|2:0;
(Horse_beta-delta.2.1:2,((Human_beta:1,Human_delta:1).2D@0|0.4|Human:1,(Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.05|Cow:2).2:1)D@2|1|2:2)D@2|1.3|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.1|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.1|Human:1).2:1)D@2|1.35|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.1|2:0;
((Human_gamma:5,(Cow_beta-delta.1:1,Cow_gamma.1:1)D@1|0.5|1:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.2|Human:1).2:1)D@2|1.05|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@1|0.55|Human:1).2:1)D@2|1.05|2:0;
# of     Duplications   Transfers       Losses  Speciations
Total   3.2     0       2.5     4.3

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     0.9     0       1       2
S_terminal_branch       Horse   0       0       1.1     1
S_terminal_branch       Human   1       0       0.2     3
S_internal_branch       1       0.1     0       0.2     2.1
S_internal_branch       2       1.2     0       0       2.2
HuHoCo.tree_Zukerkandl-Pauling.tree.ale.ml_rec (END)
```

species tree

ML log-likelihood (tau=0)

ML rates (tau=0)



10 random reconciled gene trees
sampled according to joint likelihood

mean number of events per branch in sampled reconciliations

sum over reconciled gene trees

Hemoglobin/

```
ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale tau=0 sample=10
```

```
#ALEml using ALE v0.5 by Szollosi GJ et al.; ssolo@elte.hu; CC BY-SA 3.0;

S:      (Human:1,(Horse:0.5,Cow:0.5)1:0.5)2;


Input ale from: Zukerkandl-Pauling.tree.ale
>logl: -10.0385
rate of  Duplications   Transfers       Losses
ML      0.721451        0               0.699903

..
# of     Duplications   Transfers       Losses  Speciations
Total    3.4            0               2.9     4.5

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     0.9     0       1       2
S_terminal_branch       Horse   0       0       1.1     1
S_terminal_branch       Human   1       0       0.4     3
S_internal_branch       1       0.1     0       0.4     2.1
S_internal_branch       2       1.4     0       0       2.4
HuHoCo.tree_Zukerkandl-Pauling.tree.ale.ml_rec (END)
```

```
ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10
```

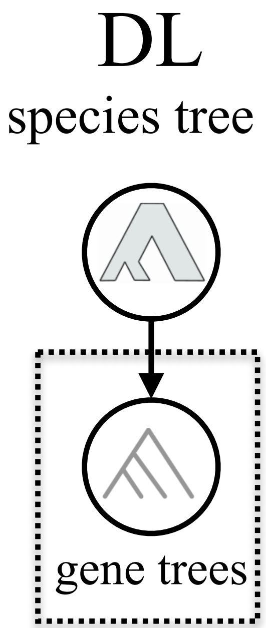
```
#ALEml using ALE v0.5 by Szollosi GJ et al.; ssolo@elte.hu; CC BY-SA 3.0;

S:      (Human:1,(Horse:0.5,Cow:0.5)1:0.5)2;


Input ale from: Hemoglobin.tree.ale
>logl: -4.45543
rate of  Duplications   Transfers       Losses
ML      0.76128         0               1e-10

..
# of     Duplications   Transfers       Losses  Speciations
Total    3              0               0       2

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     1       0       0       2
S_terminal_branch       Horse   0       0       0       1
S_terminal_branch       Human   2       0       0       3
S_internal_branch       1       0       0       0       1
S_internal_branch       2       0       0       0       1
HuHoCo.tree_Hemoglobin.tree.ale.ml_rec (END)
```



Hemoglobin/

ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

```
#ALEml using ALE v0.5 by Szollosi GJ et al.; ssolo@elte.hu; CC BY-SA 3.0;

S:      (Human:1,(Horse:0.5,Cow:0.5)1:0.5)2;


Input ale from: Zukerkandl-Pauling.tree.ale
>logl: -25.1341
rate of  Duplications   Transfers       Losses
ML      0.01    0       0.01

..
# of     Duplications   Transfers       Losses  Speciations
Total    3              0               2       4

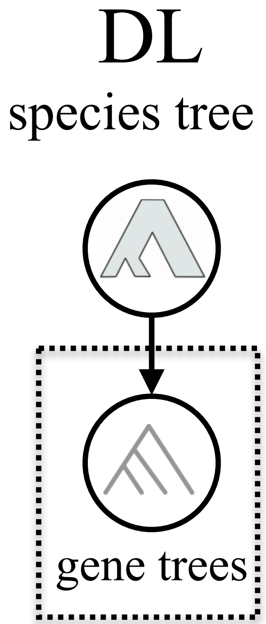
# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     1       0       1       2
S_terminal_branch       Horse   0       0       1       1
S_terminal_branch       Human   1       0       0       3
S_internal_branch       1       0       0       0       2
S_internal_branch       2       1       0       0       2
HuHoCo.tree_Zukerkandl-Pauling.tree.ale.ml_rec (END)
```

ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale tau=0 sample=10

```
Input ale from: Zukerkandl-Pauling.tree.ale
>logl: -10.0385
rate of  Duplications   Transfers       Losses
ML      0.721451        0               0.699903

..
# of     Duplications   Transfers       Losses  Speciations
Total    3.4            0               2.9     4.5

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     0.9     0       1       2
S_terminal_branch       Horse   0       0       1.1     1
S_terminal_branch       Human   1       0       0.4     3
S_internal_branch       1       0.1     0       0.4     2.1
S_internal_branch       2       1.4     0       0       2.4
HuHoCo.tree_Zukerkandl-Pauling.tree.ale.ml_rec (END)
```



ALEml HuHoCo.tree Hemoglobin.tree.ale tau=0 sample=10

```
#ALEml using ALE v0.5 by Szollosi GJ et al.; ssolo@elte.hu; CC BY-SA 3.0;

S:      (Human:1,(Horse:0.5,Cow:0.5)1:0.5)2;


Input ale from: Hemoglobin.tree.ale
>logl: -4.45543
rate of  Duplications   Transfers       Losses
ML      0.76128         0               1e-10

..
# of     Duplications   Transfers       Losses  Speciations
Total    3              0               0       2

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     1       0       0       2
S_terminal_branch       Horse   0       0       0       1
S_terminal_branch       Human   2       0       0       3
S_internal_branch       1       0       0       0       1
S_internal_branch       2       0       0       0       1
HuHoCo.tree_Hemoglobin.tree.ale.ml_rec (END)
```

Hemoglobin/

ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

```
#ALEml using ALE v0.5 by Szollosi GJ et al.; ssolo@elte.hu; CC BY-SA 3.0;

S:      (Human:1,(Horse:0.5,Cow:0.5)1:0.5)2;


Input ale from: Zukerkandl-Pauling.tree.ale
>logl: -25.1341
rate of  Duplications   Transfers       Losses
ML      0.01    0       0.01

10 reconciled G-s:

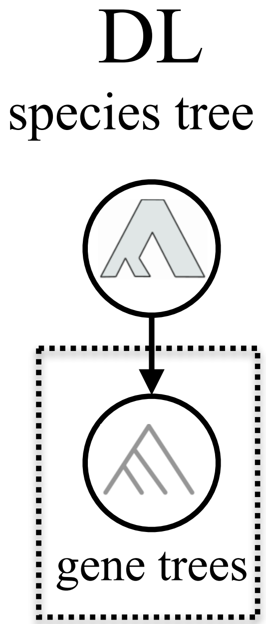
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@1|0.5|Human:1).2:1)D@2|1.45|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.3|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.45|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.45|Human:1).2:1)D@2|1.35|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.05|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@1|0.55|Human:1).2:1)D@2|1.65|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.45|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@1|0.95|Human:1).2:1)D@2|1.55|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.25|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.1|Human:1).2:1)D@2|1.05|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.25|Human:1).2:1)D@2|1.6|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.35|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.35|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@1|0.55|Human:1).2:1)D@2|1.1|2:0;
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.25|Human:1).2:1)D@2|1.7|2:0;
# of     Duplications   Transfers       Losses  Speciations
Total   3       0       2       4

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     1       0       1       2
S_terminal_branch       Horse   0       0       1       1
S_terminal_branch       Human   1       0       0       3
S_internal_branch       1       0       0       0       2
S_internal_branch       2       1       0       0       2
HuHoCo.tree_Zukerkandl-Pauling.tree.ale.ml_rec (END)
```

species tree

log-likelihood

fixed rates



10 random reconciled gene trees
sampled according to joint likelihood

mean number of events per branch in sampled reconciliations

sum over reconciled gene trees

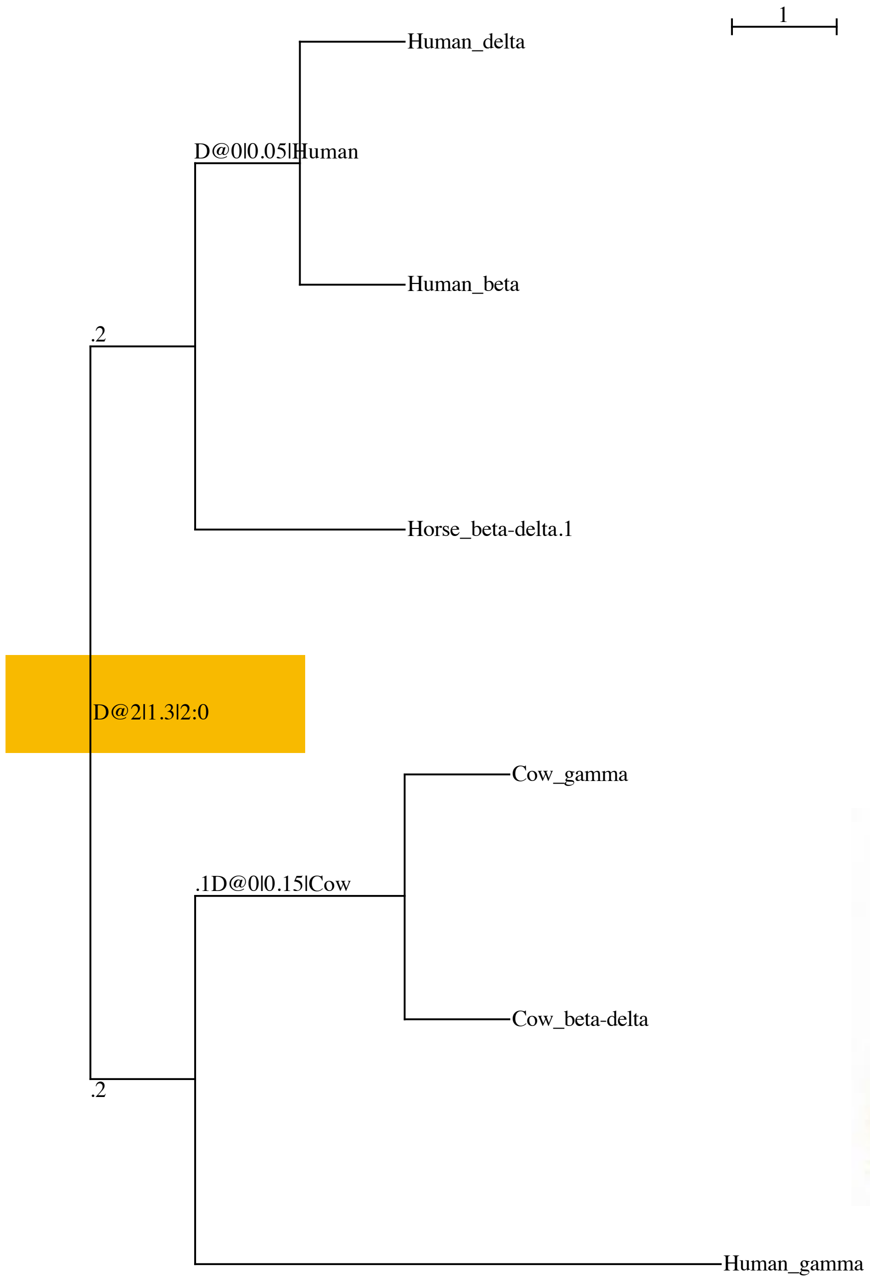
Hemoglobin/

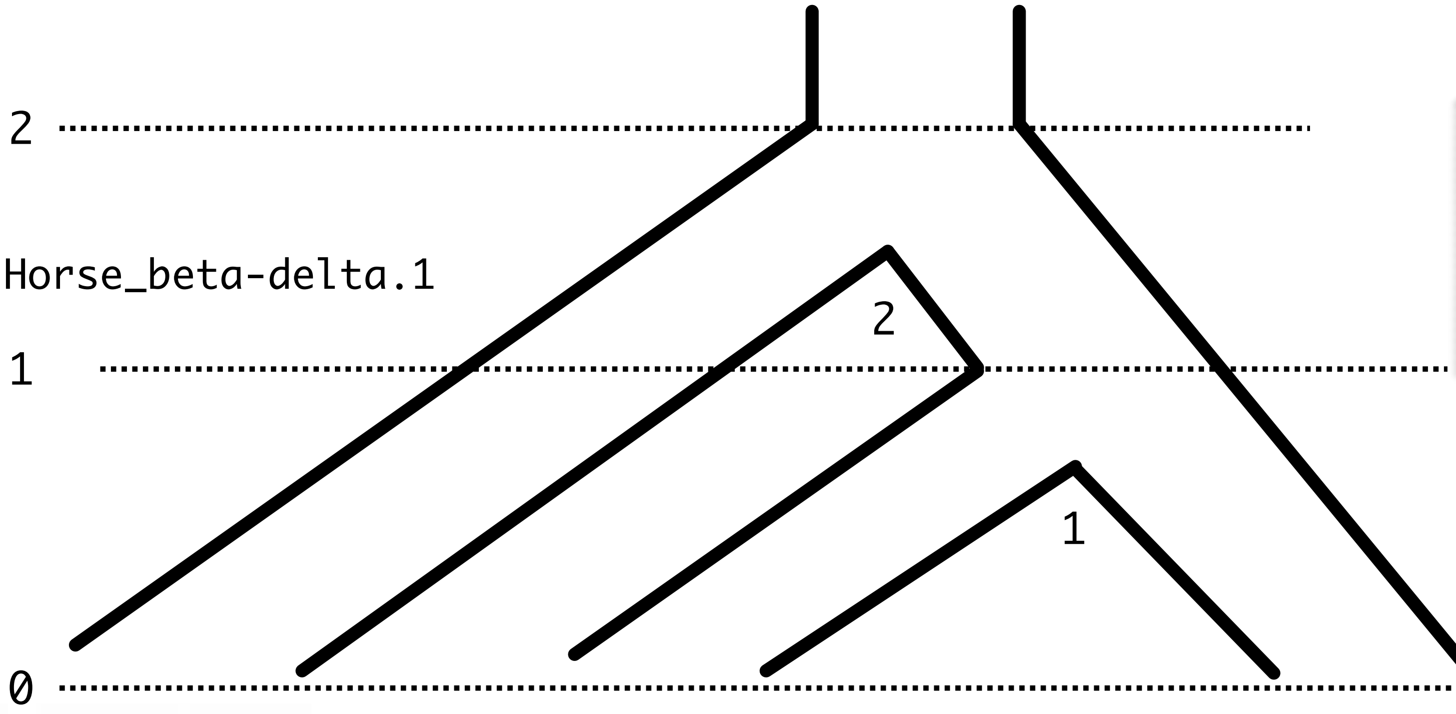
ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

```
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.3|2:0;
```

```
# of     Duplications   Transfers       Losses  Speciations
Total    3              0               2       4

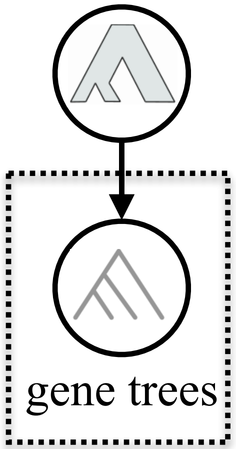
# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     1       0       1       2
S_terminal_branch       Horse   0       0       1       1
S_terminal_branch       Human   1       0       0       3
S_internal_branch       1       0       0       0       2
S_internal_branch       2       1       0       0       2
Zukerkandl-Pauling.tree.ale.ml_rec (END)
```





DL

species tree



Human

Horse

Cow

view the tree using either phylo.io, seaview or FigTree!

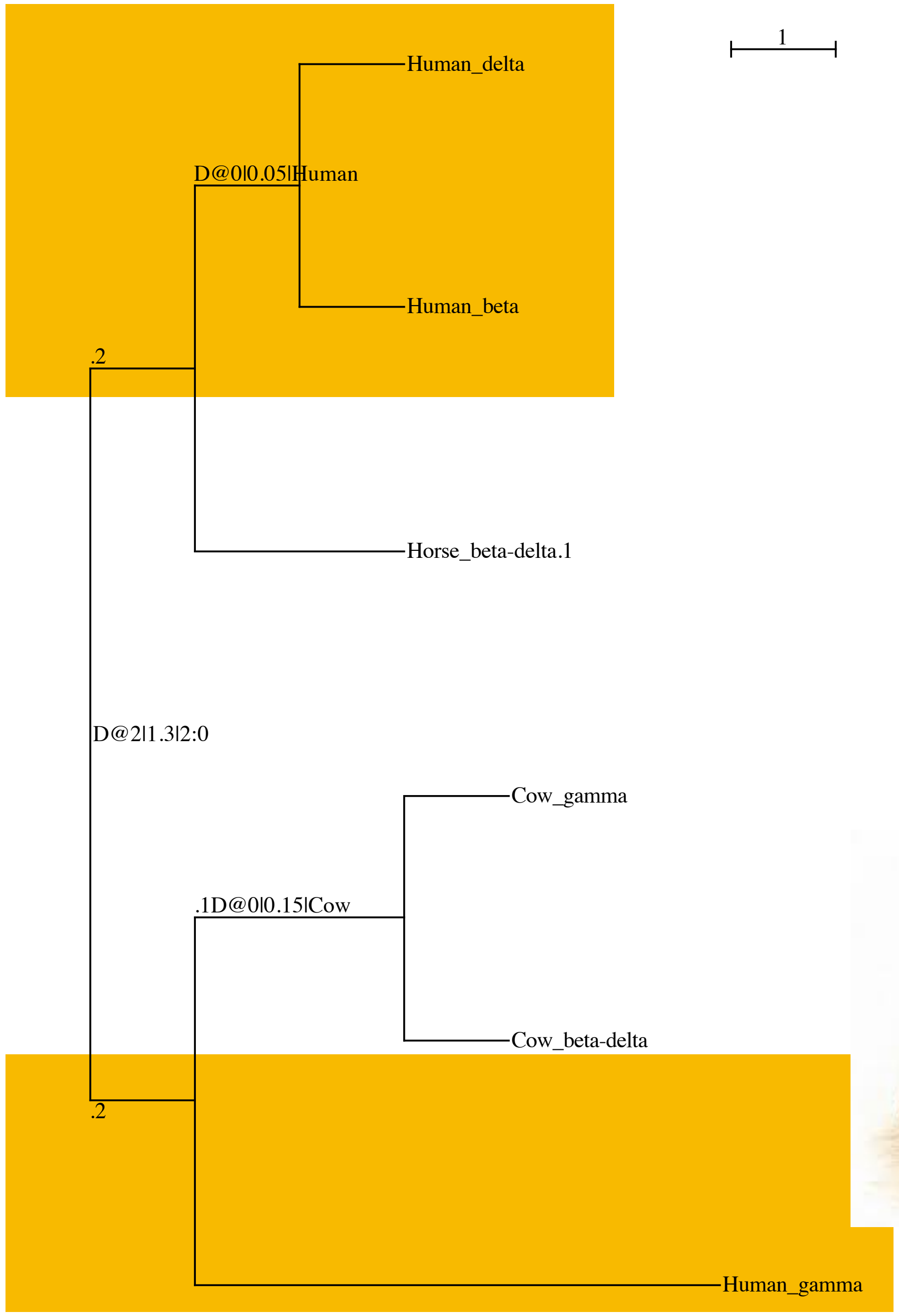
Hemoglobin/

ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

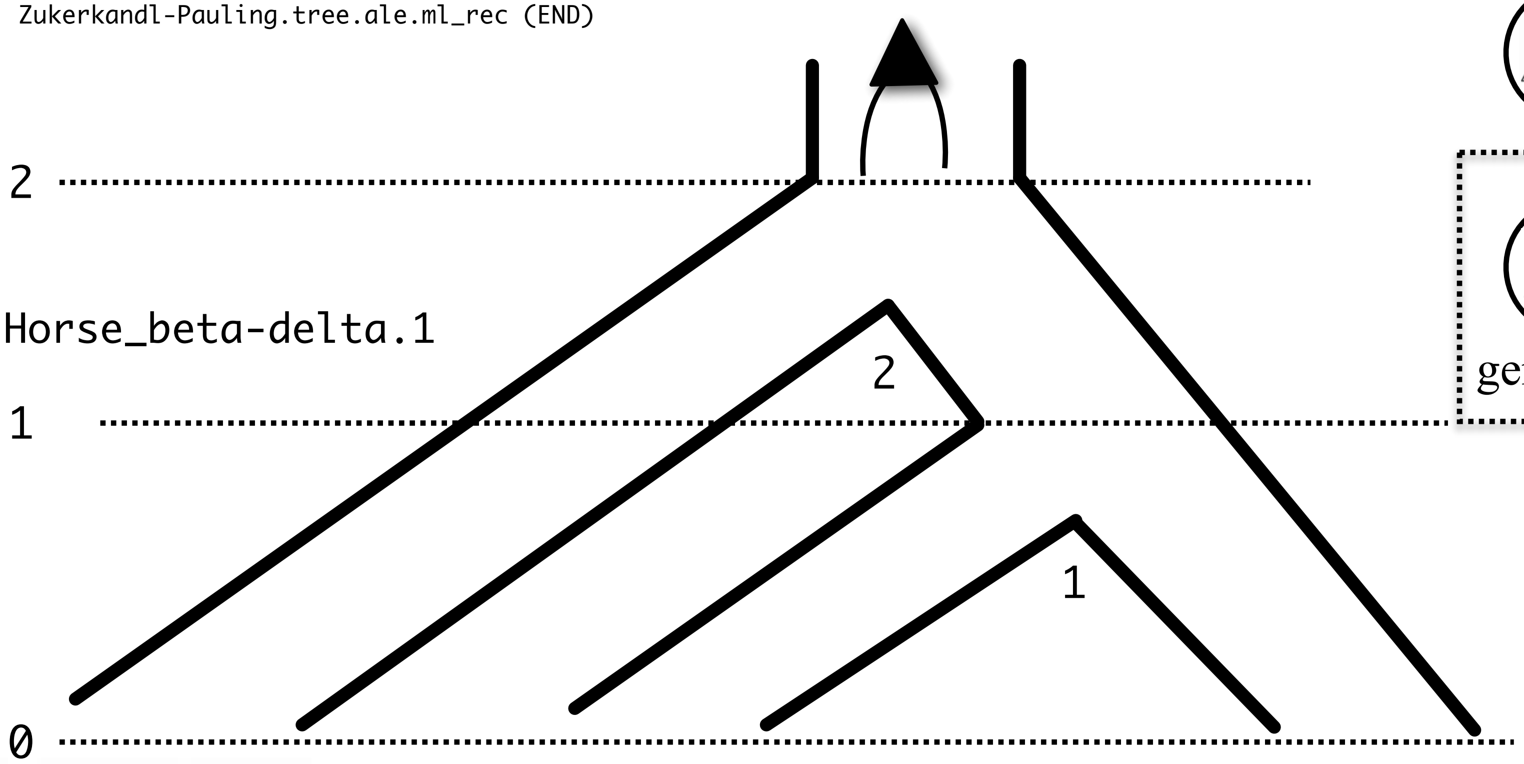
```
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.3|2:0;
```

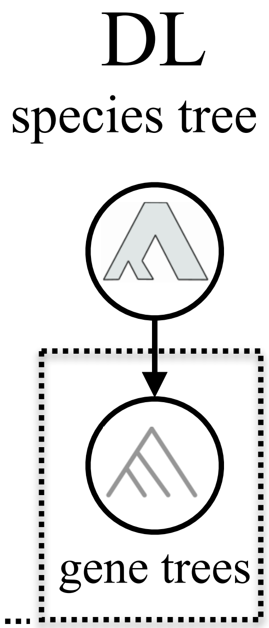
```
# of     Duplications   Transfers       Losses  Speciations
Total    3              0               2       4

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     1       0       1       2
S_terminal_branch       Horse   0       0       1       1
S_terminal_branch       Human   1       0       0       3
S_internal_branch       1       0       0       0       2
S_internal_branch       2       1       0       0       2
Zukerkandl-Pauling.tree.ale.ml_rec (END)
```



view the tree using either phylo.io, seaview or FigTree!





Human

Horse

Cow

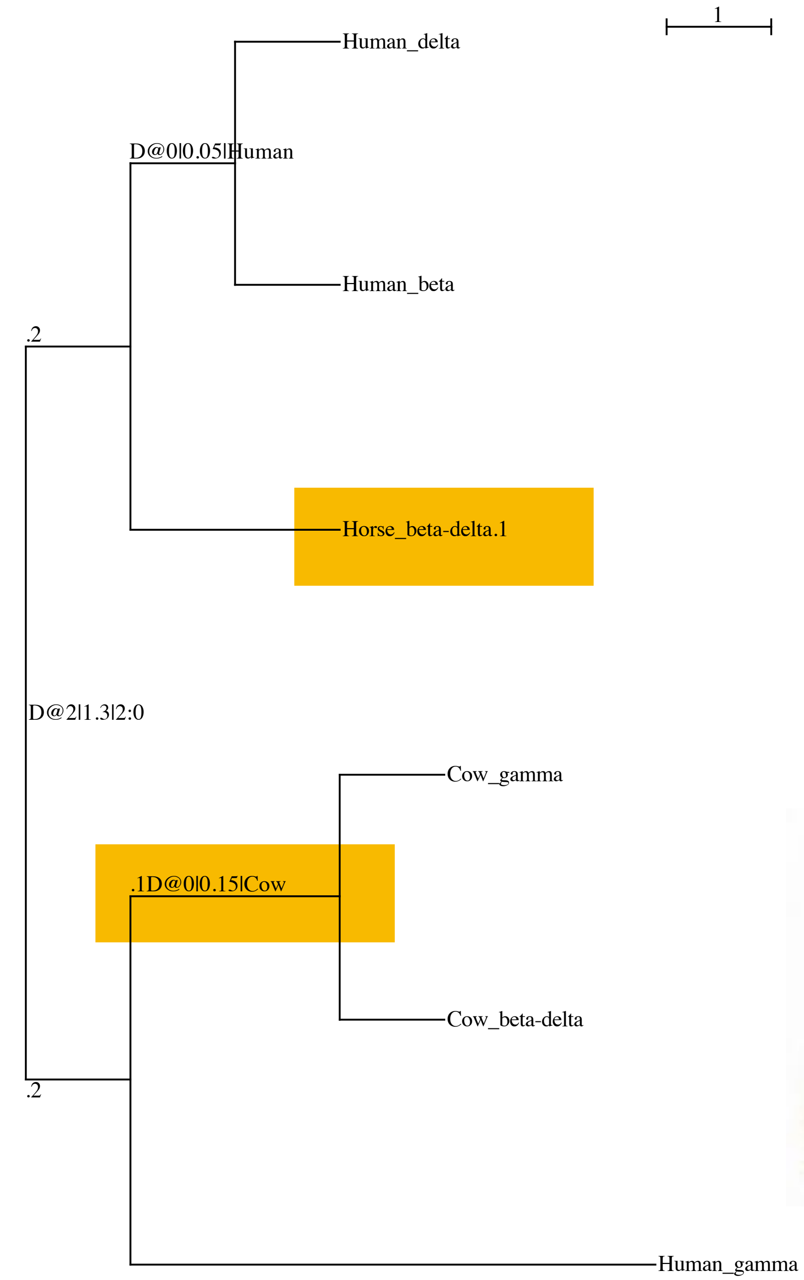
Hemoglobin/

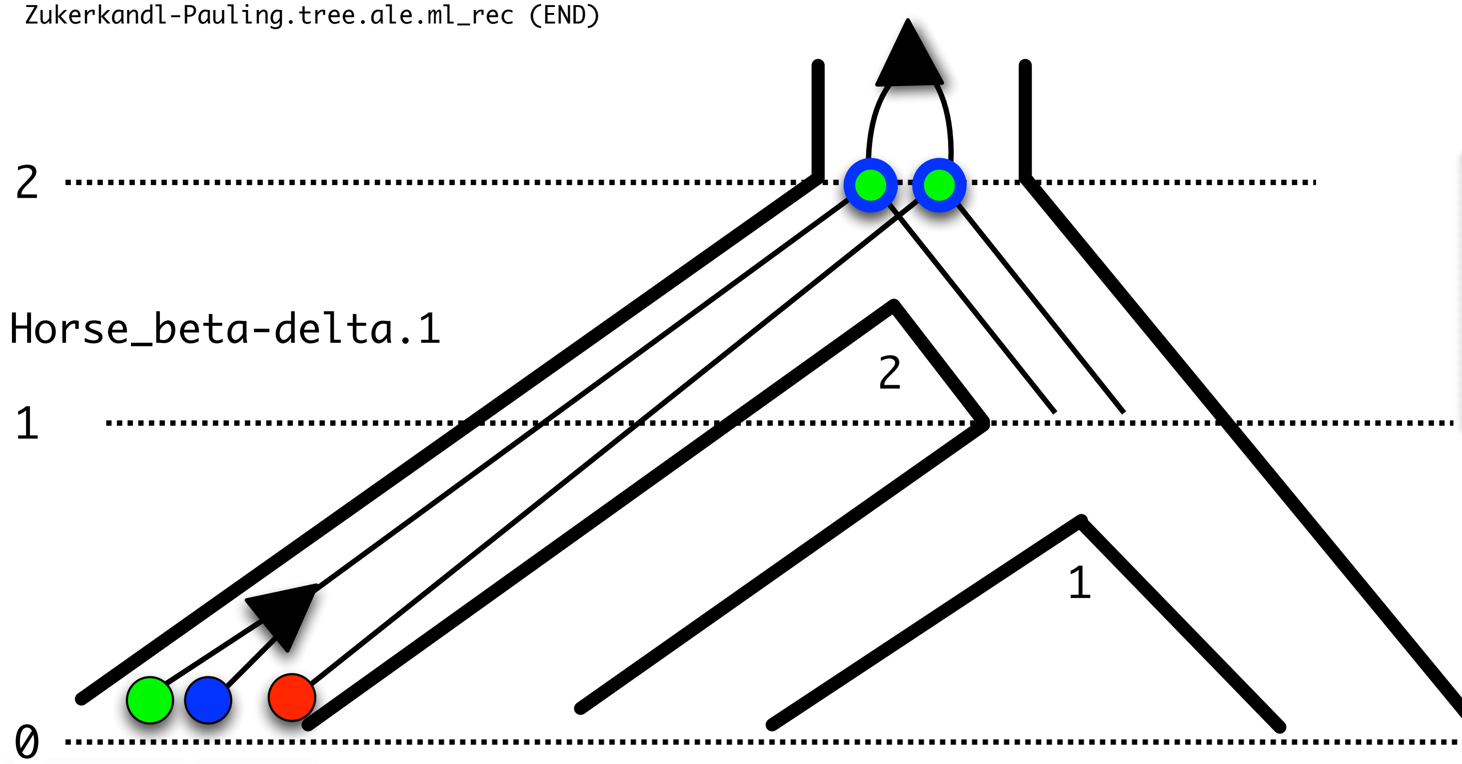
ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

```
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.3|2:0;
```

```
# of      Duplications    Transfers       Losses  Speciations
Total     3               0               2       4

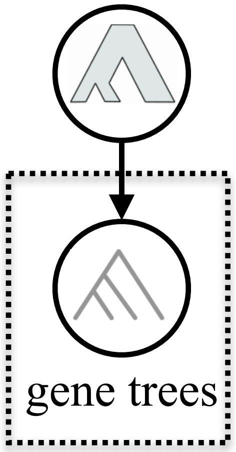
# of      Duplications    Transfers       Losses  copies
S_terminal_branch         Cow     1       0       1       2
S_terminal_branch         Horse   0       0       1       1
S_terminal_branch         Human   1       0       0       3
S_internal_branch         1       0       0       0       2
S_internal_branch         2       1       0       0       2
Zukerkandl-Pauling.tree.ale.ml_rec (END)
```





DL

species tree



Human

Horse

Cow

view the tree using either phylo.io, seaview or FigTree!

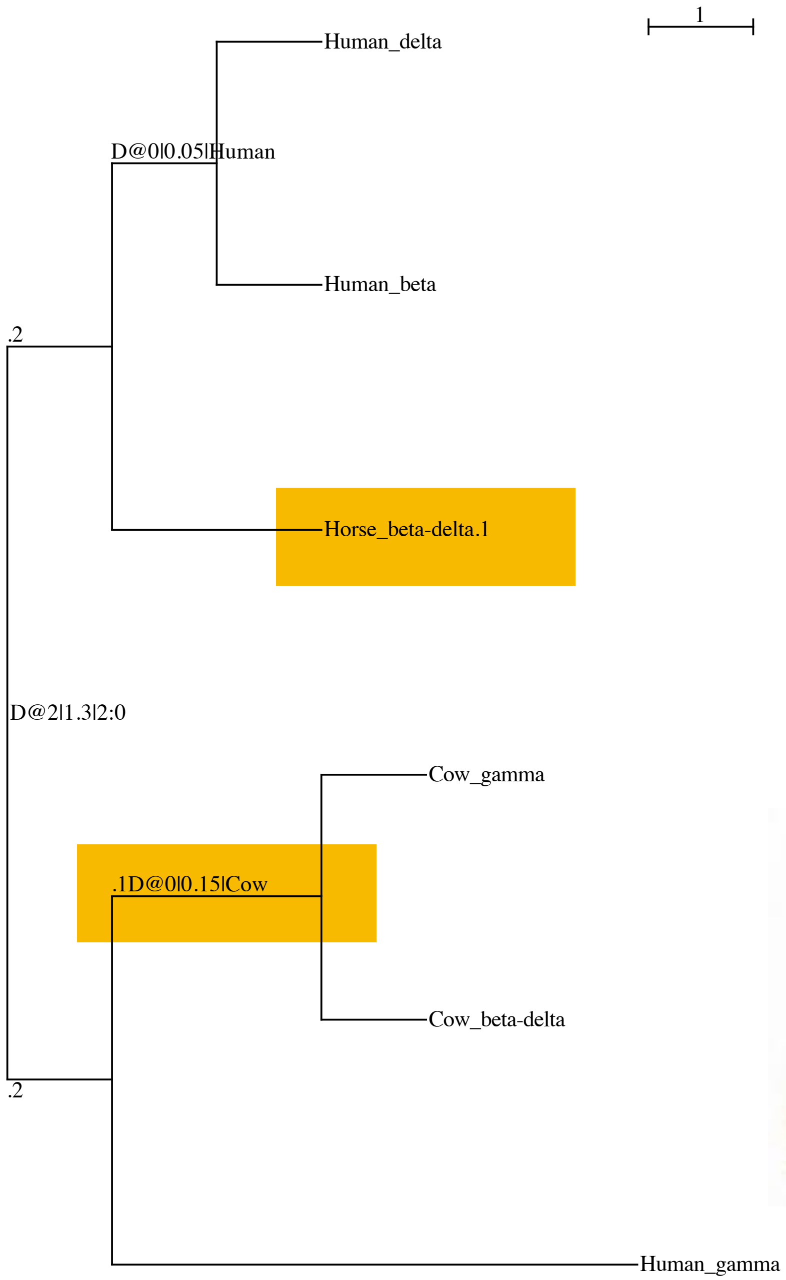
Hemoglobin/

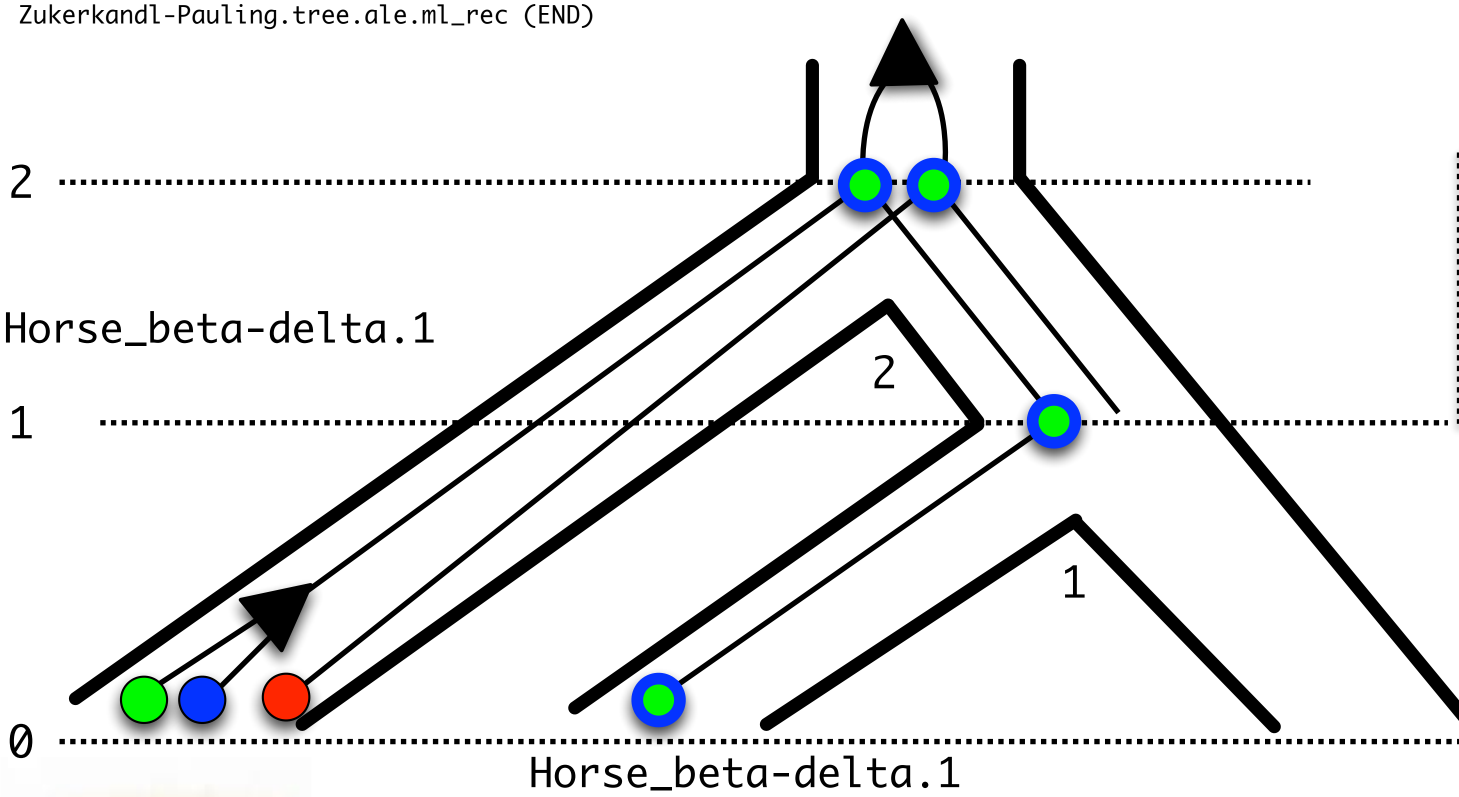
ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

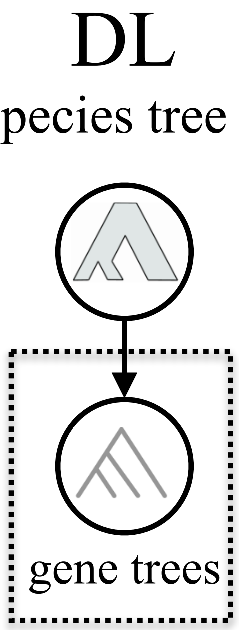
```
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.3|2:0;
```

```
# of    Duplications    Transfers       Losses  Speciations
Total   3               0               2       4

# of    Duplications    Transfers       Losses  copies
S_terminal_branch       Cow     1       0       1       2
S_terminal_branch       Horse   0       0       1       1
S_terminal_branch       Human   1       0       0       3
S_internal_branch       1       0       0       0       2
S_internal_branch       2       1       0       0       2
Zukerkandl-Pauling.tree.ale.ml_rec (END)
```







Human

Horse

Cow

view the tree using either
phylo.io, seaview or FigTree!

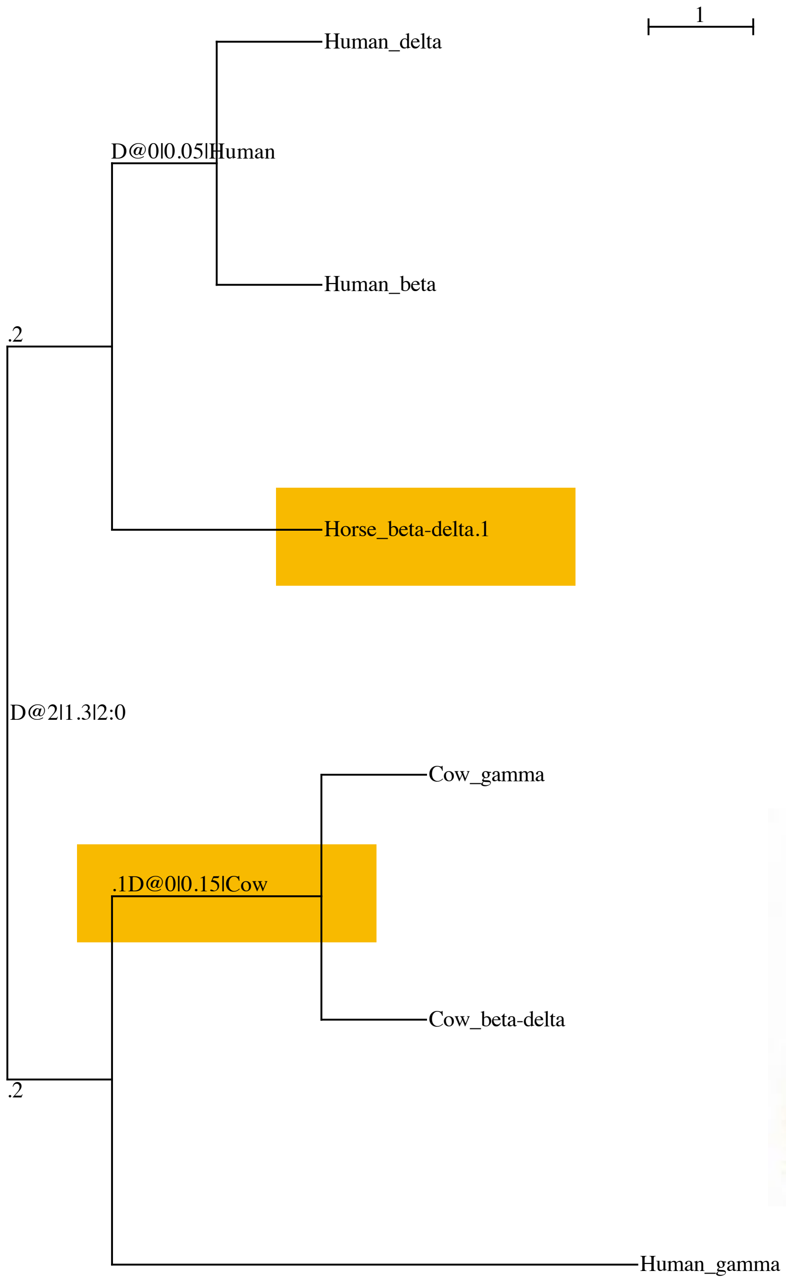
Hemoglobin/

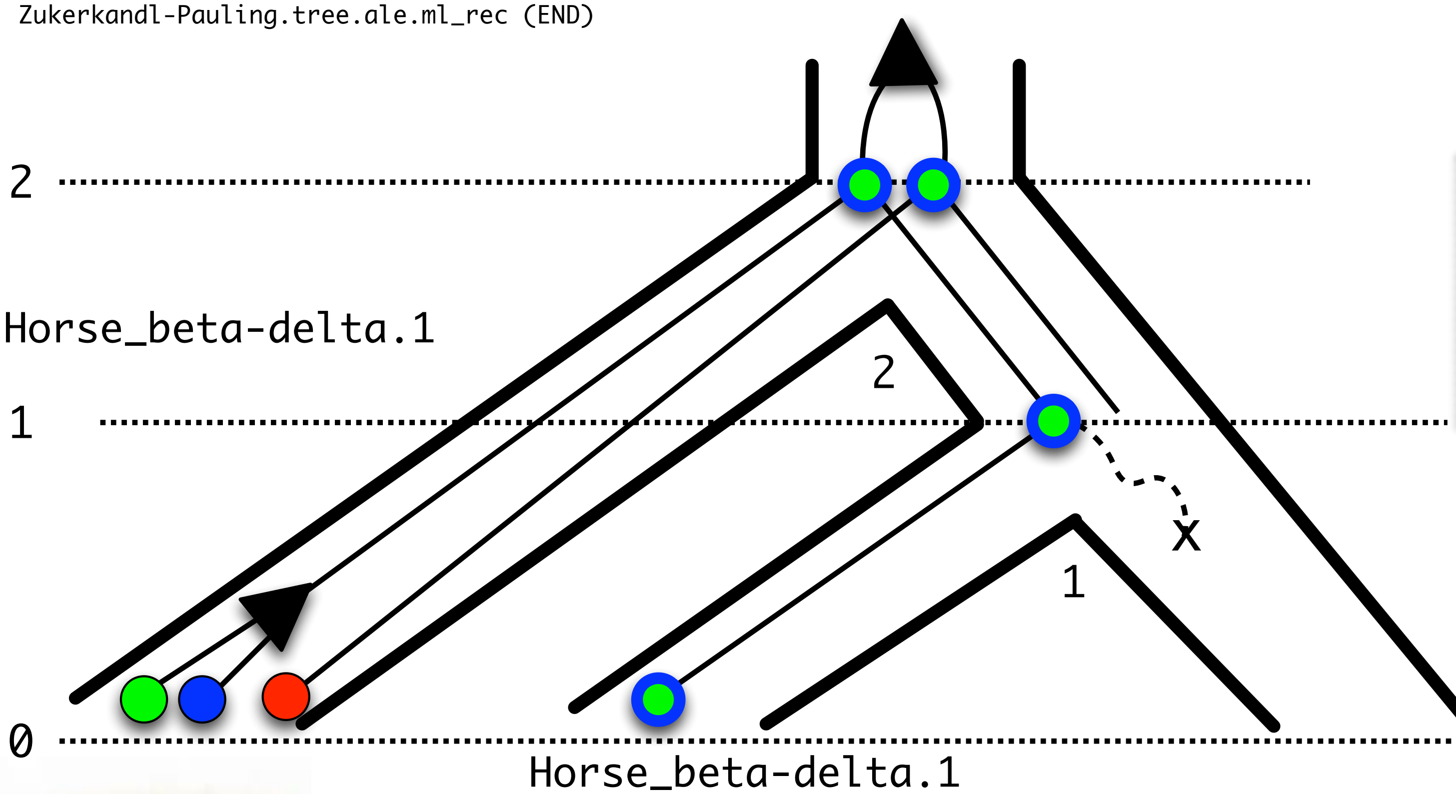
ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

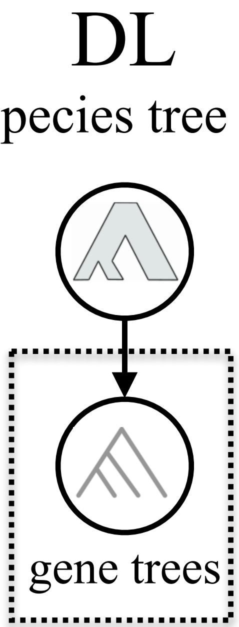
```
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.3|2:0;
```

```
# of      Duplications   Transfers      Losses  Speciations
Total     3              0              2       4

# of      Duplications   Transfers      Losses  copies
S_terminal_branch        Cow     1      0       1       2
S_terminal_branch        Horse   0      0       1       1
S_terminal_branch        Human   1      0       0       3
S_internal_branch        1       0      0       0       2
S_internal_branch        2       1      0       0       2
Zukerkandl-Pauling.tree.ale.ml_rec (END)
```








Human


Horse


Cow

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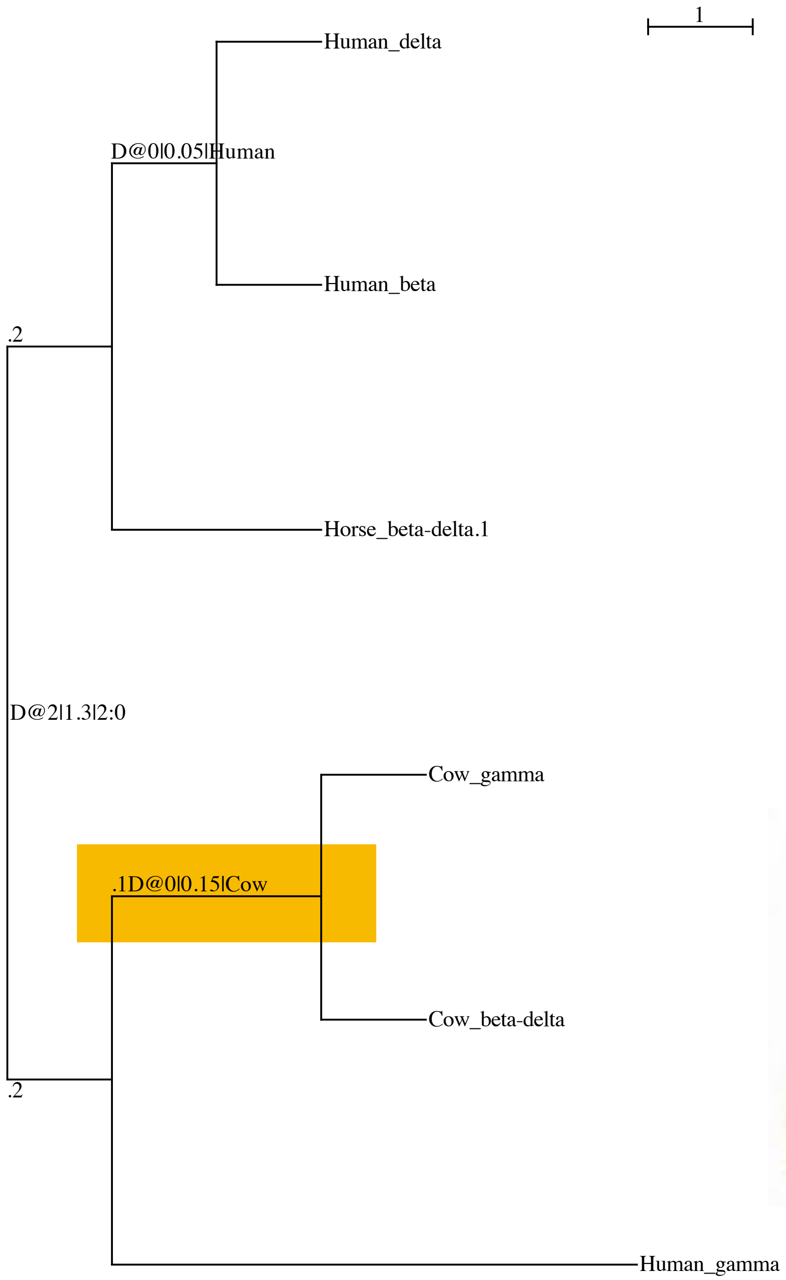
Hemoglobin/

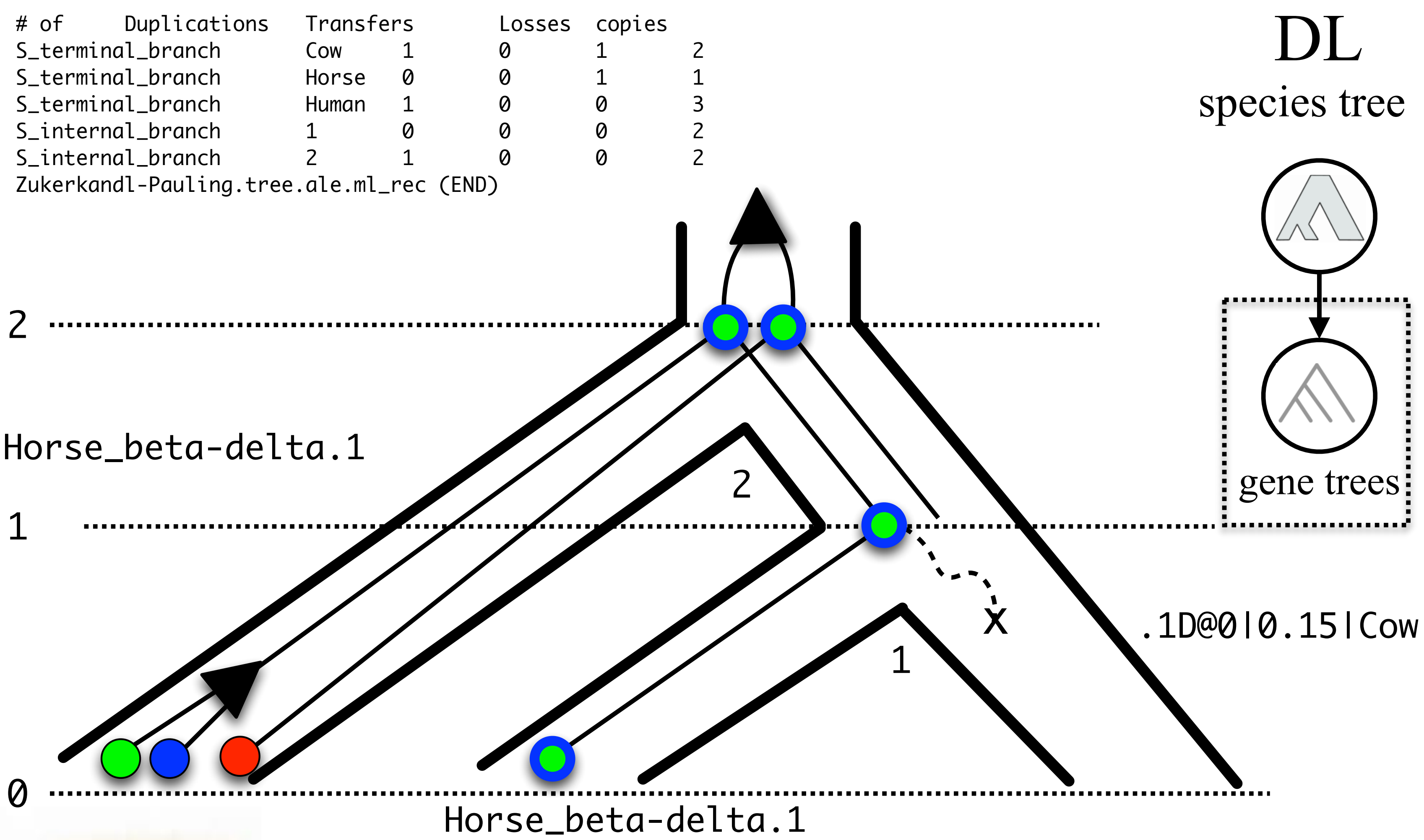
ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

```
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.3|2:0;
```

```
# of	Duplications	Transfers	Losses	Speciations
Total	3		0		2	4

# of	Duplications	Transfers	Losses	copies
S_terminal_branch	Cow	1	0	1	2
S_terminal_branch	Horse	0	0	1	1
S_terminal_branch	Human	1	0	0	3
S_internal_branch	1	0	0	0	2
S_internal_branch	2	1	0	0	2
Zukerkandl-Pauling.tree.ale.ml_rec (END)
```





Human

Horse

Cow

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Hemoglobin/

ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

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```

```
# of      Duplications    Transfers       Losses  Speciations
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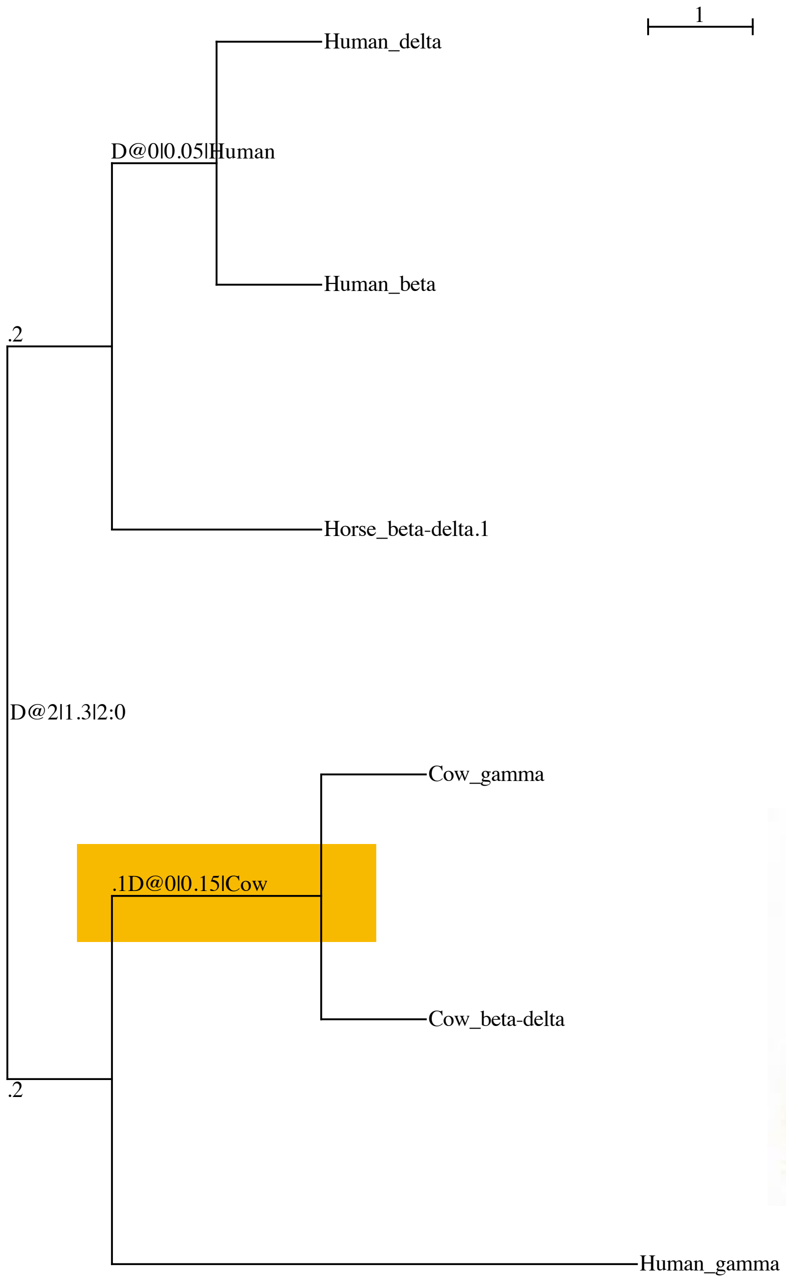
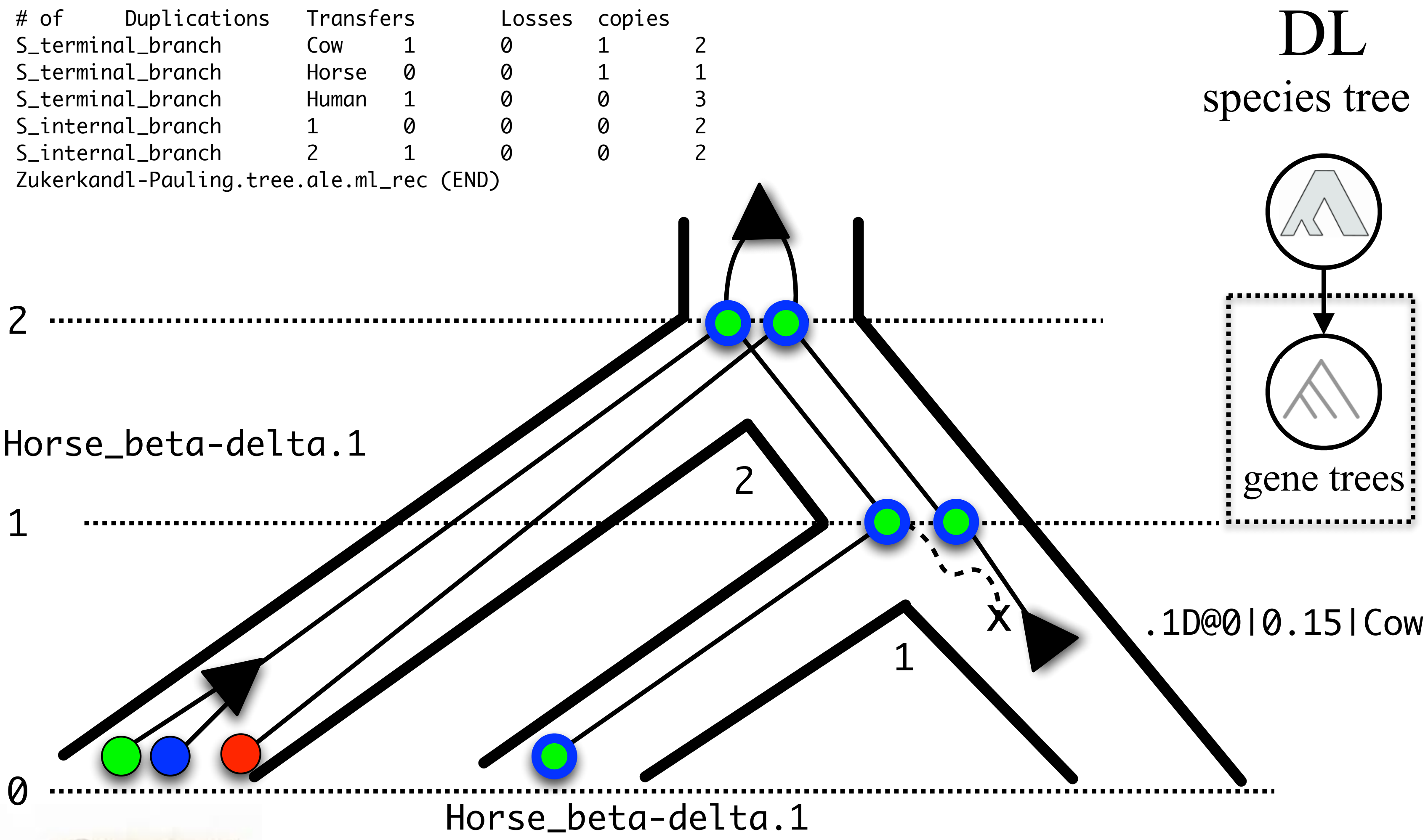
S_internal_branch         1       0       0       0       2
S_internal_branch         2       1       0       0       2
Zukerkandl-Pauling.tree.ale.ml_rec (END)
```





Human

Horse

Cow

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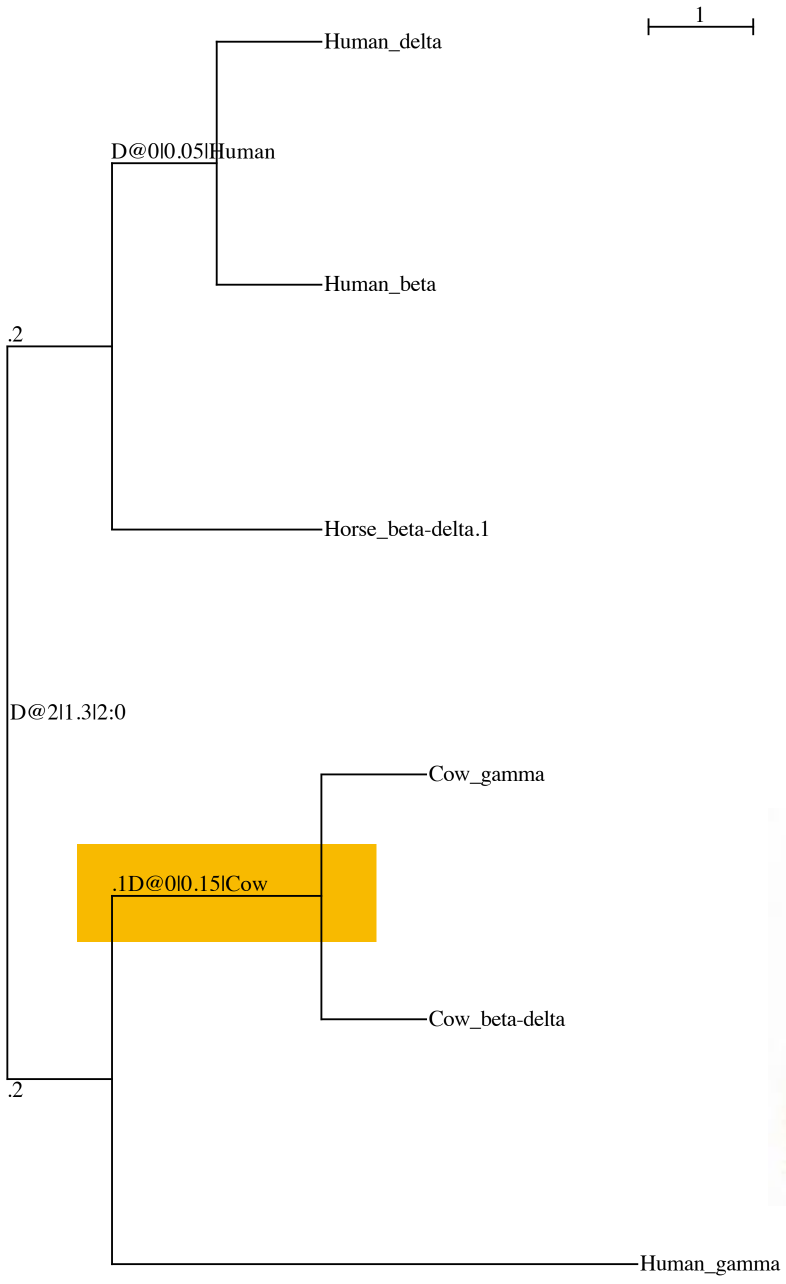
Hemoglobin/

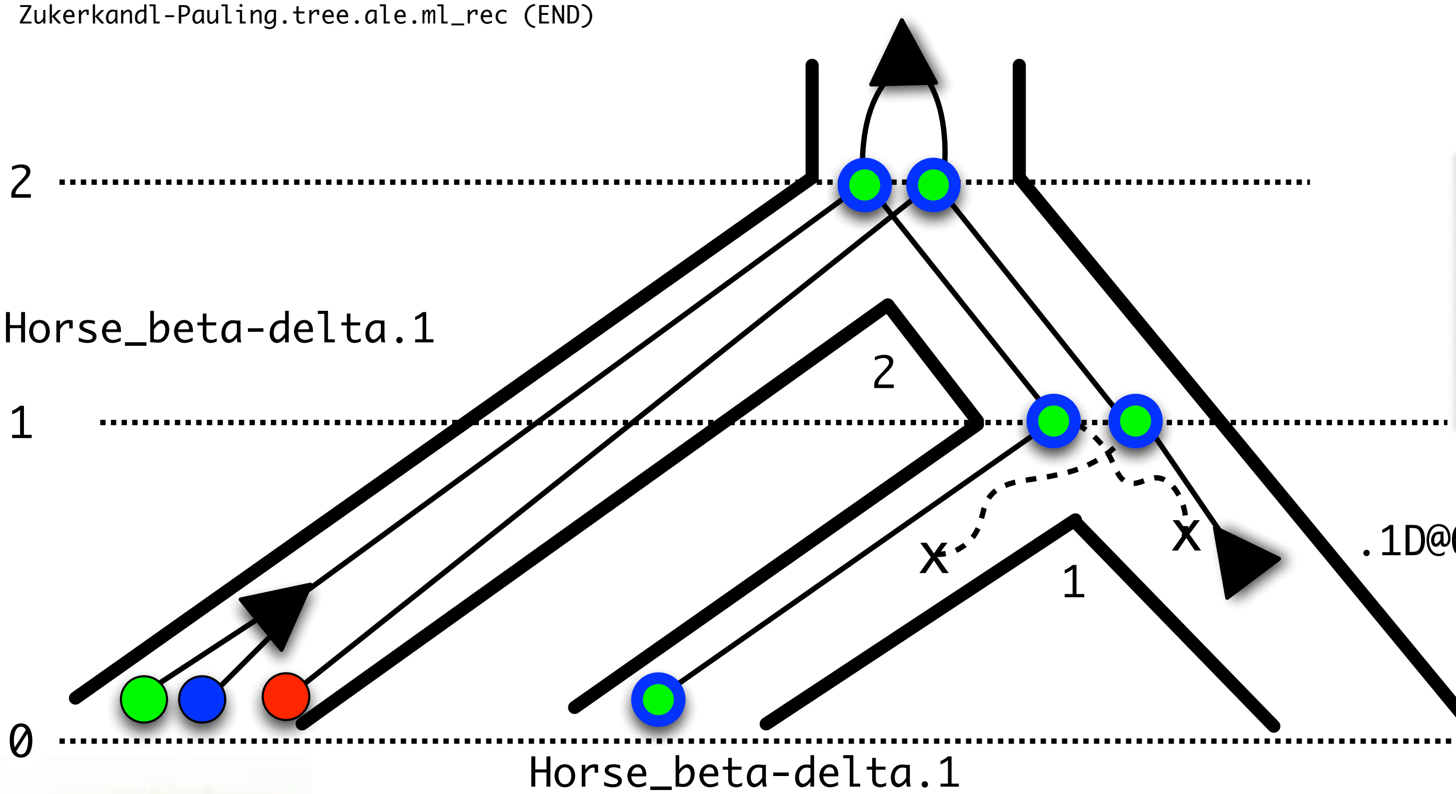
ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

```
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.3|2:0;
```

```
# of      Duplications    Transfers        Losses  Speciations
Total     3               0                2       4

# of      Duplications    Transfers        Losses  copies
S_terminal_branch         Cow      1       0       1       2
S_terminal_branch         Horse    0       0       1       1
S_terminal_branch         Human    1       0       0       3
S_internal_branch         1        0       0       0       2
S_internal_branch         2        1       0       0       2
Zukerkandl-Pauling.tree.ale.ml_rec (END)
```

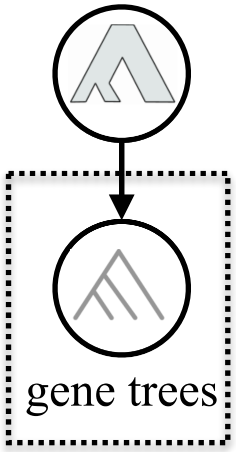




Human

Horse

Cow



view the tree using either phylo.io, seaview or FigTree!

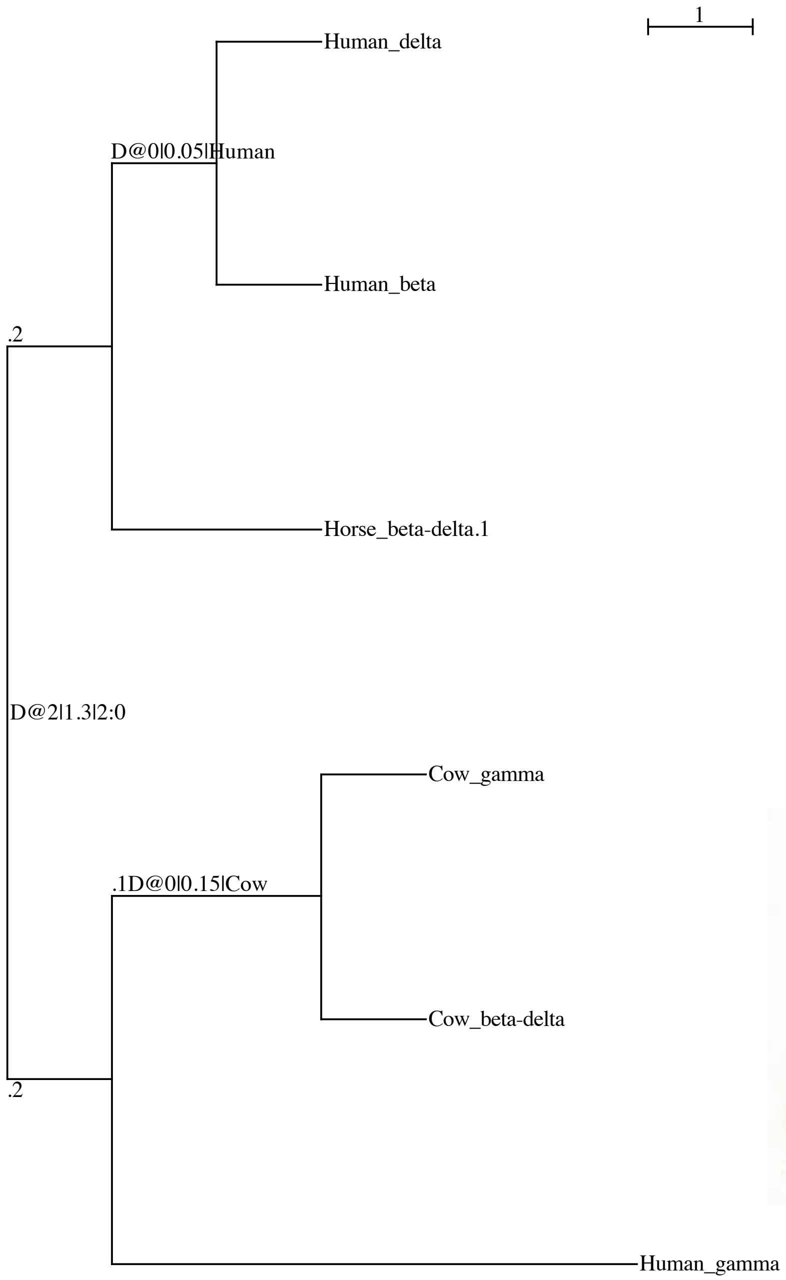
Hemoglobin/

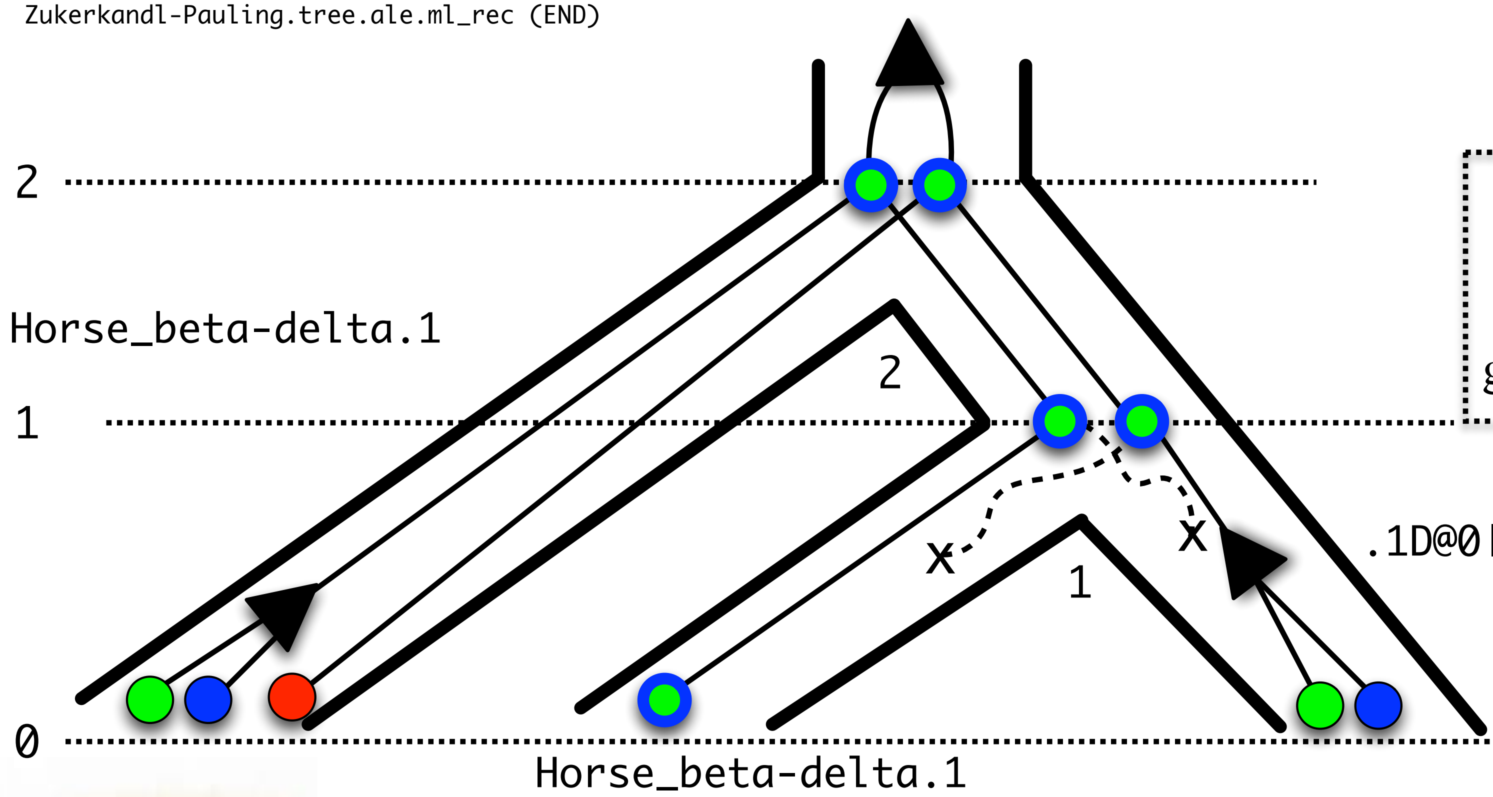
ALEml HuHoCo.tree Zukerkandl-Pauling.tree.ale **delta=0.01 lambda=0.01** tau=0 sample=10

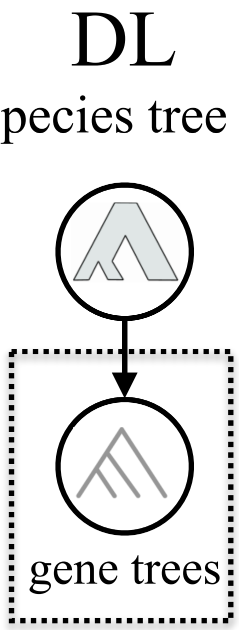
```
((Human_gamma:5,(Cow_beta-delta:1,Cow_gamma:1).1D@0|0.15|Cow:2).2:1,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@0|0.05|Human:1).2:1)D@2|1.3|2:0;
```

```
# of      Duplications   Transfers       Losses  Speciations
Total     3              0               2       4

# of      Duplications   Transfers       Losses  copies
S_terminal_branch        Cow     1       0       1       2
S_terminal_branch        Horse   0       0       1       1
S_terminal_branch        Human   1       0       0       3
S_internal_branch        1       0       0       0       2
S_internal_branch        2       1       0       0       2
Zukerkandl-Pauling.tree.ale.ml_rec (END)
```







Human

Horse

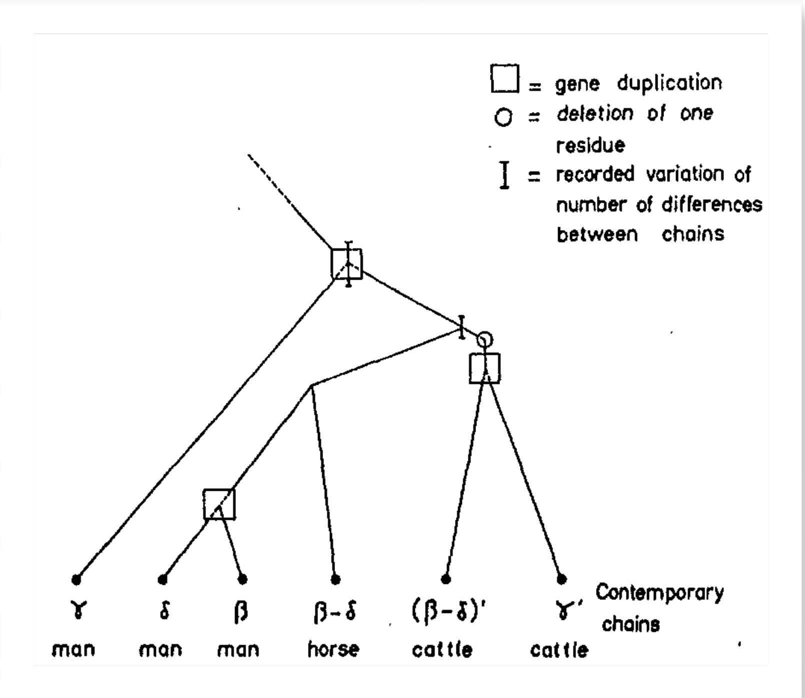
Cow

view the tree using either
phylo.io, seaview or FigTree!

Hemoglobin/

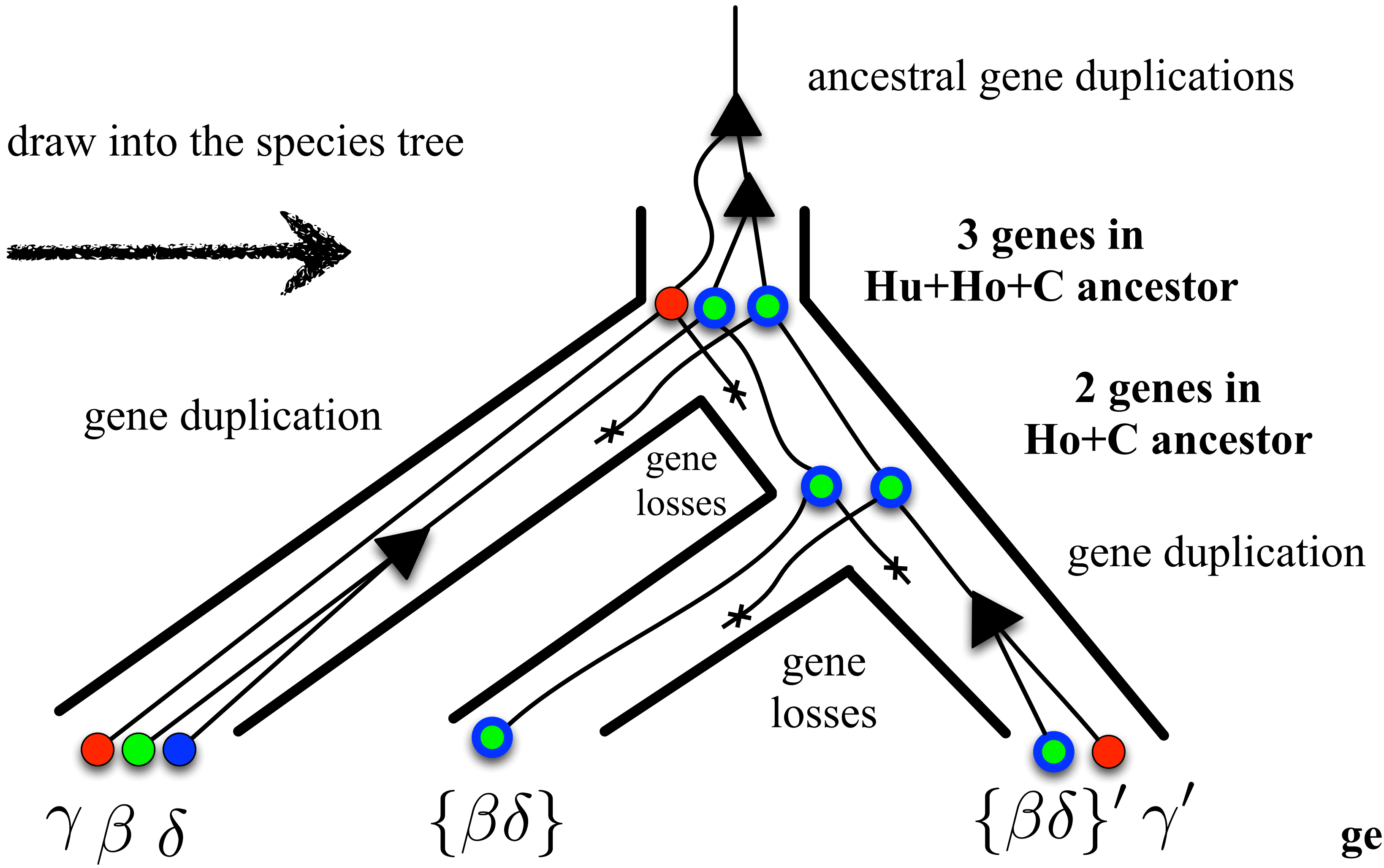
The story of individual gene families is often blurred

Errors in gene trees will result in conflicts with the species tree that imply spurious evolutionary events.



Zukerkandl & Pauling 1965

gene tree draw into the species tree



ancestral gene duplications

3 genes in Hu+Ho+C ancestor

2 genes in Ho+C ancestor

gene duplication

gene losses

gene duplication

gene losses

genes

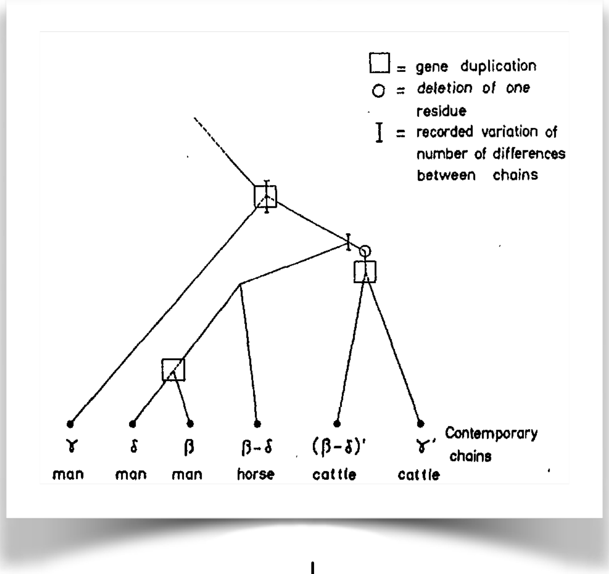
Human

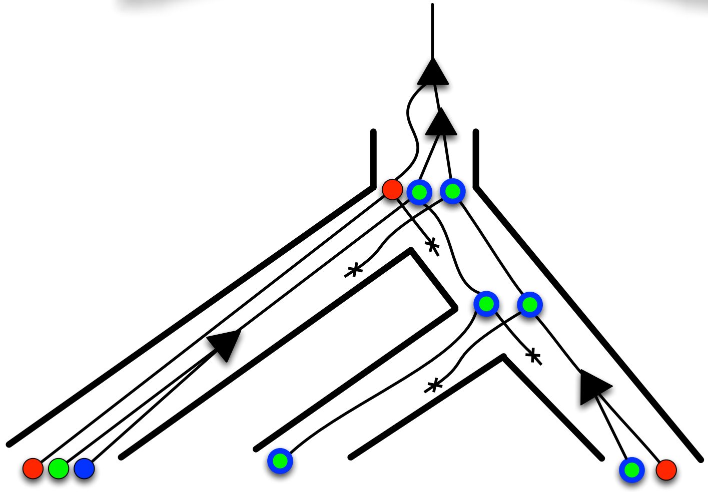
Horse

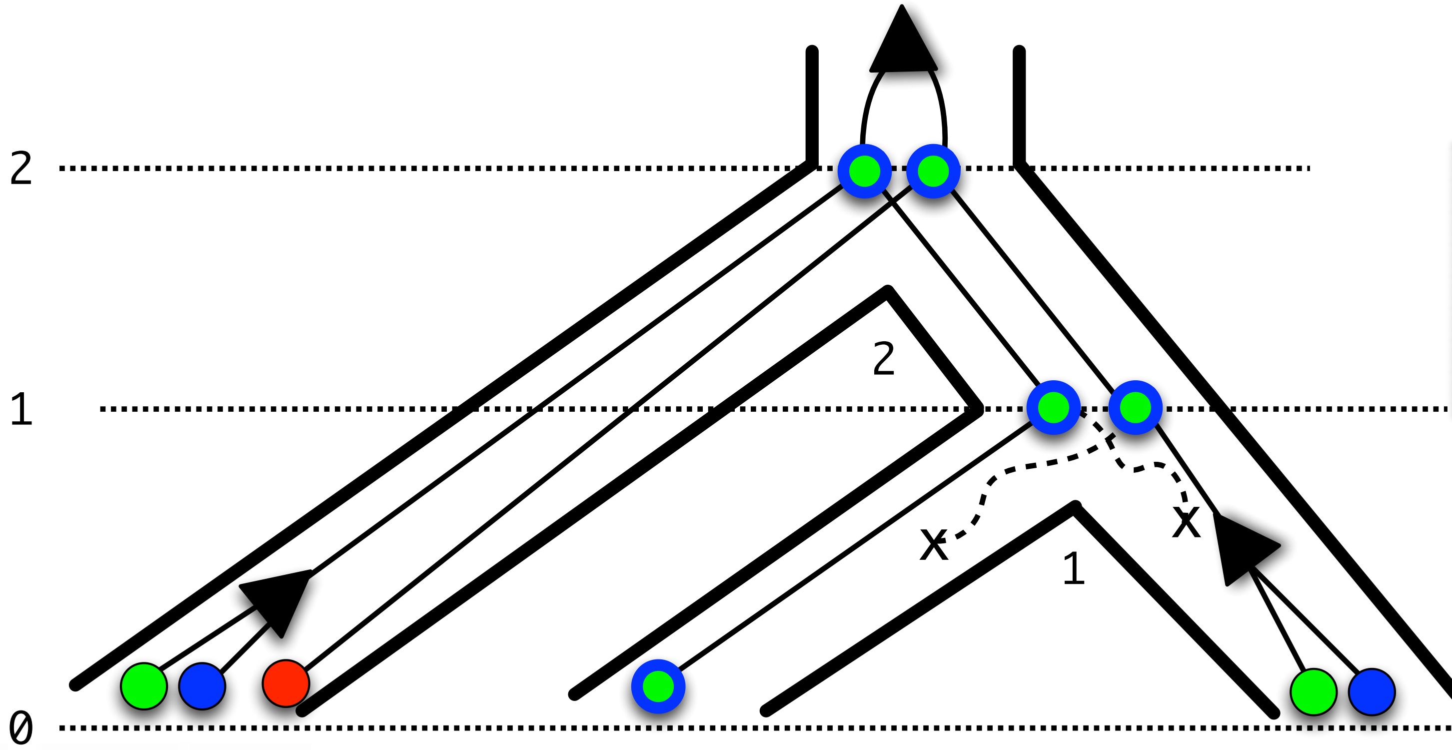
Cow

species

Hemoglobin/

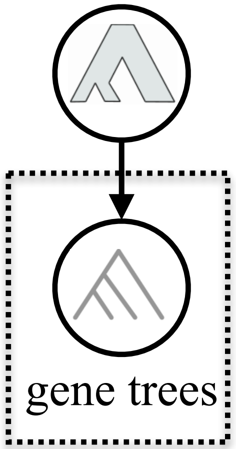






DL

species tree



gene trees

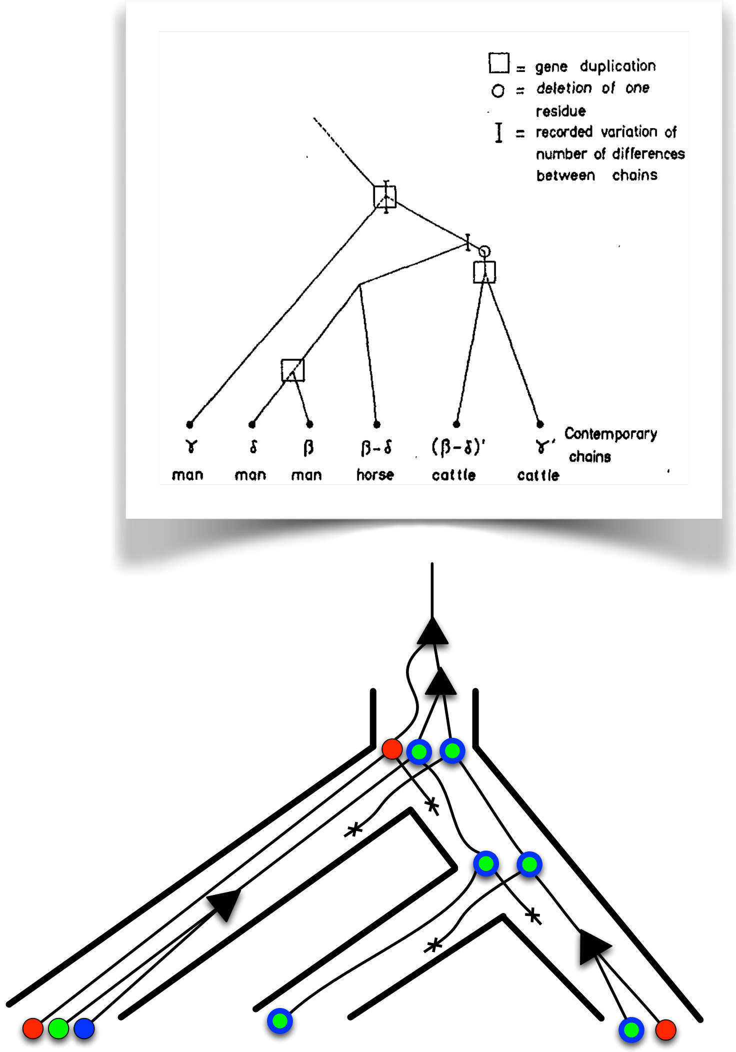
Human

Horse

Cow

Hemoglobin/

```
ALEobserve Zukerkandl-Pauling_OUT.tree
ALEml HuHoCo_OUT.tree Zukerkandl-Pauling_OUT.tree.ale delta=0.01 lambda=0.01 tau=0 sample=10
```



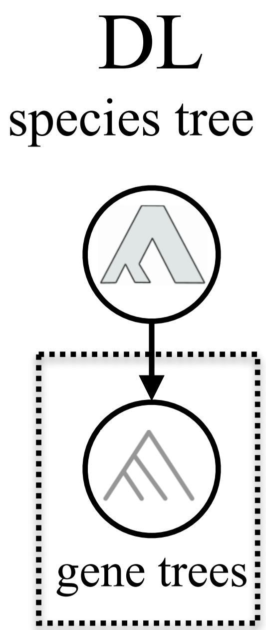
```
S:      ((Human:0.571429,(Horse:0.285714,Cow:0.285714)1:0.285714)2:0.428571,OUT:1)3;


Input ale from: Zukerkandl-Pauling_OUT.tree.ale
>logl: -44.1068
rate of  Duplications   Transfers       Losses
ML      0.01    0       0.01

10 reconciled G-s:


..
# of     Duplications   Transfers       Losses  Speciations
Total   4       0       4       6

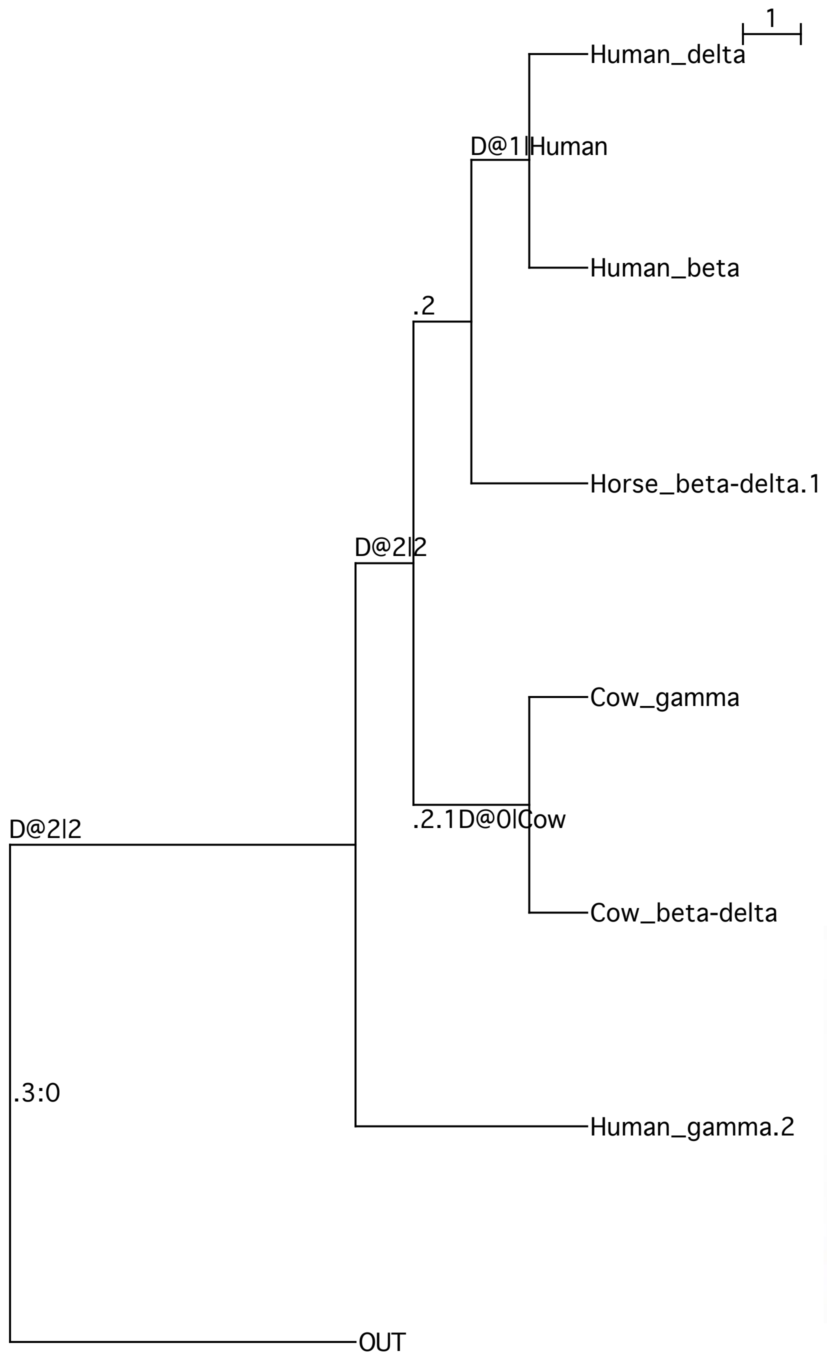
# of     Duplications   Transfers       Losses  copies
S_terminal_branch       Cow     1       0       1       2
S_terminal_branch       Horse   0       0       1       1
S_terminal_branch       Human   1       0       1       3
S_terminal_branch       OUT     0       0       0       1
S_internal_branch       1       0       0       1       2
S_internal_branch       2       2       0       0       3
S_internal_branch       3       0       0       0       1
HuHoCo_OUT.tree_Zukerkandl-Pauling_OUT.tree.ale.ml_rec (END)
```



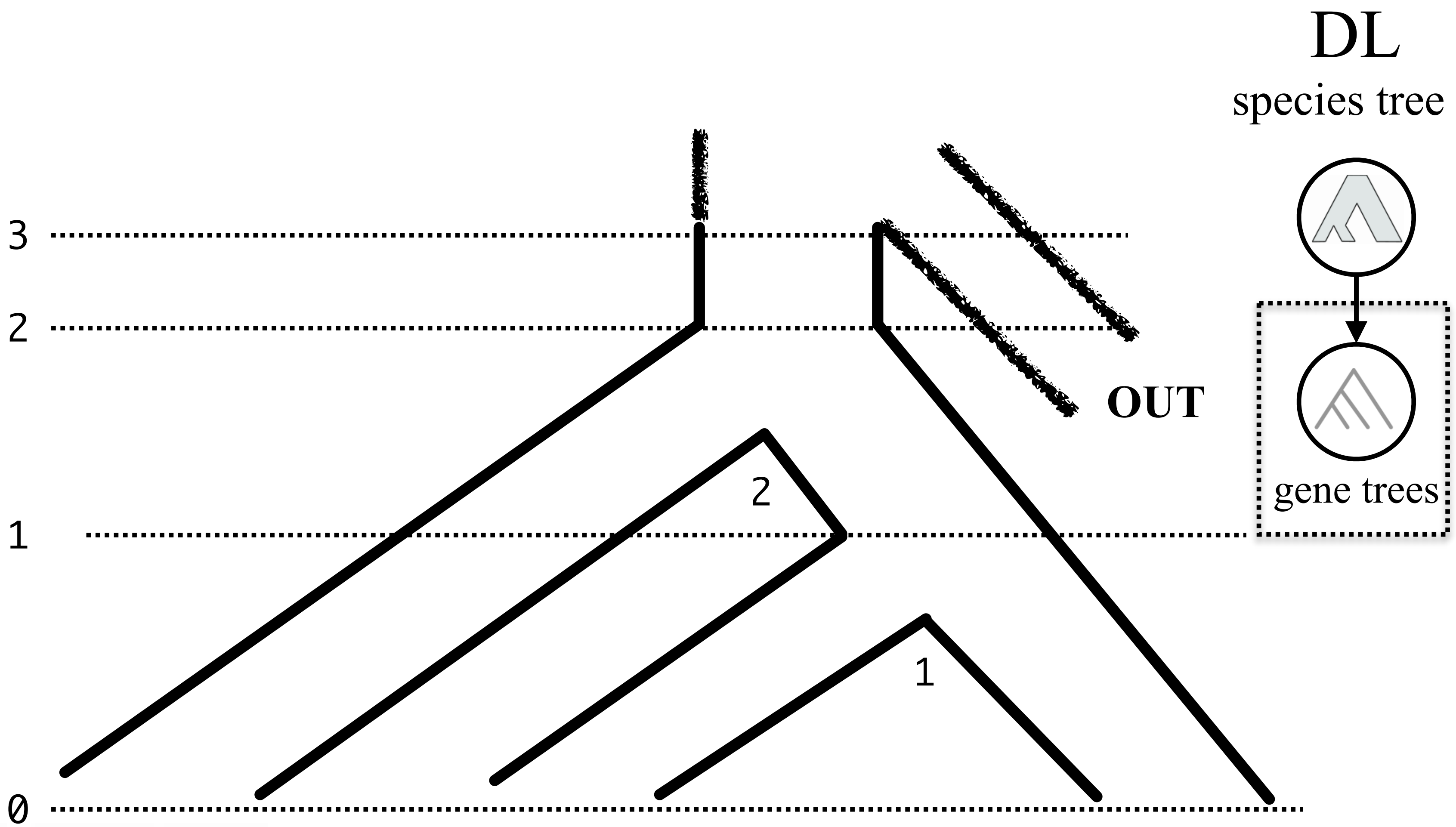
Hemoglobin/

```
ALEml HuHoCo_OUT.tree Zukerkandl-Pauling_OUT.tree.ale delta=0.01 lambda=0.01 tau=0 sample=10
```

```
(OUT:6,(Human_gamma.2:4,((Cow_beta-delta:1,Cow_gamma:1).2.1D@0|Cow:2,(Horse_beta-delta.1:2,(Human_beta:1,Human_delta:1)D@1|Human:1).2:1)D@2|2:1)D@2|2:6).3:0;
```



view the tree using either phylo.io, seaview or FigTree!



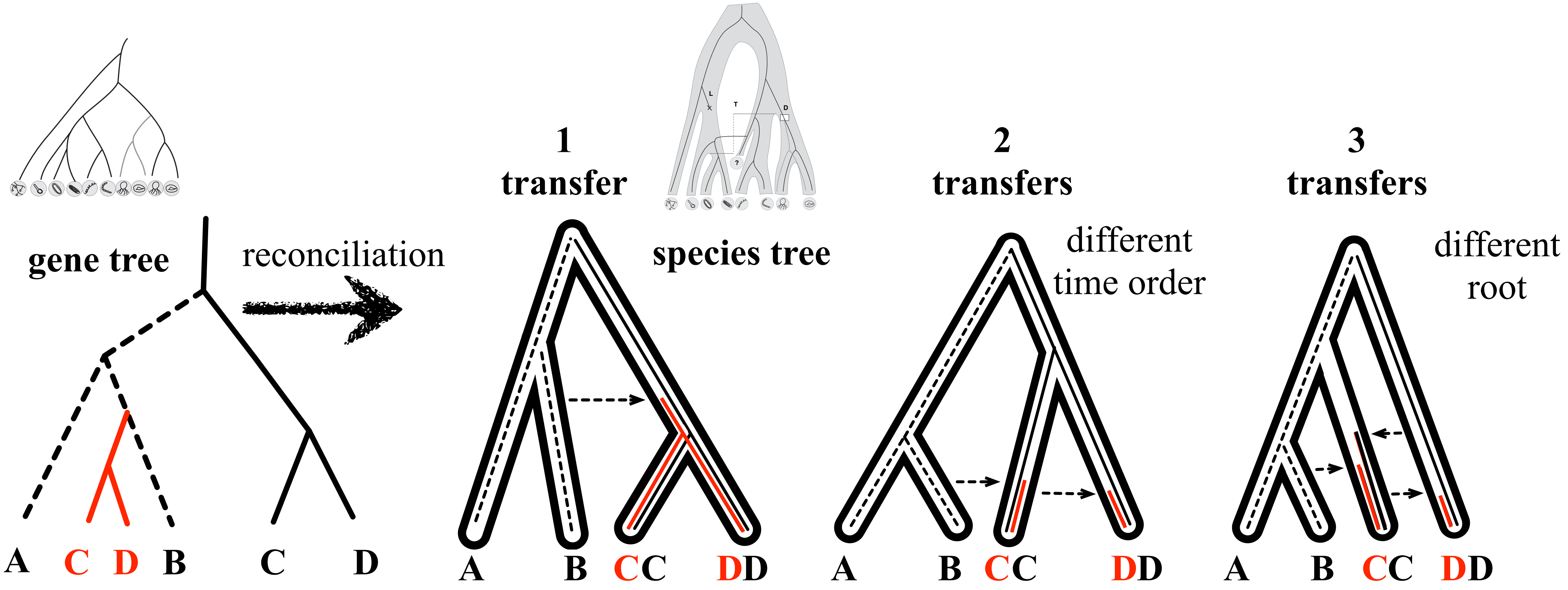
Human

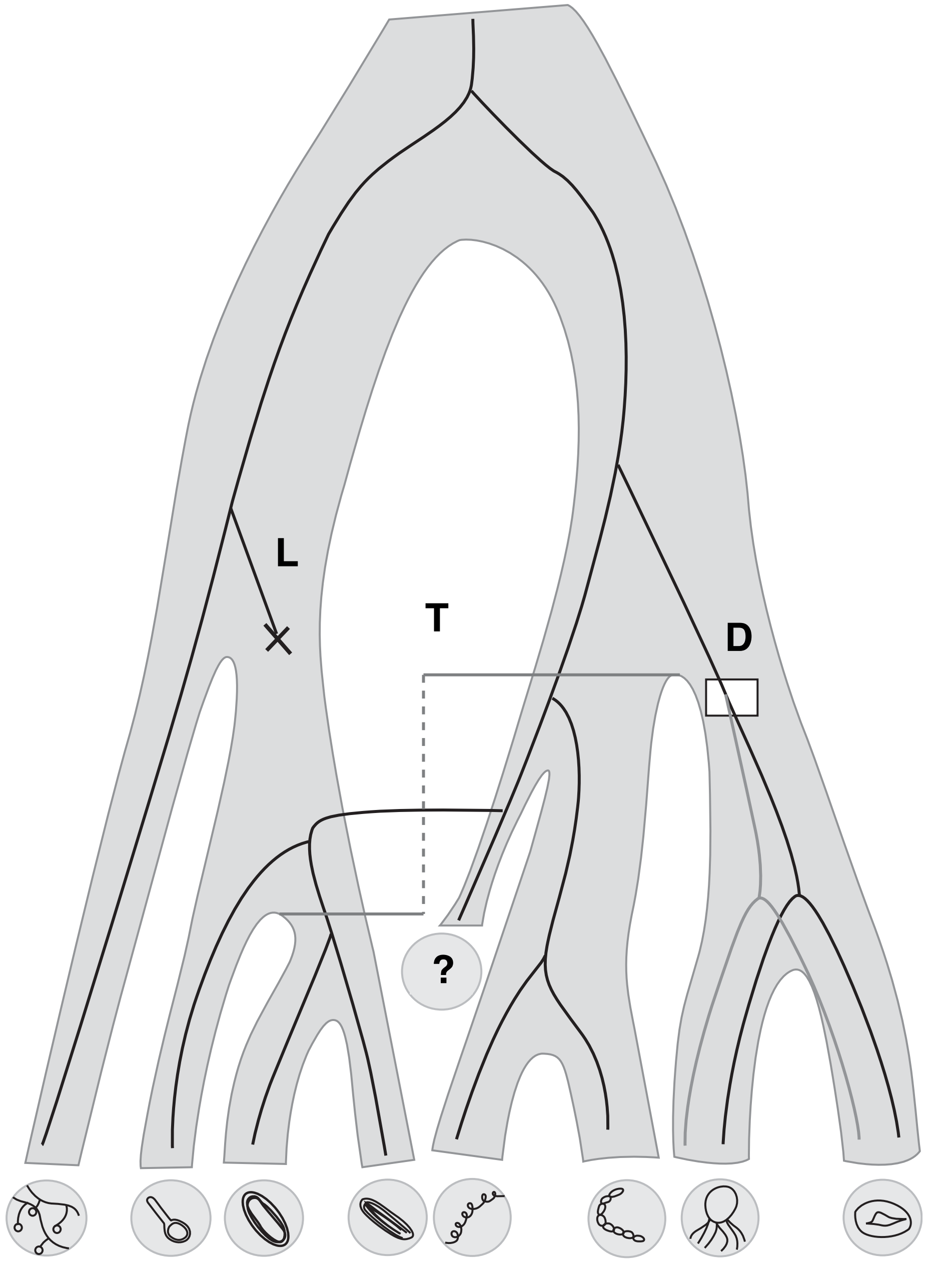
Horse

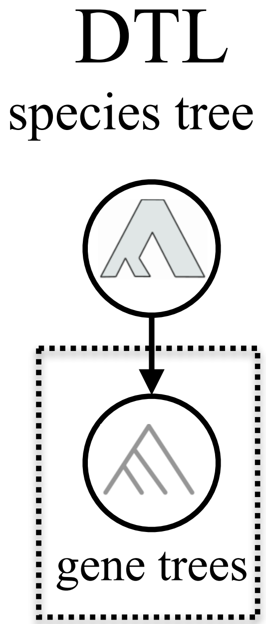
Cow

Horizontal gene transfer as information

Transfer events, encoded in the topologies of gene trees can be thought of as "*molecular fossils*" that record the order of speciation events.






DTL

species tree

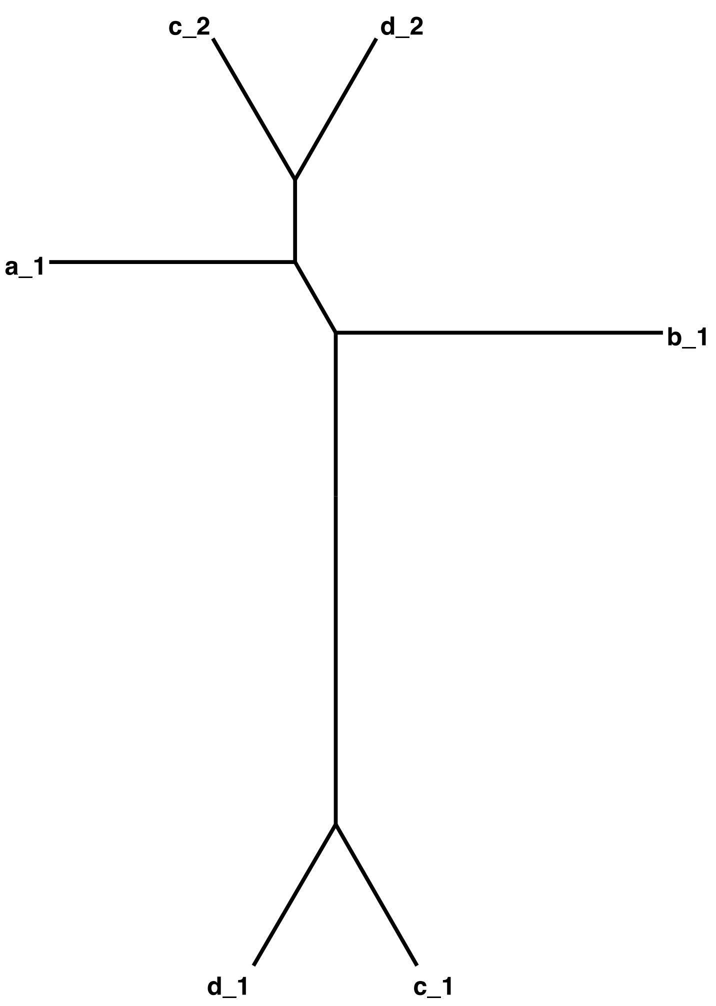
gene trees

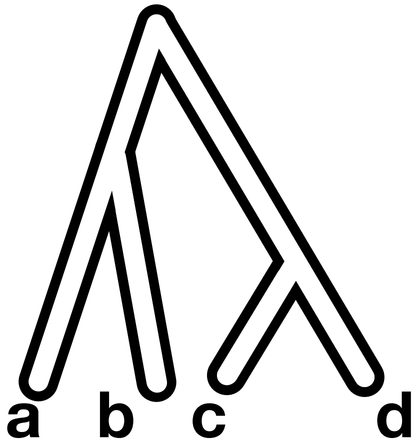
`abcd/`

```
$ cd ~/workshop_materials/lab_data/abcd
```

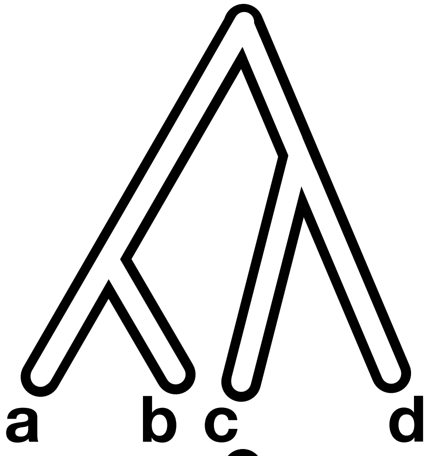
gene tree

`g.tree`

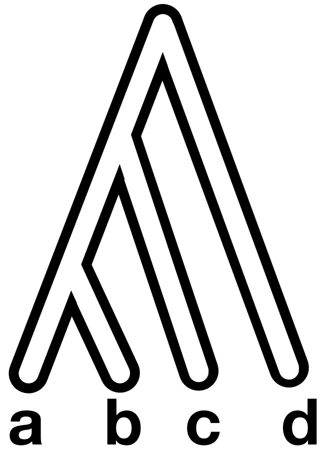




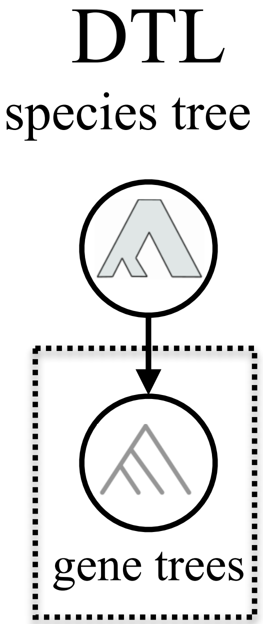
`abcd_S.tree`



`cdab_S.tree`



`abc-d_S.tree`



DTL

species tree

gene trees

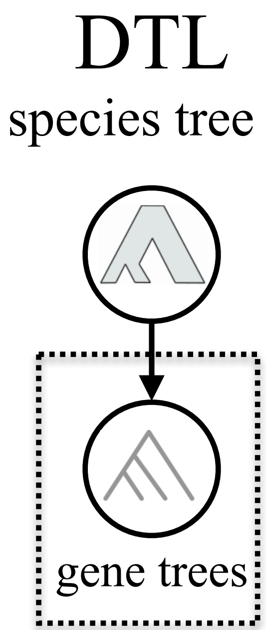
abcd/

```
ALEobserve g.tree
```

ALEml **abcd_S.tree** g.tree.ale sample=10

ALEml **cdab_S.tree** g.tree.ale sample=10

ALEml **abc-d_S.tree** g.tree.ale sample=10

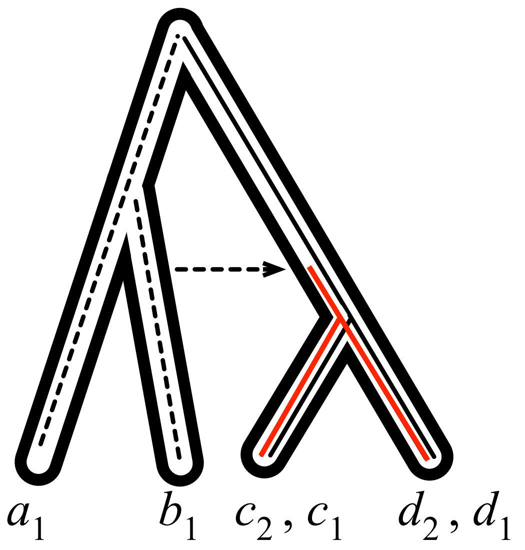


abcd/

abcd_S.tree
ML log-likelihood →

```
..
>logl: -5.93738
rate of  Duplications   Transfers       Losses
ML      4.17809e-07     0.372863        1e-10
..
# of     Duplications   Transfers       Losses  Speciations
Total   0       1.6     0       3.8

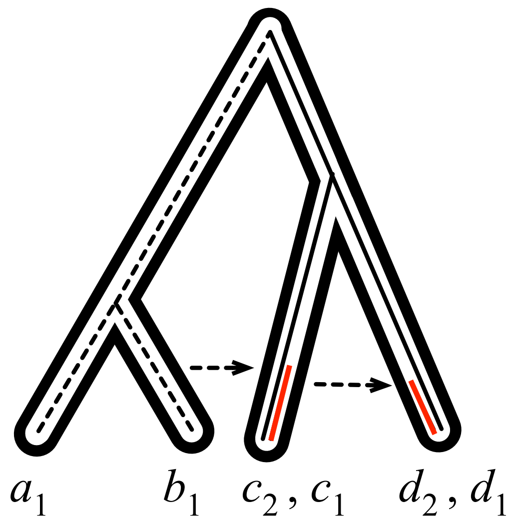
# of     Duplications   Transfers       Losses  copies
S_terminal_branch       a       0       0       0       1
S_terminal_branch       b       0       0       0       1
S_terminal_branch       c       0       0       0       2
S_terminal_branch       d       0       0       0       2
S_internal_branch       1       0       1.2     0       2
S_internal_branch       2       0       0.1     0       1
S_internal_branch       3       0       0.3     0       0.8
abcd_S.tree_g.tree.ale.ml_rec (END)
```



cdab_S.tree
ML log-likelihood →

```
..
>logl: -9.86434
rate of  Duplications   Transfers       Losses
ML      1e-10   1.05185 1e-10
..
# of     Duplications   Transfers       Losses  Speciations
Total   0       3       0       2.3

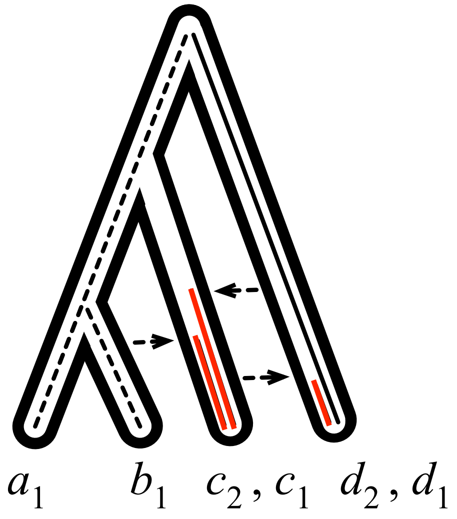
# of     Duplications   Transfers       Losses  copies
S_terminal_branch       a       0       0.1     0       1
S_terminal_branch       b       0       0.1     0       1
S_terminal_branch       c       0       1.2     0       2
S_terminal_branch       d       0       1.2     0       2
S_internal_branch       1       0       0.2     0       0.9
S_internal_branch       2       0       0.1     0       0.8
S_internal_branch       3       0       0.1     0       0.6
cdab_S.tree_g.tree.ale.ml_rec (END)
```

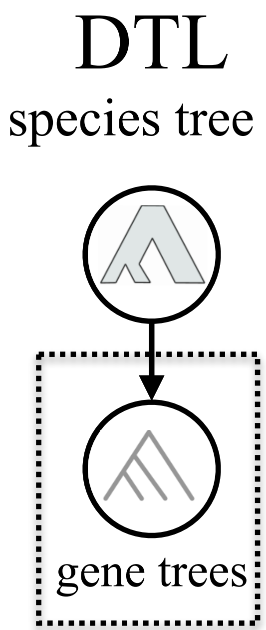


abc-d_S.tree
ML log-likelihood →

```
..
>logl: -9.83179
rate of  Duplications   Transfers       Losses
ML      3.74258e-06     1.06978 1e-10
..
# of     Duplications   Transfers       Losses  Speciations
Total   0       2.6     0       2.6

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       a       0       0       0       1
S_terminal_branch       b       0       0       0       1
S_terminal_branch       c       0       1       0       2
S_terminal_branch       d       0       1.4     0       2
S_internal_branch       1       0       0       0       1
S_internal_branch       2       0       0.2     0       1
S_internal_branch       3       0       0       0       0.6
abc-d_S.tree_g.tree.ale.ml_rec (END)
```





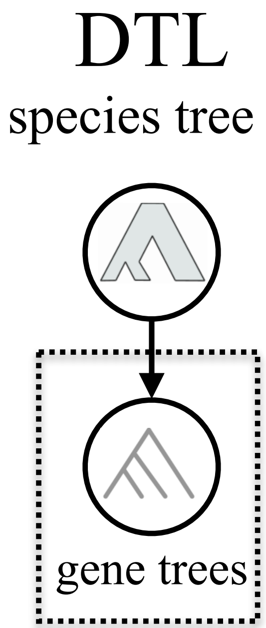
abcd/

```
ALEobserve g.tree
```

```
ALEml abcd_S.tree g.tree.ale sample=10 delta=0.0 tau=0.01 lambda=0.01
```

```
ALEml cdab_S.tree g.tree.ale sample=10 delta=0.0 tau=0.01 lambda=0.01
```

```
ALEml abc-d_S.tree g.tree.ale sample=10 delta=0.0 tau=0.01 lambda=0.01
```



abcd/

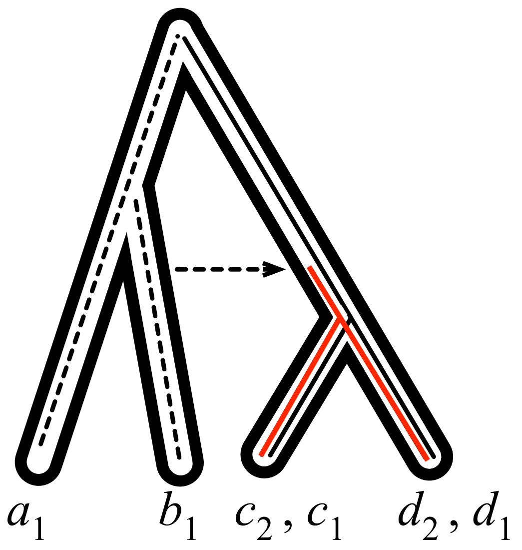
log-likelihood →

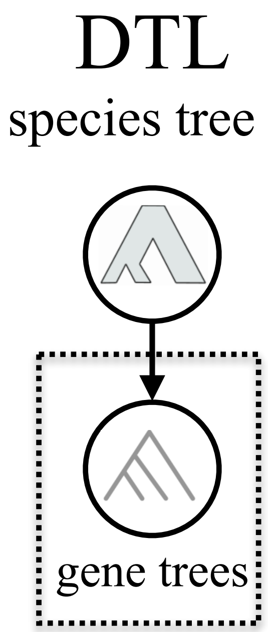
events →

ALEml **abcd_S.tree** g.tree.ale sample=10 **delta=0.0 tau=0.01 lambda=0.01**

```
..
>logl: -8.61538
..
# of     Duplications   Transfers       Losses  Speciations
Total   0       1       0       4

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       a       0       0       0       1
S_terminal_branch       b       0       0       0       1
S_terminal_branch       c       0       0       0       2
S_terminal_branch       d       0       0       0       2
S_internal_branch       1       0       1       0       2
S_internal_branch       2       0       0       0       1
S_internal_branch       3       0       0       0       1
abcd_S.tree_g.tree.ale.ml_rec (END)
```





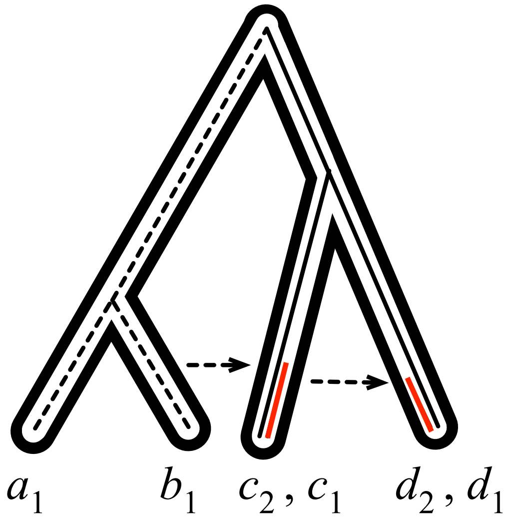
log-likelihood →

events →

ALEml **cdab_S.tree** g.tree.ale sample=10 **delta=0.0 tau=0.01 lambda=0.01**

```
..
>logl: -16.7168
..
# of     Duplications   Transfers       Losses  Speciations
Total   0       1.9     0.3     3.4

# of     Duplications   Transfers       Losses  copies
S_terminal_branch       a       0       0       0.1     1
S_terminal_branch       b       0       0.1     0.2     1
S_terminal_branch       c       0       0.8     0       2
S_terminal_branch       d       0       0.8     0       2
S_internal_branch       1       0       0       0       1.1
S_internal_branch       2       0       0.1     0       1.2
S_internal_branch       3       0       0.1     0       1.1
cdab_S.tree_g.tree.ale.ml_rec (END)
```



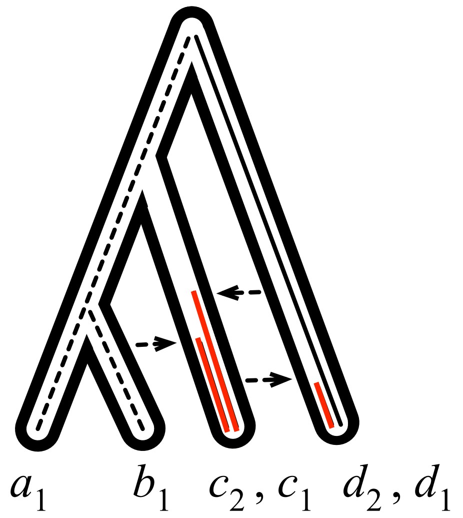
log-likelihood →

events →

ALEml **abc-d_S.tree** g.tree.ale sample=10 **delta=0.0 tau=0.01 lambda=0.01**

```
..
>logl: -16.8563
rate of  Duplications   Transfers       Losses
ML      3.74258e-06     1.06978 1e-10
..
# of     Duplications   Transfers       Losses  Speciations
Total   0       2       0       3

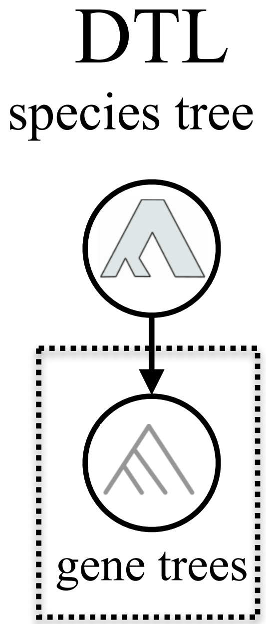
# of     Duplications   Transfers       Losses  copies
S_terminal_branch       a       0       0       0       1
S_terminal_branch       b       0       0       0       1
S_terminal_branch       c       0       1       0       2
S_terminal_branch       d       0       1       0       2
S_internal_branch       1       0       0       0       1
S_internal_branch       2       0       0       0       1
S_internal_branch       3       0       0       0       1
abc-d_S.tree_g.tree.ale.ml_rec (END)
```

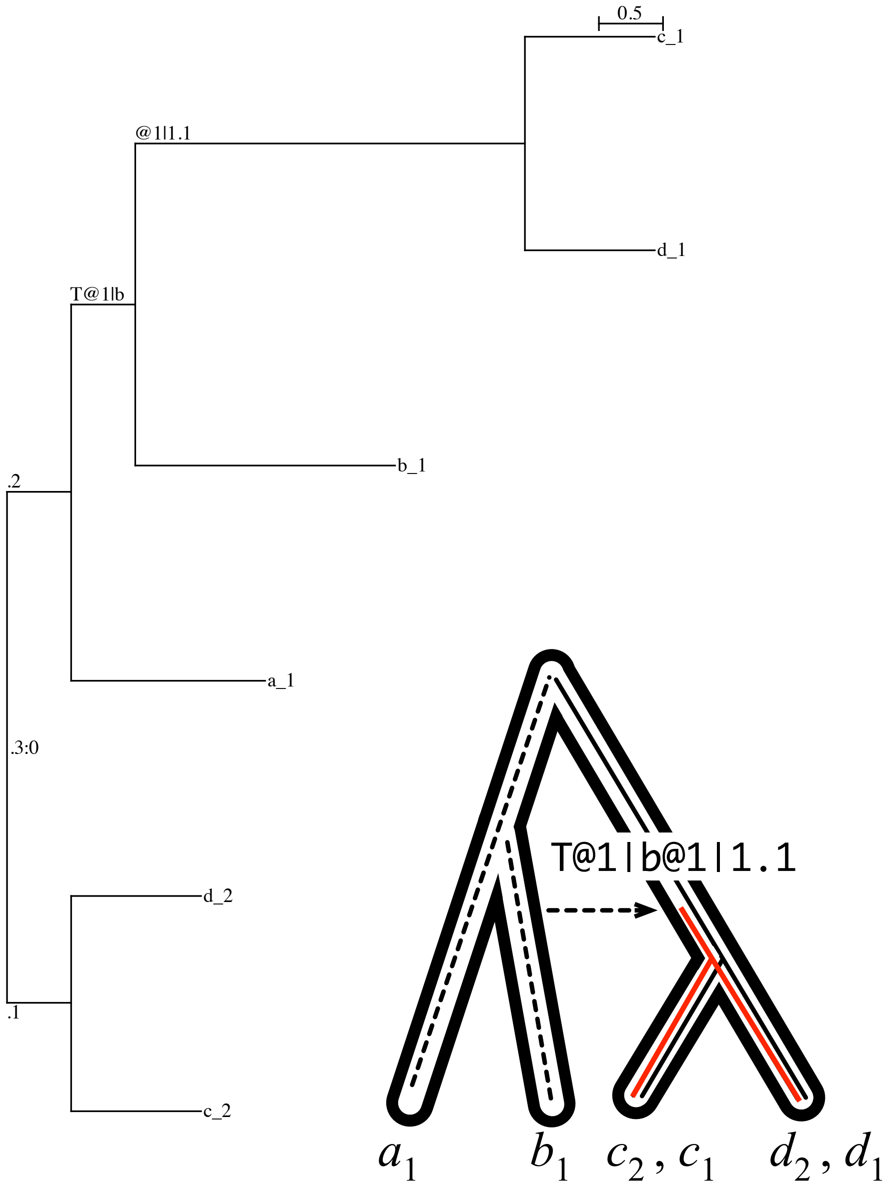


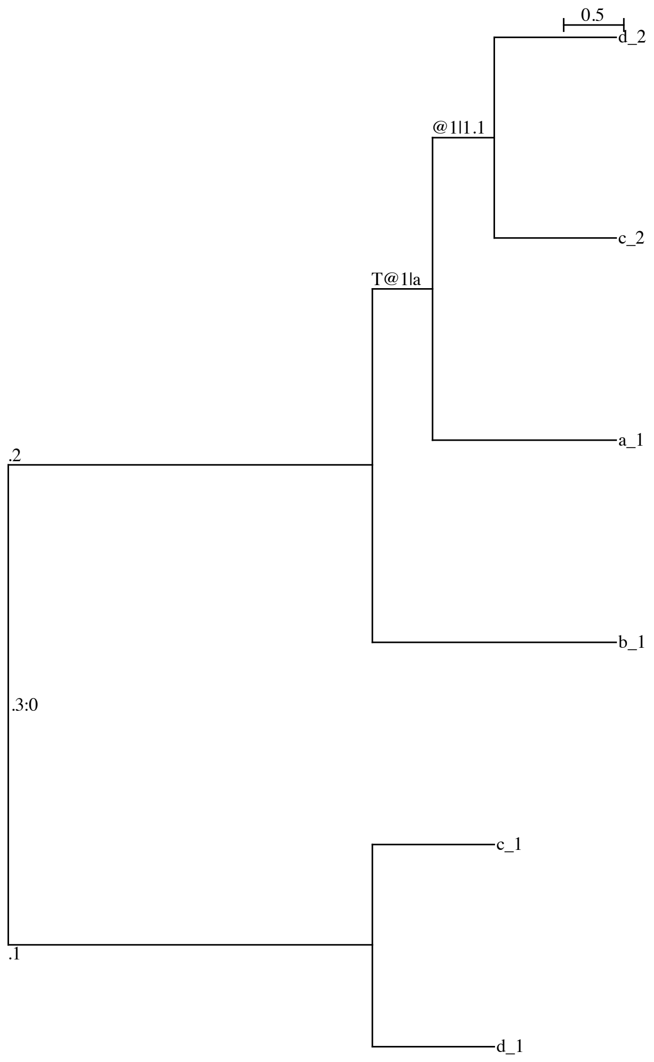
abcd/

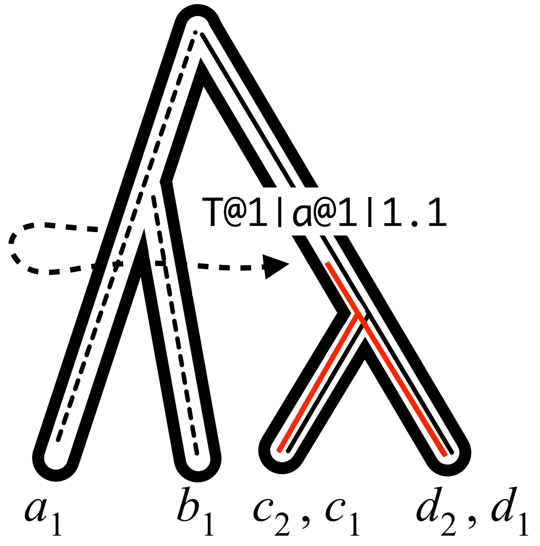
```
ALEml abcd_S.tree g.tree.ale sample=10 delta=0.0 tau=0.01 lambda=0.01
```

```
((d_1:1,c_1:1).1:3,(b_1:2,(a_1:1.5,(c_2:1,d_2:1)@1|1.1:0.5)T@1|a:0.5).2:3).3:0;
((d_1:1,c_1:1).1:3,(b_1:2,(a_1:1.5,(c_2:1,d_2:1)@1|1.1:0.5)T@1|a:0.5).2:3).3:0;
((c_2:1,d_2:1).1:0.5,(a_1:1.5,(b_1:2,(d_1:1,c_1:1)@1|1.1:3)T@1|b:0.5).2:0.5).3:0;
((c_2:1,d_2:1).1:0.5,(a_1:1.5,(b_1:2,(d_1:1,c_1:1)@1|1.1:3)T@1|b:0.5).2:0.5).3:0;
((c_2:1,d_2:1).1:0.5,(a_1:1.5,(b_1:2,(d_1:1,c_1:1)@1|1.1:3)T@1|b:0.5).2:0.5).3:0;
((d_1:1,c_1:1).1:3,(b_1:2,(a_1:1.5,(c_2:1,d_2:1)@1|1.1:0.5)T@1|a:0.5).2:3).3:0;
((d_1:1,c_1:1).1:3,(b_1:2,(a_1:1.5,(c_2:1,d_2:1)@1|1.1:0.5)T@1|a:0.5).2:3).3:0;
((c_2:1,d_2:1).1:0.5,(a_1:1.5,(b_1:2,(d_1:1,c_1:1)@1|1.1:3)T@1|b:0.5).2:0.5).3:0;
((d_1:1,c_1:1).1:3,(b_1:2,(a_1:1.5,(c_2:1,d_2:1)@1|1.1:0.5)T@1|a:0.5).2:3).3:0;
((d_1:1,c_1:1).1:3,(b_1:2,(a_1:1.5,(c_2:1,d_2:1)@1|1.1:0.5)T@1|a:0.5).2:3).3:0;
```









view the tree using either phylo.io, seaview or FigTree!

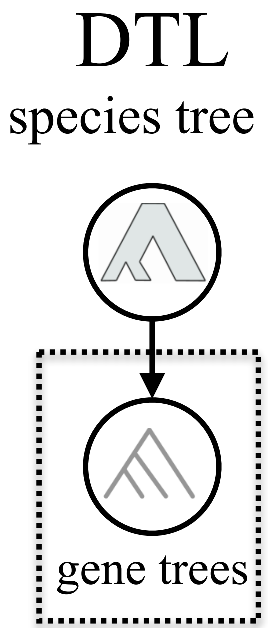
abcd/

ALEml **cdab_S.tree** g.tree.ale sample=10 **delta=0.0 tau=0.01 lambda=0.01**

```
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2@0|c:1,d_2@0|d:1)T@0|-1:0.5)T@0|a:0.5).1:3).3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3)@3|3.3:0.5)T@3|3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1@0|c:1)T@0|-1:3)T@0|b:0.5).1:0.5).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1@0|c:1)T@0|-1:3)T@0|b:0.5).1:0.5).3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1@0|b:2,(d_1:1,c_1:1)@2|2.2:3)T@2|-1:0.5)T@3|3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1@0|c:1)T@0|-1:3)T@0|b:0.5).1:0.5).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1:1)@0|cT@0|c:3)T@0|b:0.5).1:0.5).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1:1)@0|cT@0|c:3)T@0|b:0.5).1:0.5).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1:1,c_1@0|c:1)@0|dT@0|d:3)T@0|b:0.5).1:0.5).3:0;
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2:1,d_2@0|d:1)@0|cT@0|c:0.5)T@0|a:0.5).1:3).3:0;
```

ALEml cdab_S.tree g.tree.ale sample=10 **delta=0.01 tau=0.0** lambda=0.01

```
Total   0       2       0       3
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.45|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.3|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.2|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.4|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.1|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.45|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.2|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.1|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.35|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.3|3:0;
# of     Duplications   Transfers       Losses  Speciations
Total   1       0       2       6
```



DTL

species tree

gene trees

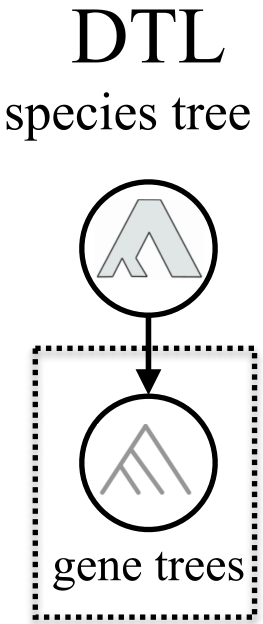
view the trees using either
phylo.io, seaview or FigTree!

`abcd/`

ALEml **cdab_S.tree** g.tree.ale sample=10 **delta=0.0 tau=0.01 lambda=0.01**

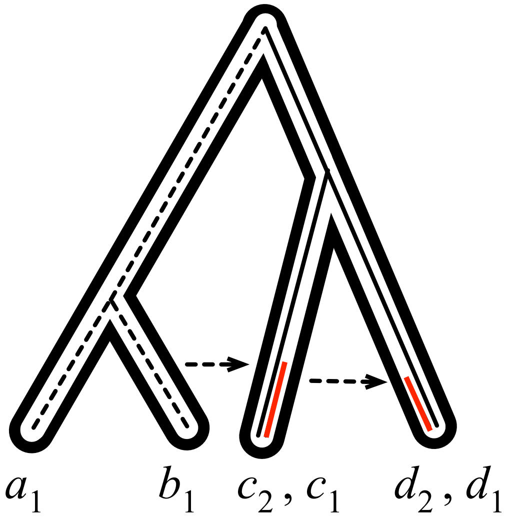
```
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2@0|c:1,d_2@0|d:1)T@0|-1:0.5)T@0|a:0.5).1:3).3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3)@3|3.3:0.5)T@3|3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1@0|c:1)T@0|-1:3)T@0|b:0.5).1:0.5).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1@0|c:1)T@0|-1:3)T@0|b:0.5).1:0.5).3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1@0|b:2,(d_1:1,c_1:1)@2|2.2:3)T@2|-1:0.5)T@3|3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1@0|c:1)T@0|-1:3)T@0|b:0.5).1:0.5).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1:1)@0|cT@0|c:3)T@0|b:0.5).1:0.5).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1:1)@0|cT@0|c:3)T@0|b:0.5).1:0.5).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1:1,c_1@0|c:1)@0|dT@0|d:3)T@0|b:0.5).1:0.5).3:0;
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2:1,d_2@0|d:1)@0|cT@0|c:0.5)T@0|a:0.5).1:3).3:0;
```

ALEml cdab_S.tree g.tree.ale sample=10 **delta=0.01 tau=0.0** lambda=0.01



```
Total   0       2       0       3
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.45|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.3|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.2|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.4|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.1|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.45|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.2|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.1|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.35|3:0;
((a_1.1:1.5,(c_2:1,d_2:1).2:0.5).3:0.5,(b_1.1:2,(d_1:1,c_1:1).2:3).3:0.5)D@3|1.3|3:0;
# of     Duplications   Transfers       Losses  Speciations
Total   1       0       2       6
```

ALEml cdab_S.tree g.tree.ale sample=10 **delta=0.0** tau=0.01 **lambda=0.0**

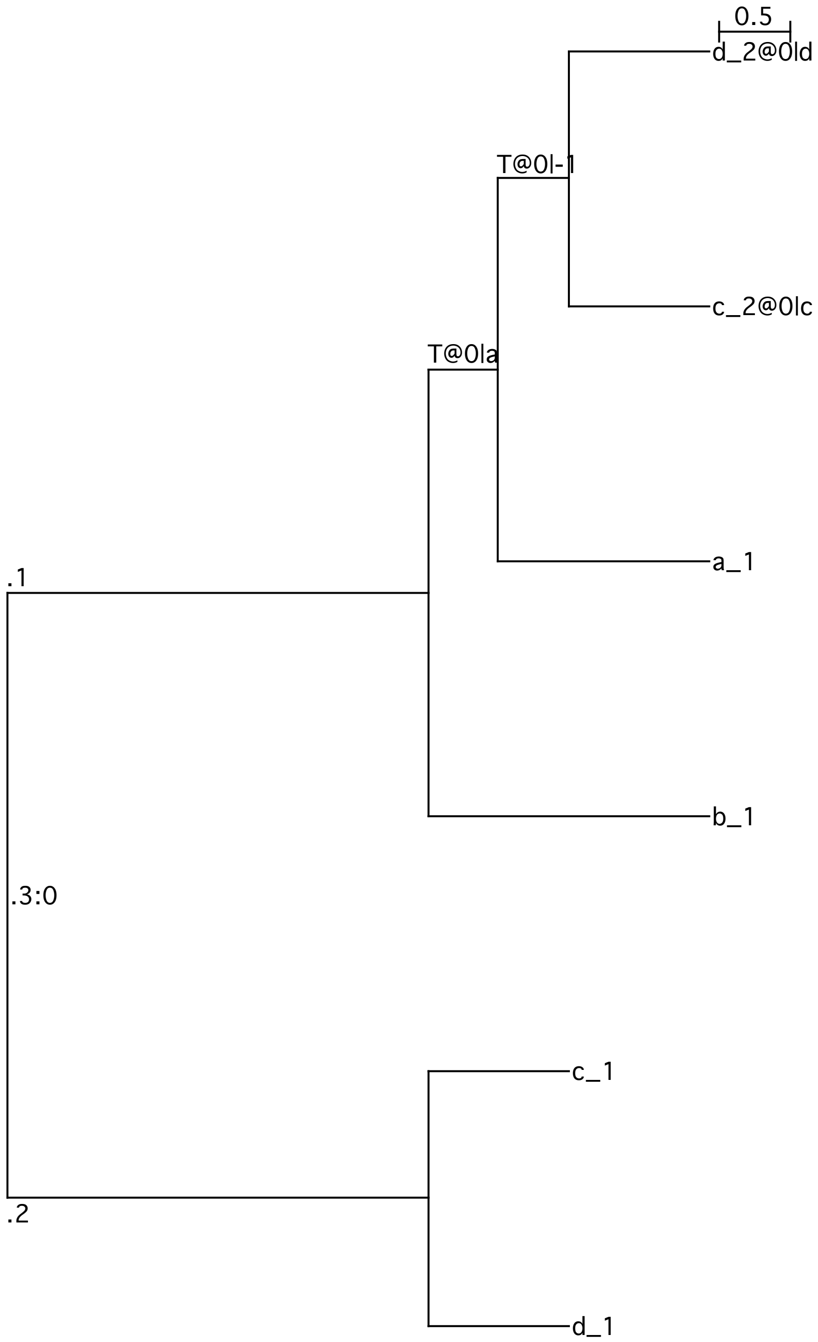


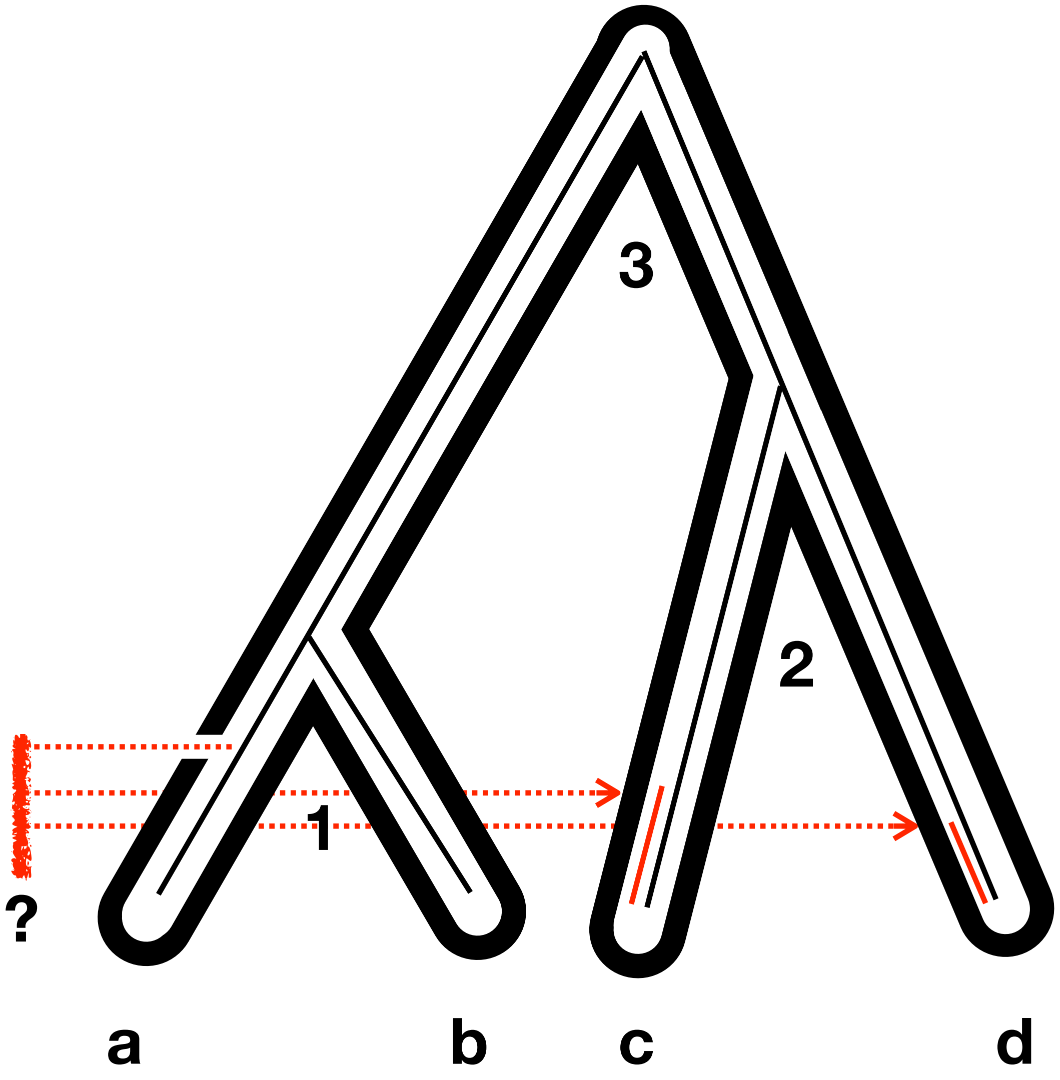
```
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2:1,d_2@0|d:1)@0|cT@0|c:0.5)T@0|a:0.5).1:3).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1@0|c:1)T@0|-1:3)T@0|b:0.5).1:0.5).3:0;
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2@0|c:1,d_2@0|d:1)T@0|-1:0.5)T@0|a:0.5).1:3).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1:1)@0|cT@0|c:3)T@0|b:0.5).1:0.5).3:0;
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2@0|c:1,d_2:1)@0|dT@0|d:0.5)T@0|a:0.5).1:3).3:0;
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2@0|c:1,d_2:1)@0|dT@0|d:0.5)T@0|a:0.5).1:3).3:0;
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2@0|c:1,d_2@0|d:1)T@0|-1:0.5)T@0|a:0.5).1:3).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1@0|d:1,c_1@0|c:1)T@0|-1:3)T@0|b:0.5).1:0.5).3:0;
((c_2:1,d_2:1).2:0.5,(a_1:1.5,(b_1:2,(d_1:1,c_1@0|c:1)@0|dT@0|d:3)T@0|b:0.5).1:0.5).3:0;
((d_1:1,c_1:1).2:3,(b_1:2,(a_1:1.5,(c_2@0|c:1,d_2:1)@0|dT@0|d:0.5)T@0|a:0.5).1:3).3:0;
# of     Duplications   Transfers       Losses  Speciations
```

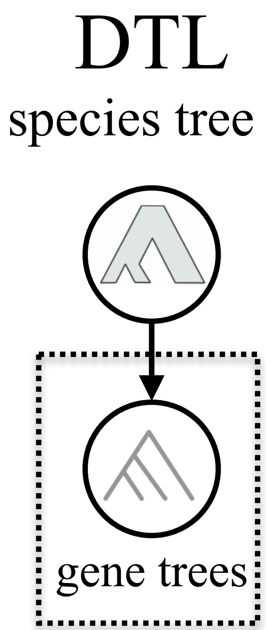
?

`T@0|-1`

abcd/







view the tree using either
phylo.io, seaview or FigTree!

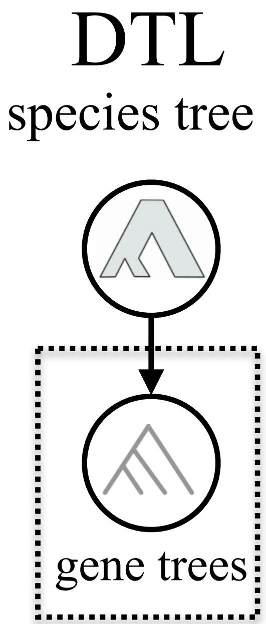
abcd/

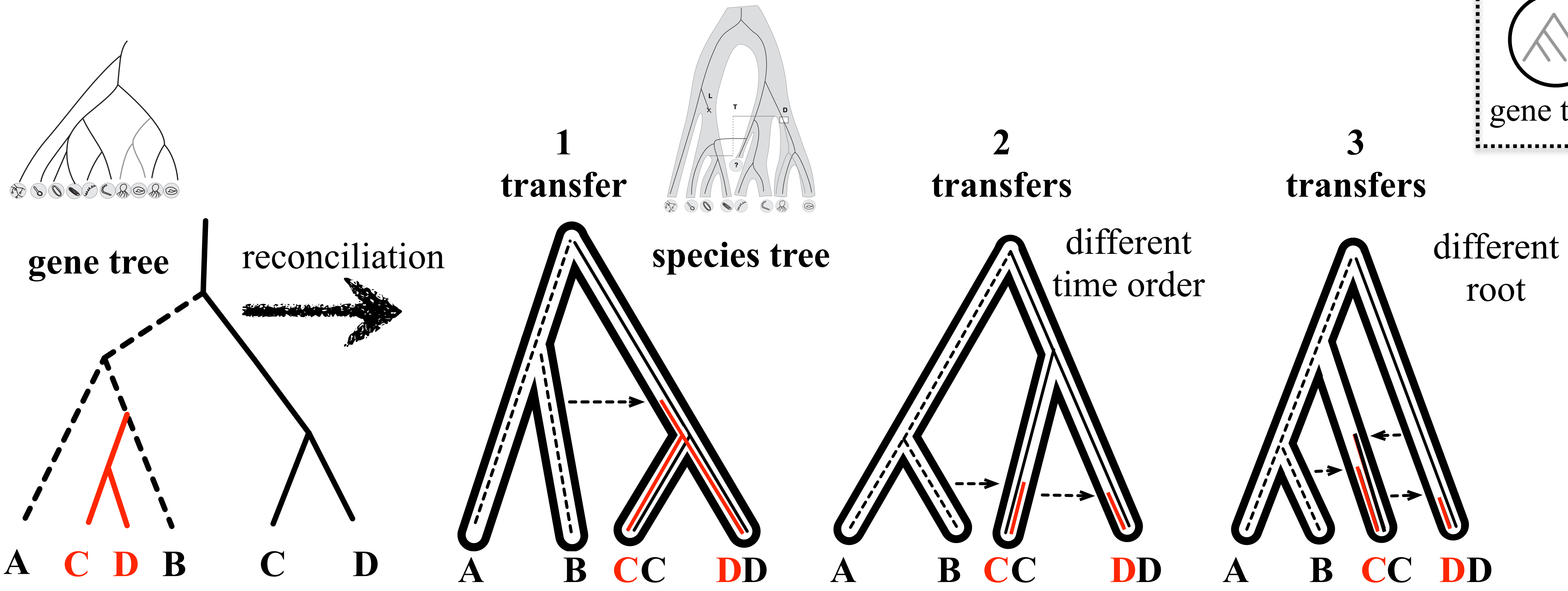
```
ALEobserve g.tree

ALEml abcd_S.tree g.tree.ale sample=10

ALEml cdab_S.tree g.tree.ale sample=10

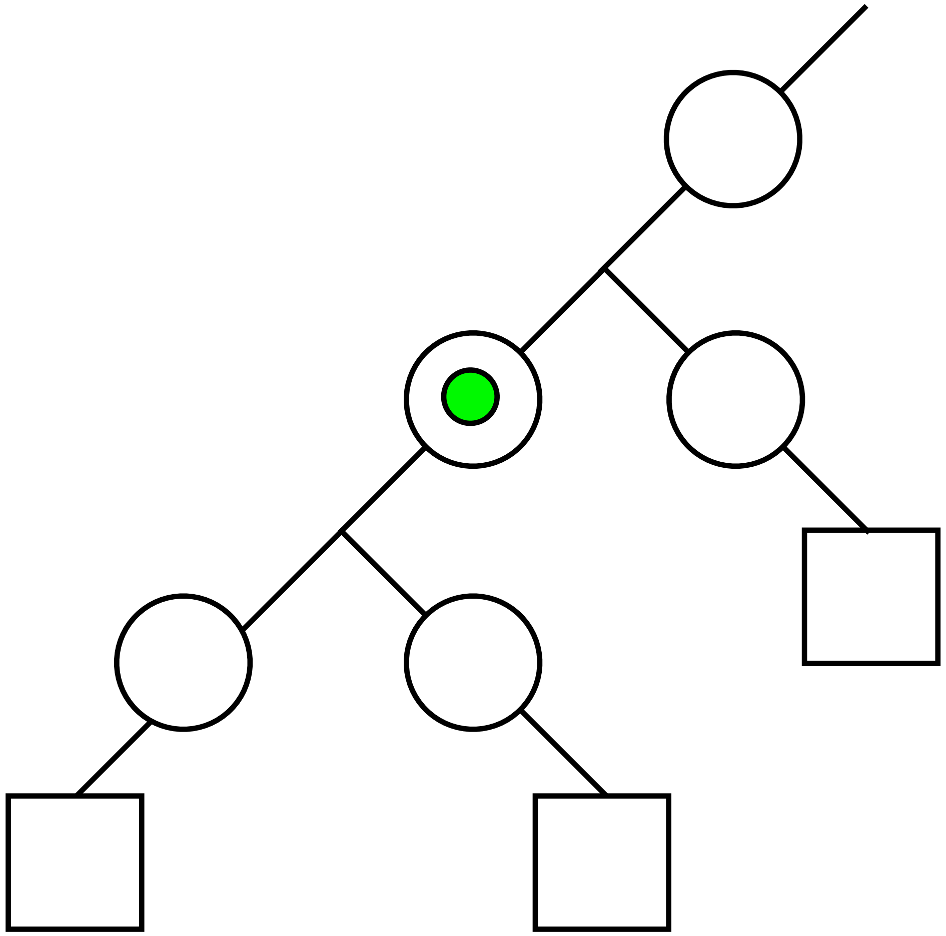
ALEml abc-d_S.tree g.tree.ale sample=10
```



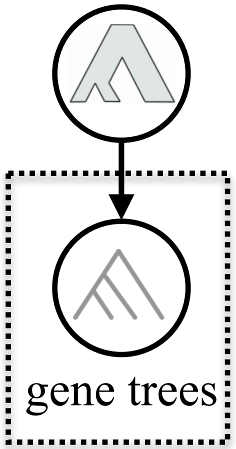


abcd/

“undated” DTL

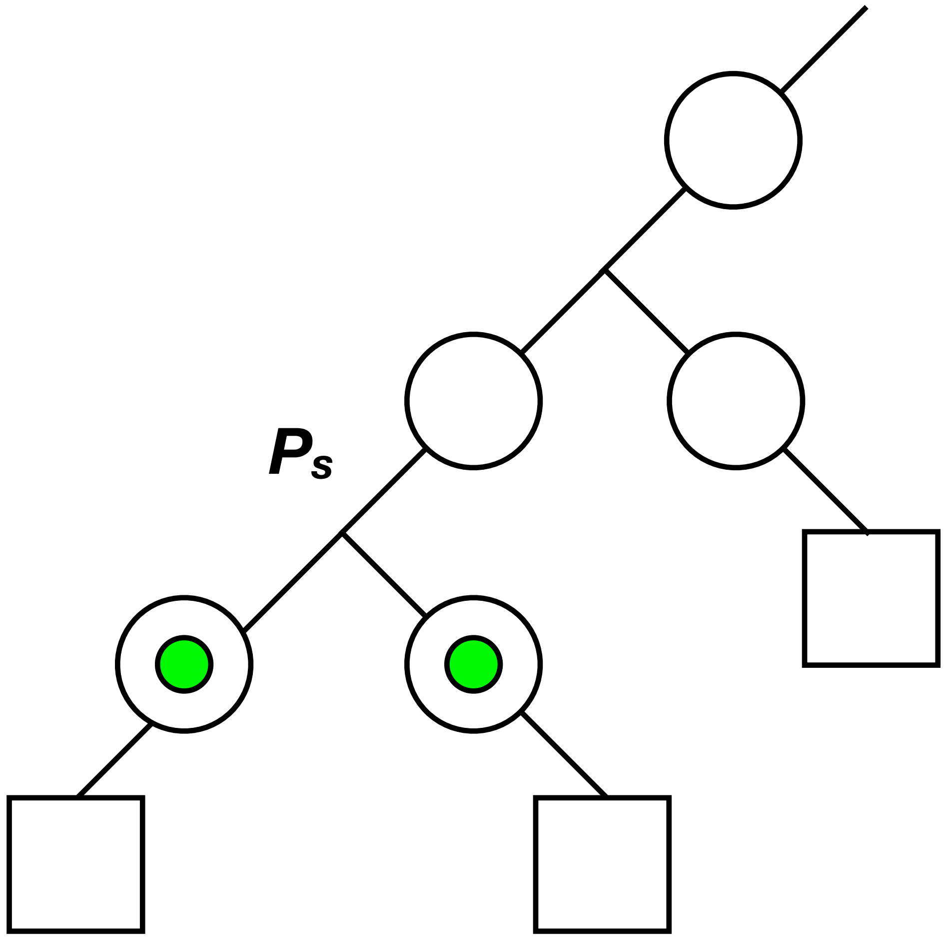


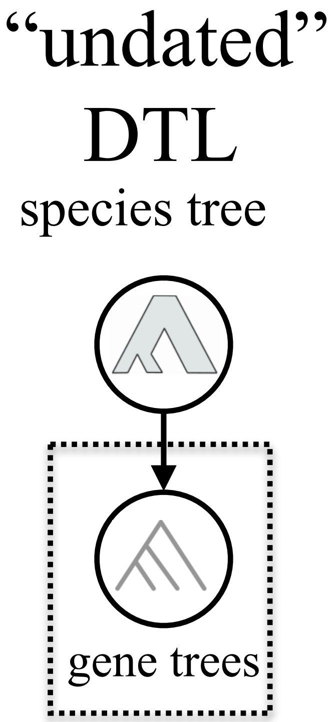
“undated”
DTL
species tree



abcd/

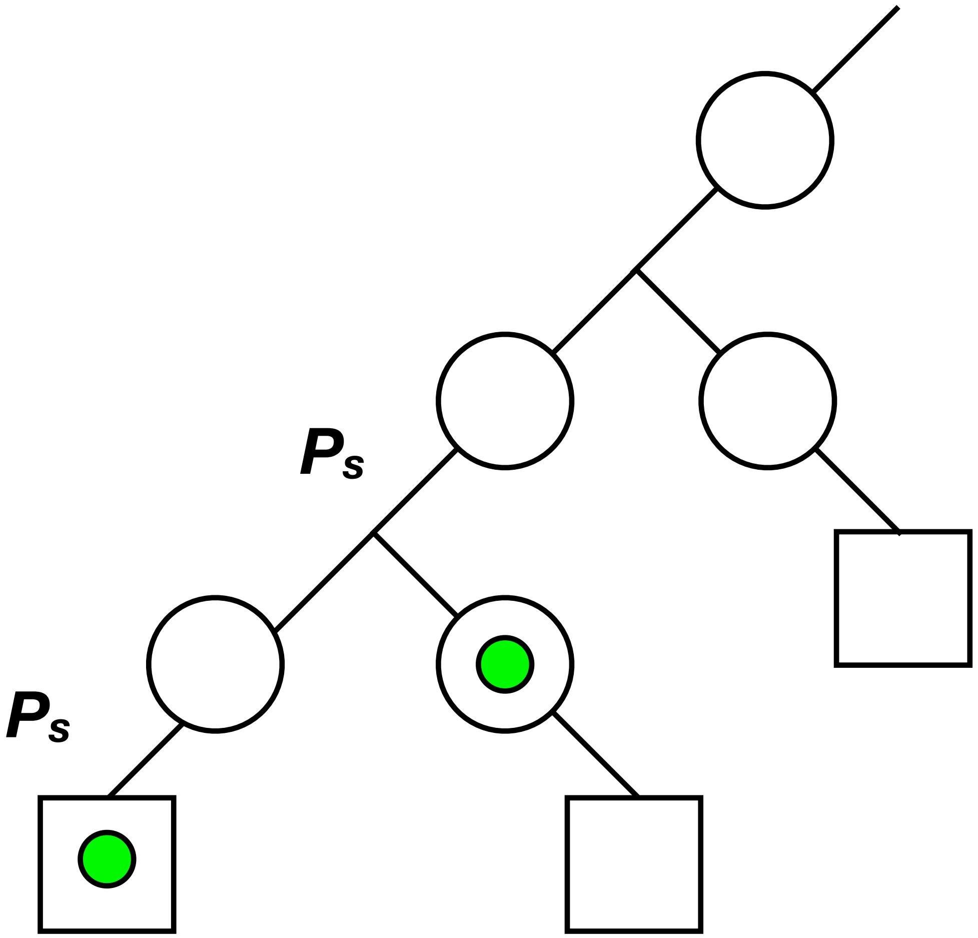
“undated” DTL



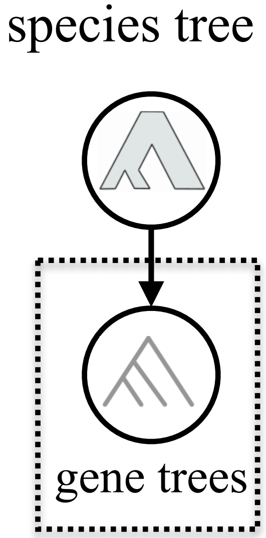


abcd/

“undated” DTL

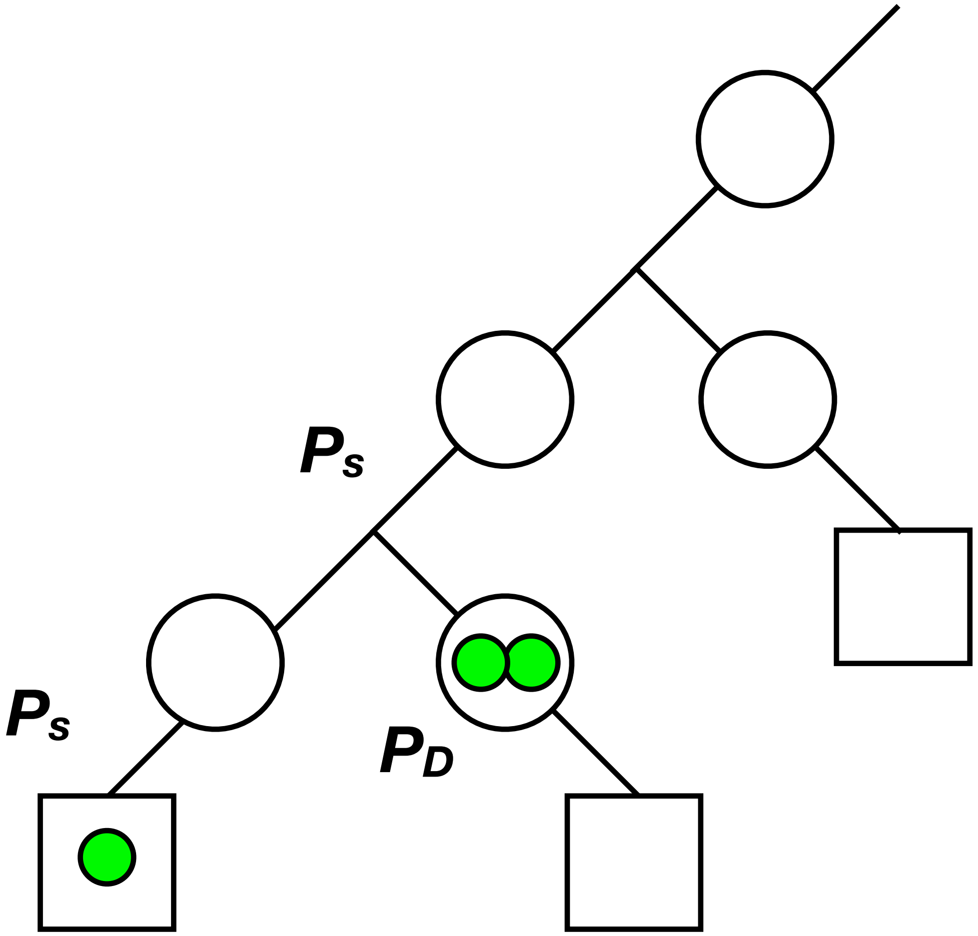


“undated”
DTL

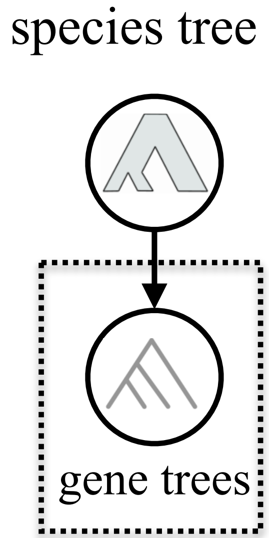


abcd/

“undated” DTL

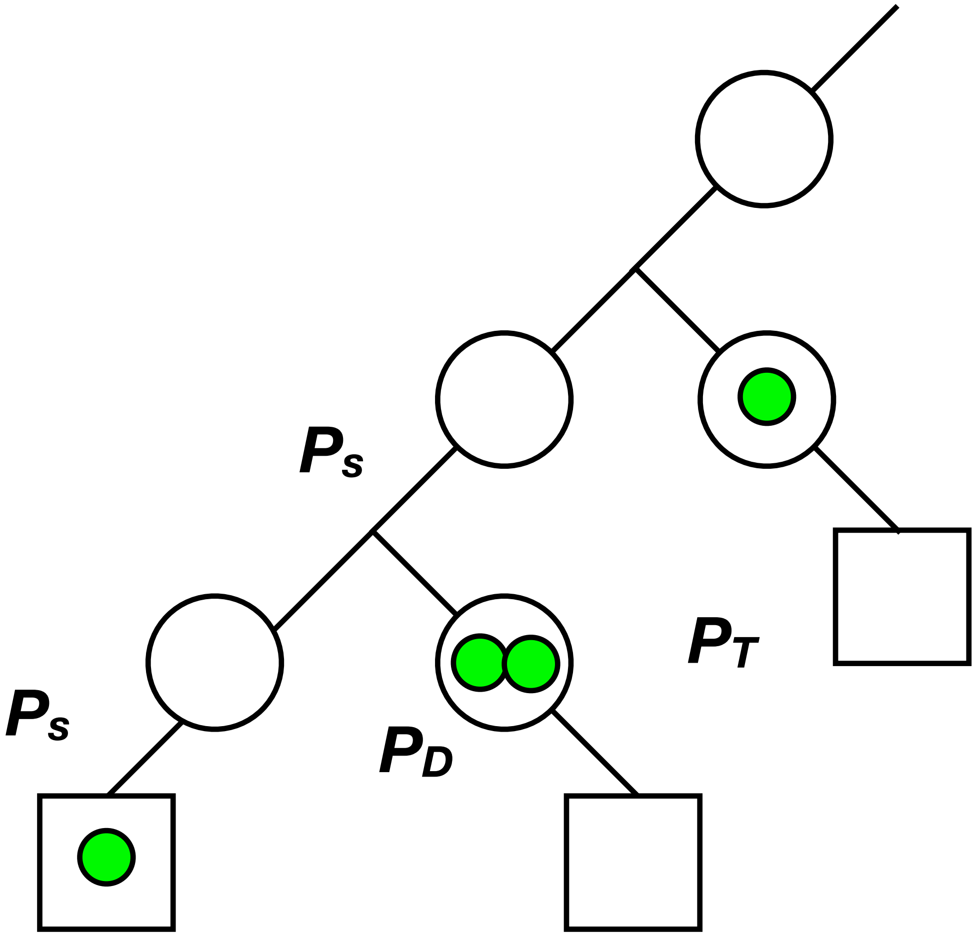


“undated”
DTL

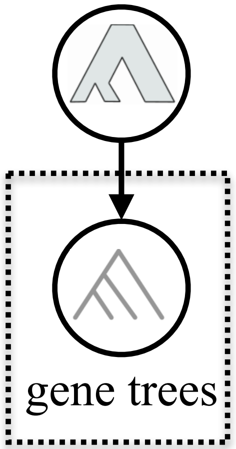


abcd/

“undated” DTL

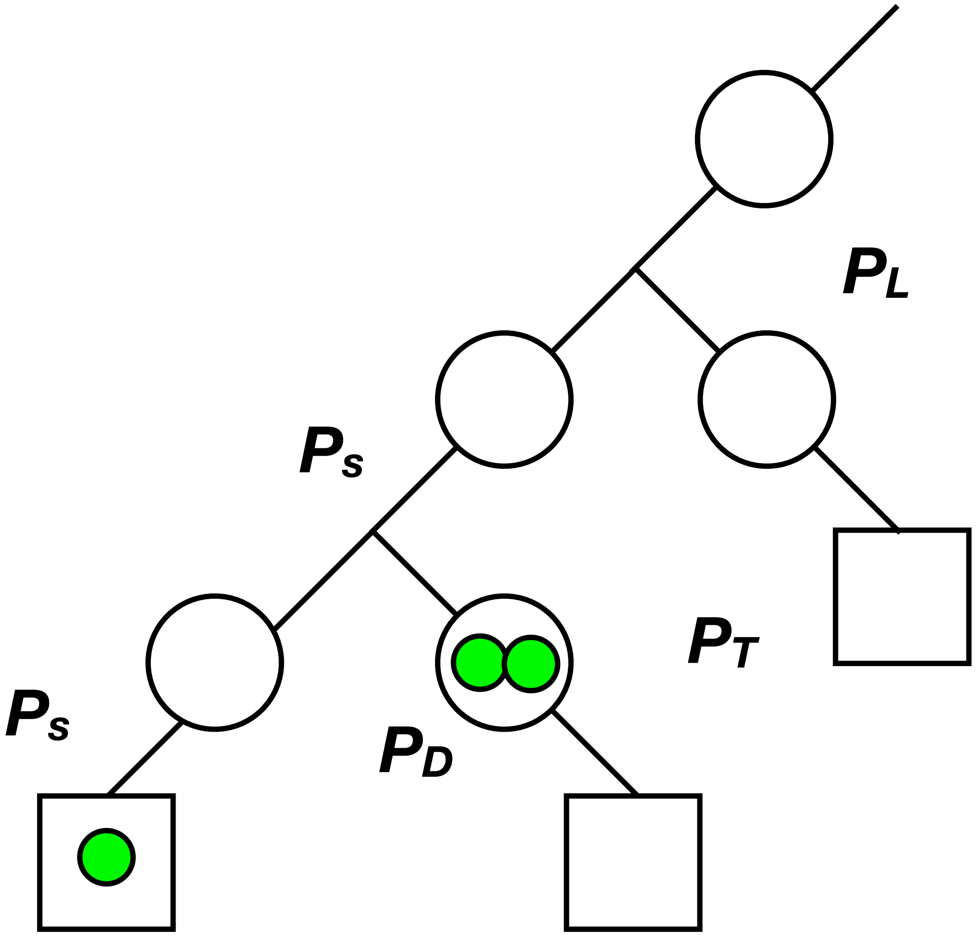


“undated”
DTL
species tree

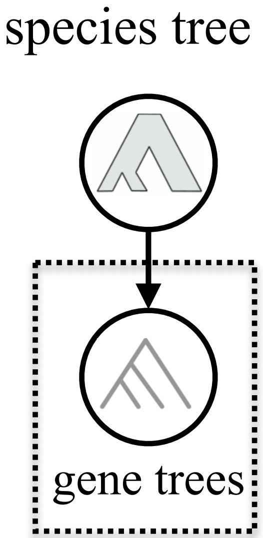


abcd/

“undated”
DTL



“undated”
DTL



`abcd/`

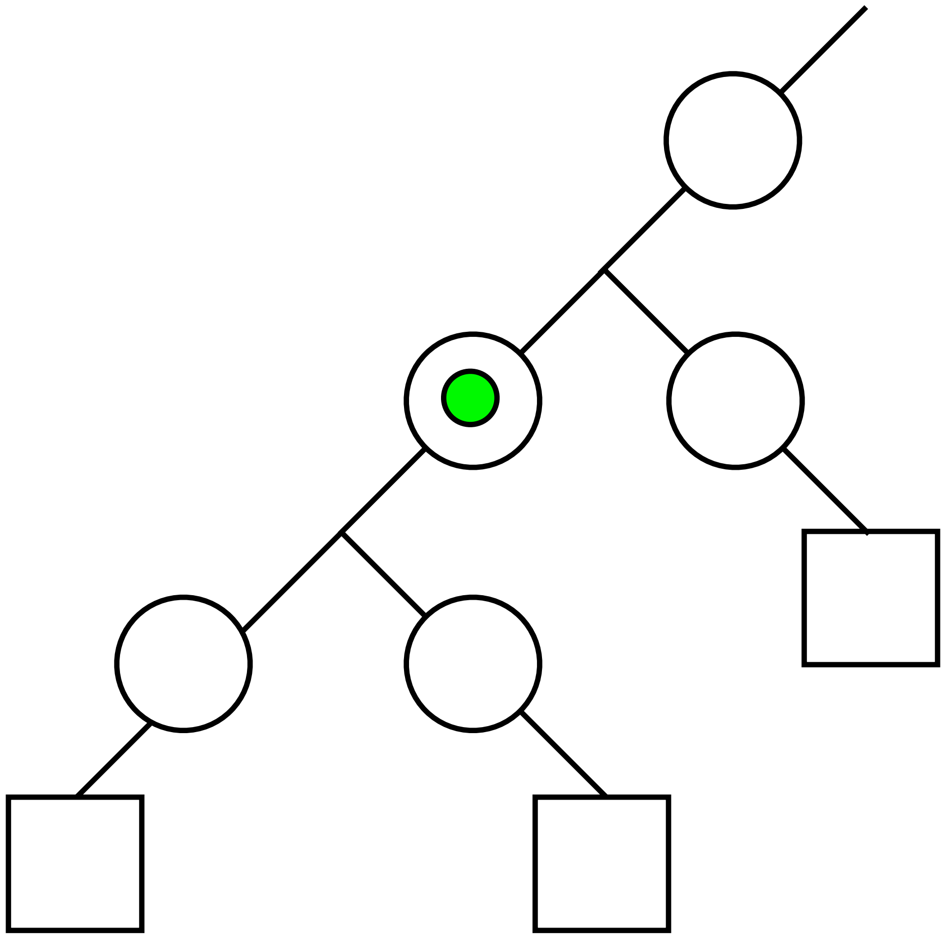
“undated” DTL

What do you see that is different compared to ALEml?

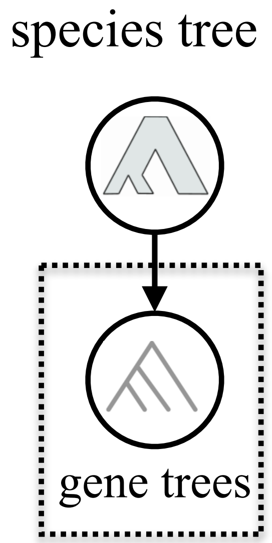
```
ALEml_undated abcd_S.tree g.tree.ale sample=10
```

```
ALEml_undated cdab_S.tree g.tree.ale sample=10
```

```
ALEml_undated abc-d_S.tree g.tree.ale sample=10
```



“undated”
DTL



`abcd/`

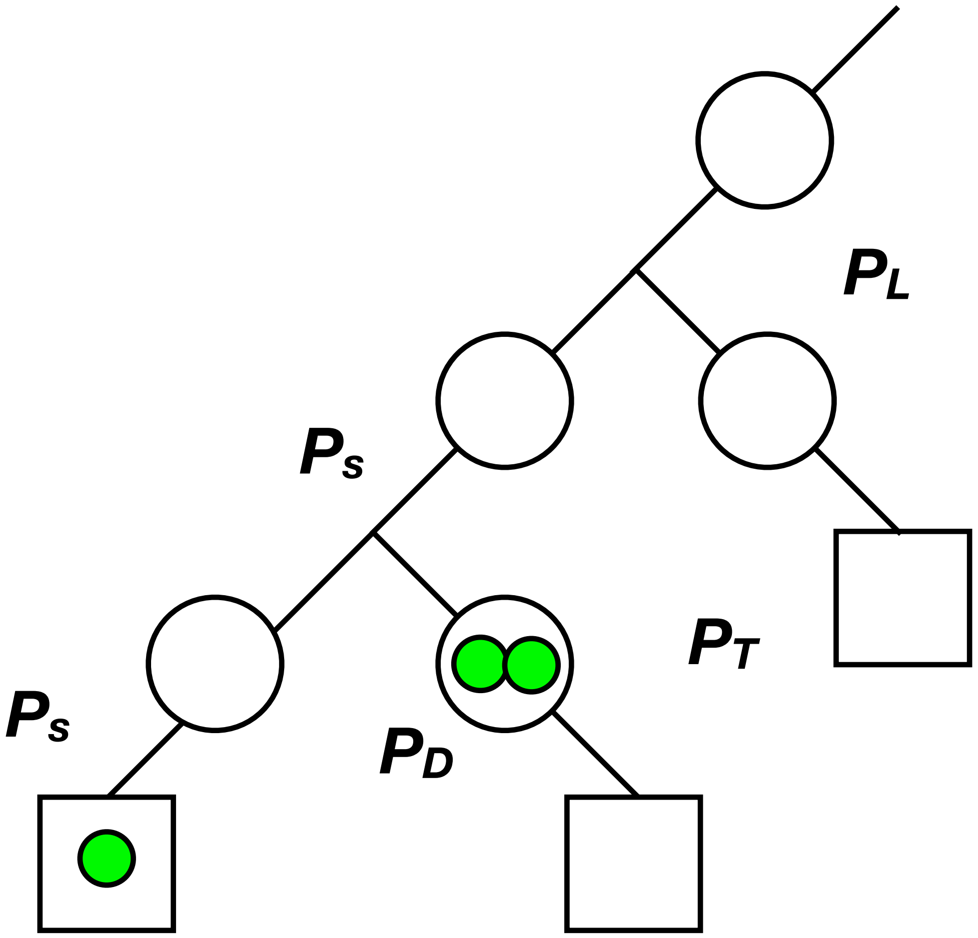
“undated” DTL

What do you see that is different compared to ALEml?

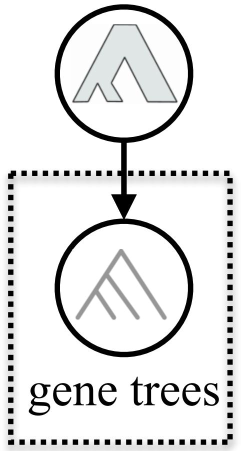
```
ALEml_undated abcd_S.tree g.tree.ale sample=10
```

```
ALEml_undated cdab_S.tree g.tree.ale sample=10
```

```
ALEml_undated abc-d_S.tree g.tree.ale sample=10
```

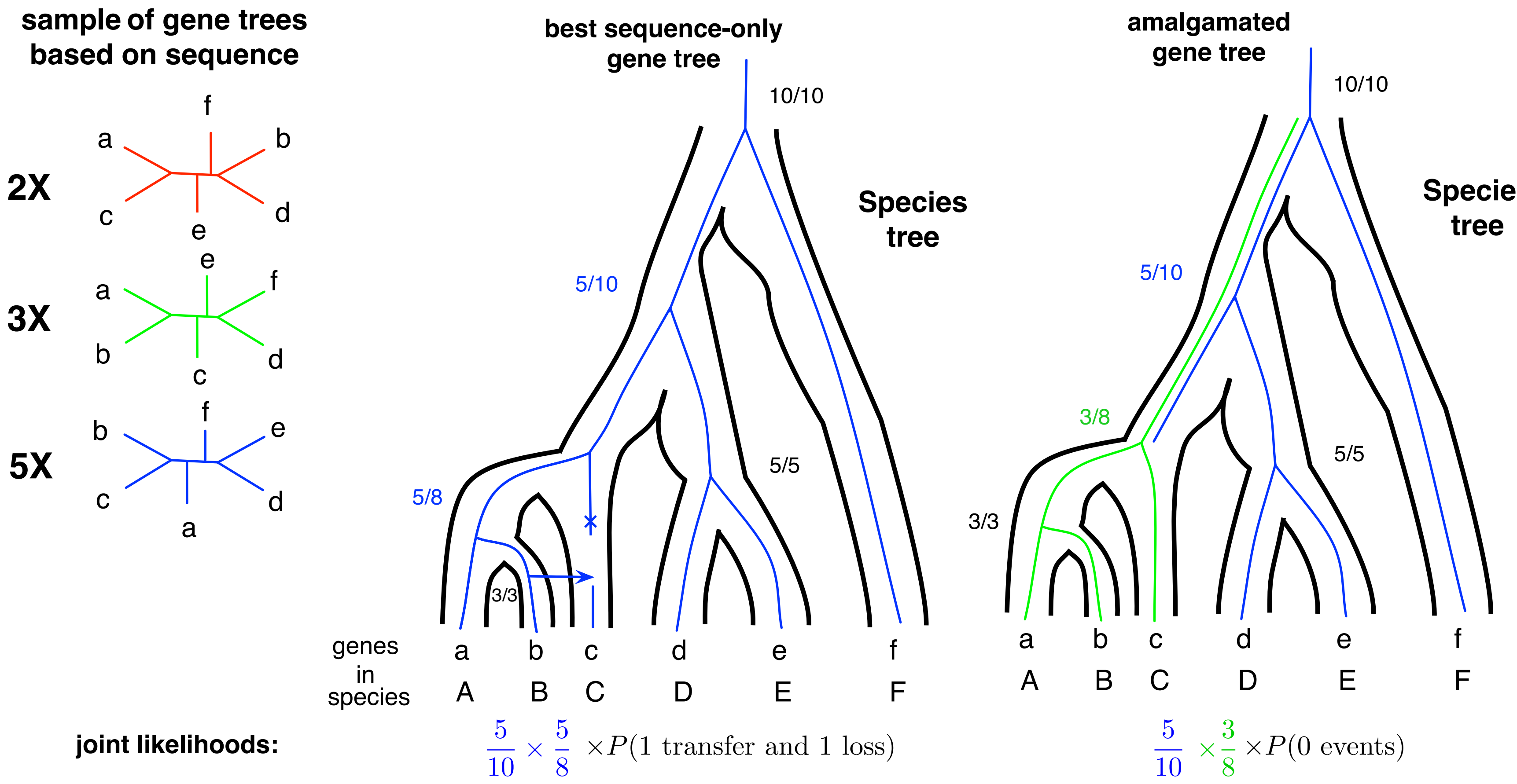


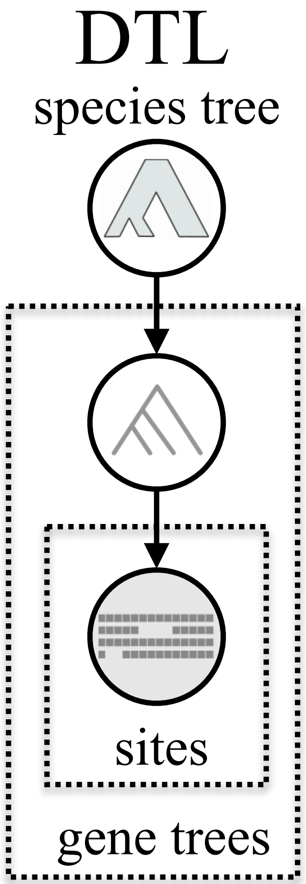
“undated” DTL



Efficiently exploring the space of reconciled gene trees

Based on a sample of trees conditional clade probabilities can be used to estimate posterior probability of any gene tree that can be amalgamated. This is usually a very large number of trees (e.g. for 10^4 samples 10^{12} trees, but up to 10^{40}). *The dynamic programming used in gene tree-species tree reconciliation can be extended to approximate the joint likelihood efficiently for a very large set of gene trees.*





implemented in ALE:

http://github.com/ssolo/ALE

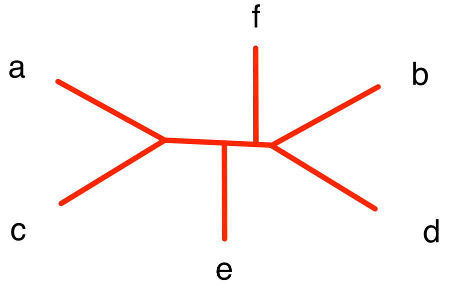
Szöllősi, Tannier, Lartillot & Daubin *Systematic Biology* (2013)
Lateral Gene Transfer from the Dead

Szöllősi, Rosikiewicz, Boussau, Tannier & Daubin *Systematic Biology* (2013)
Efficient exploration of the space of reconciled gene trees

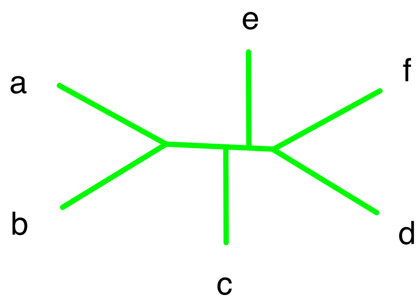
abcdef/

```
$ cd ~/workshop_materials/lab_data/abcdef
```

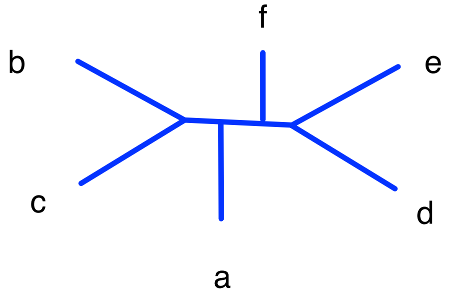
red.tree



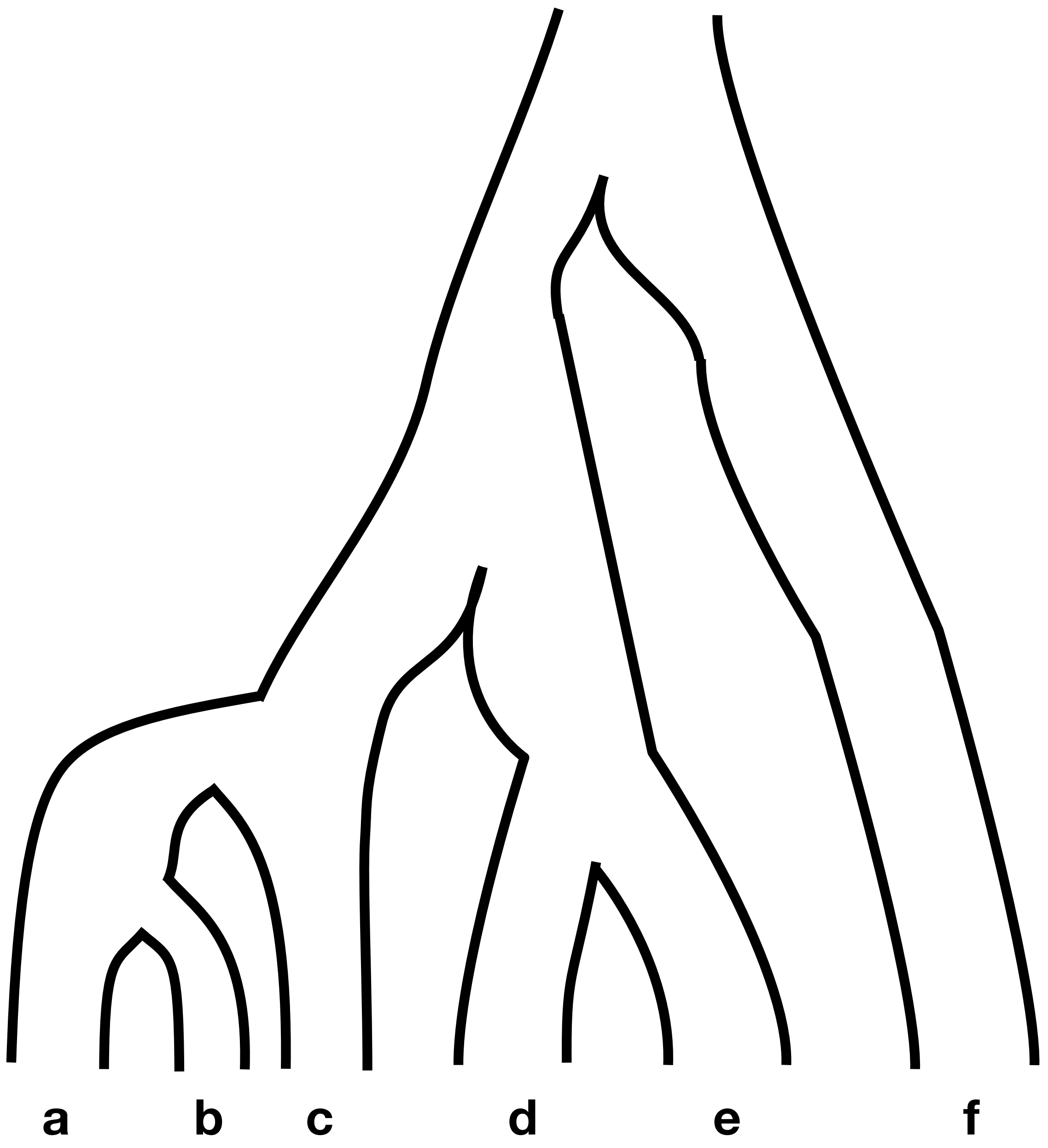
green.tree

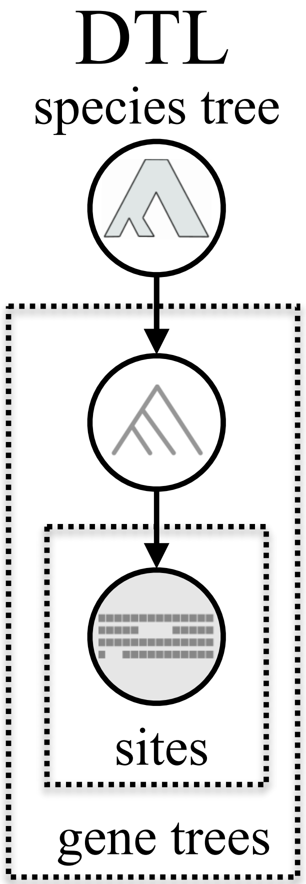


blue.tree



S.tree

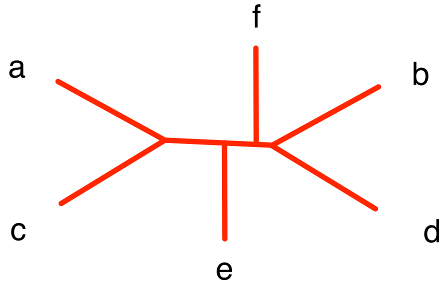




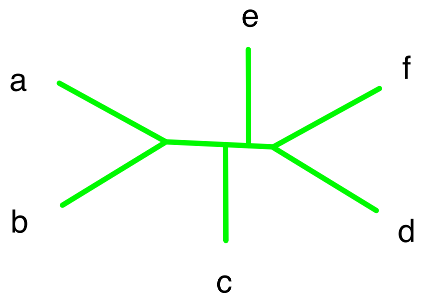
`abcdef/`

Use ALEml (and/or ALEml_undated) **on each gene tree to estimate ML rates and sample reconciliations with the specie tree**

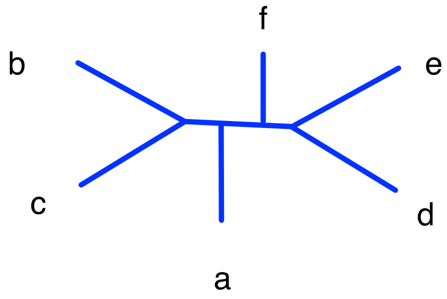
red.tree



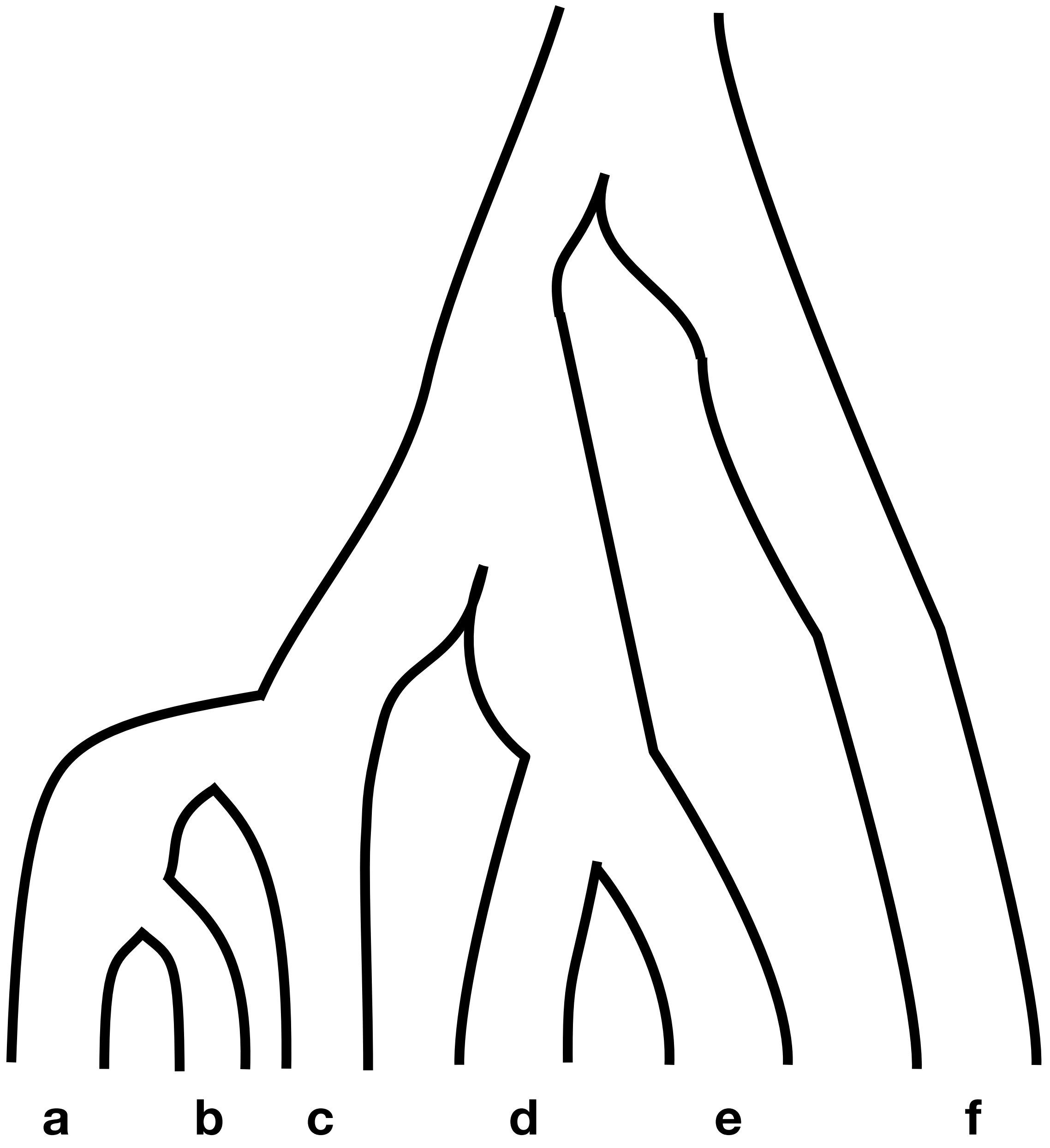
green.tree

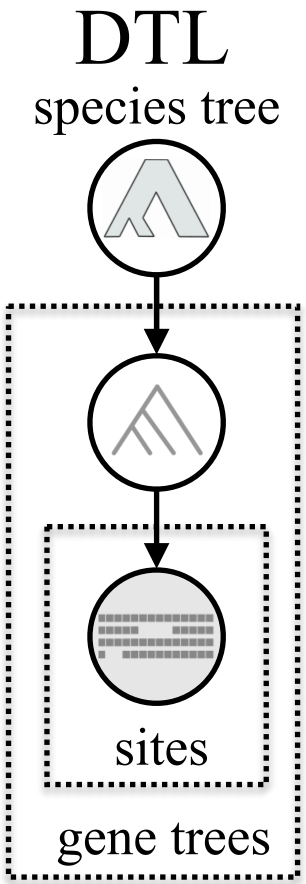


blue.tree



S.tree

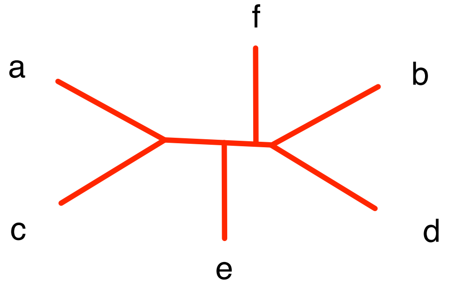




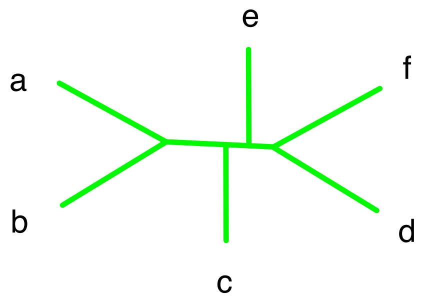
`abcdef/`

```
ALEml S.tree blue.tree.ale
ALEml S.tree green.tree.ale
ALEml S.tree red.tree.ale
```

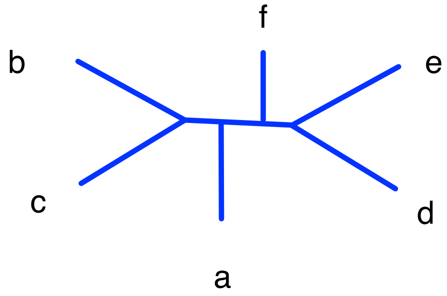
red.tree

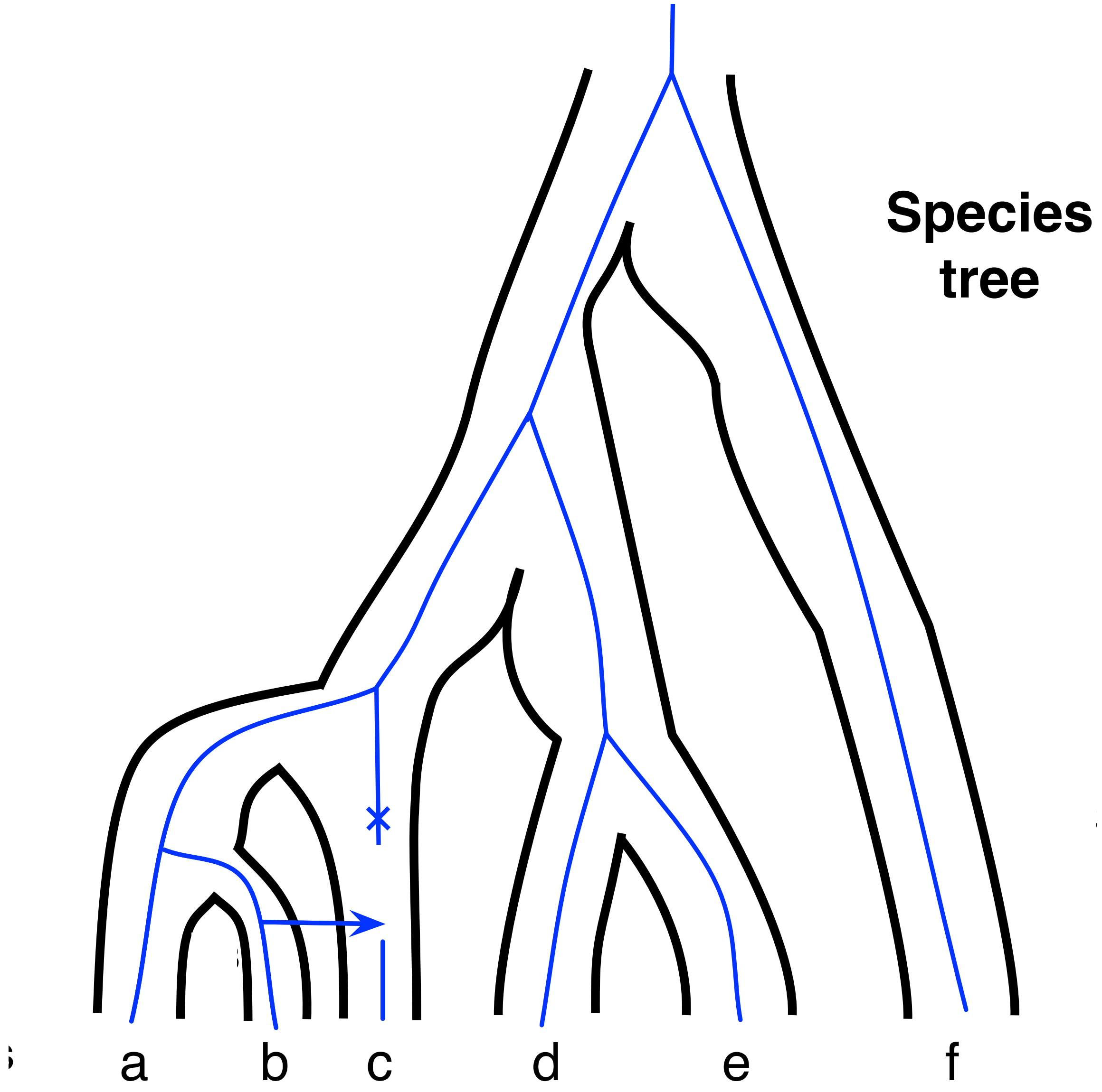


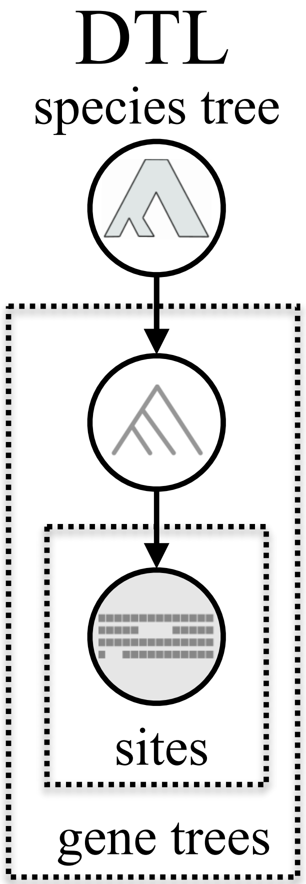
green.tree



blue.tree







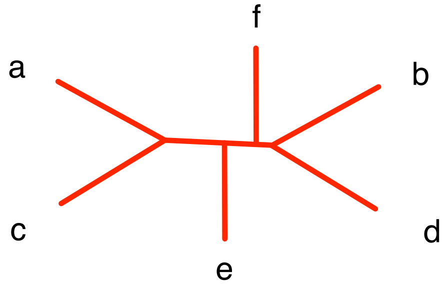
`abcdef/`

Combine the three trees into the same file to have 2x red.tree, 3x green.tree, 5x blue.tree

Then use ALEml (and/or ALEml_undated) on each gene tree to estimate ML rates and sample reconciliations with the specie tree

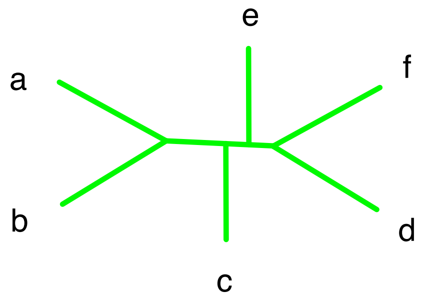
red.tree

2x



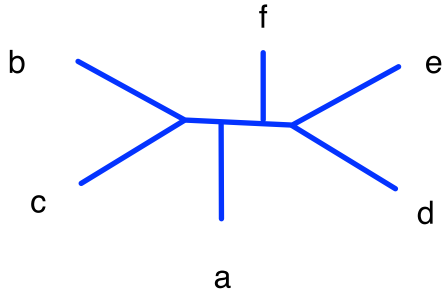
green.tree

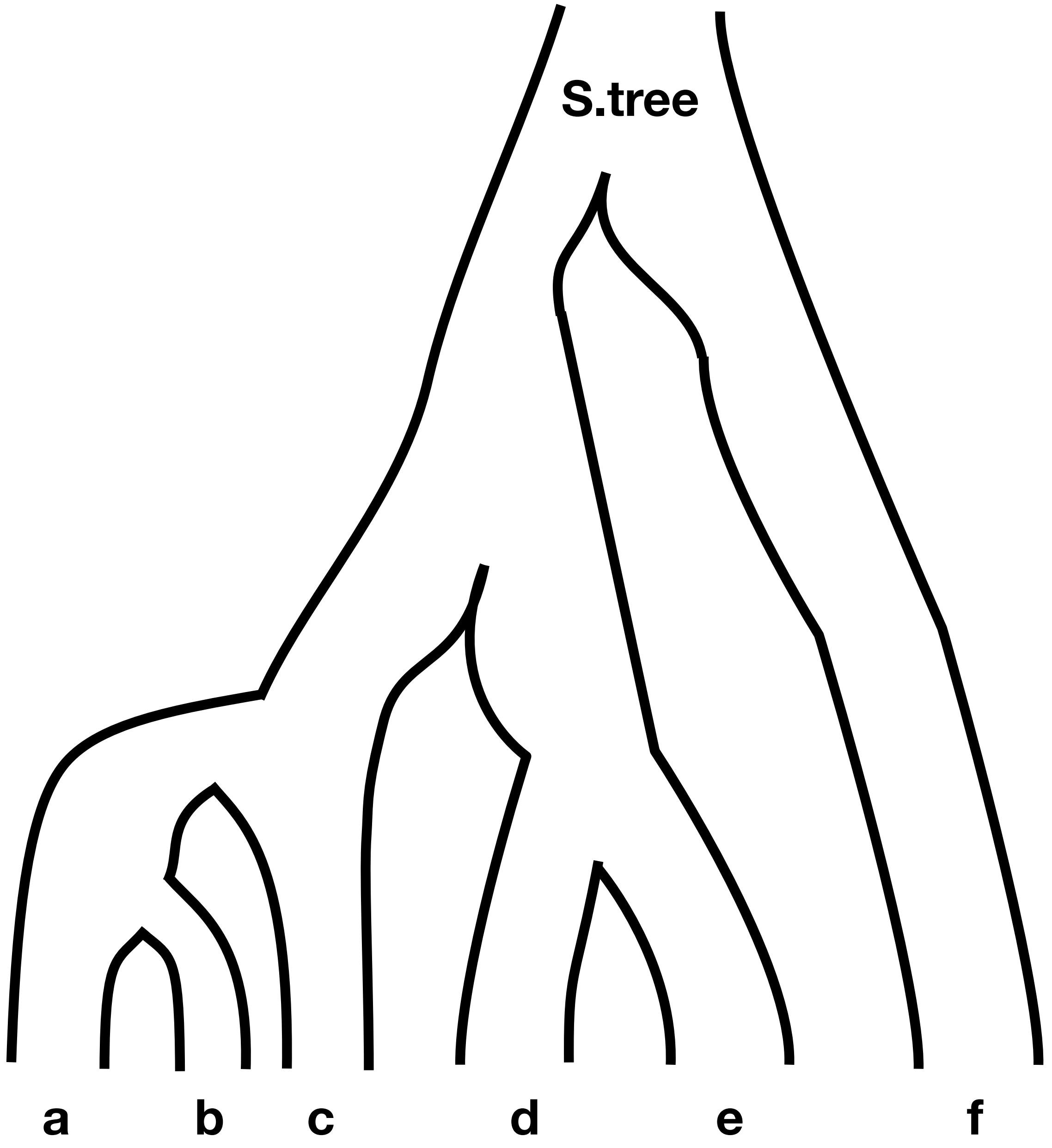
3x

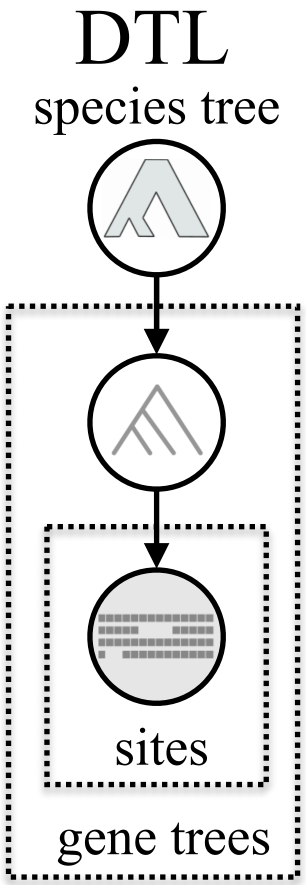


blue.tree

5x

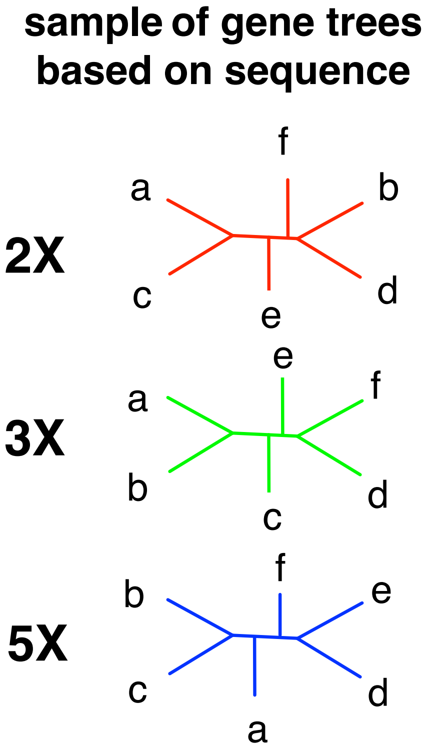


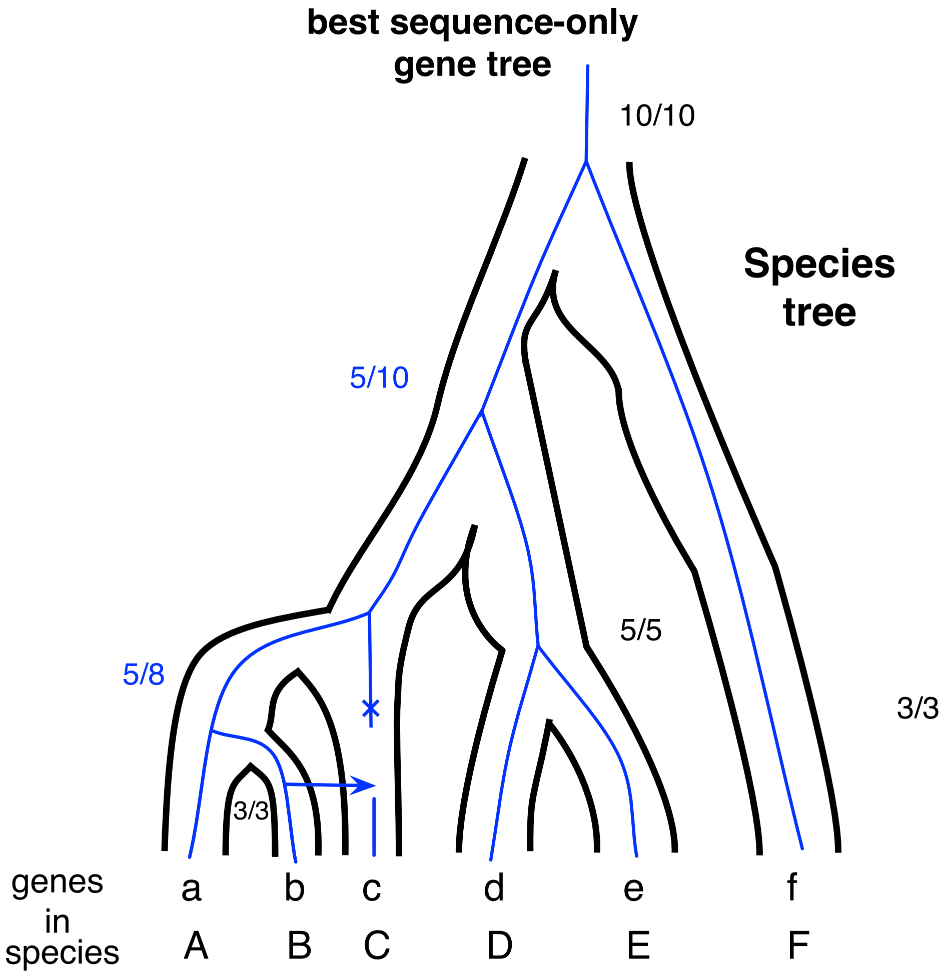


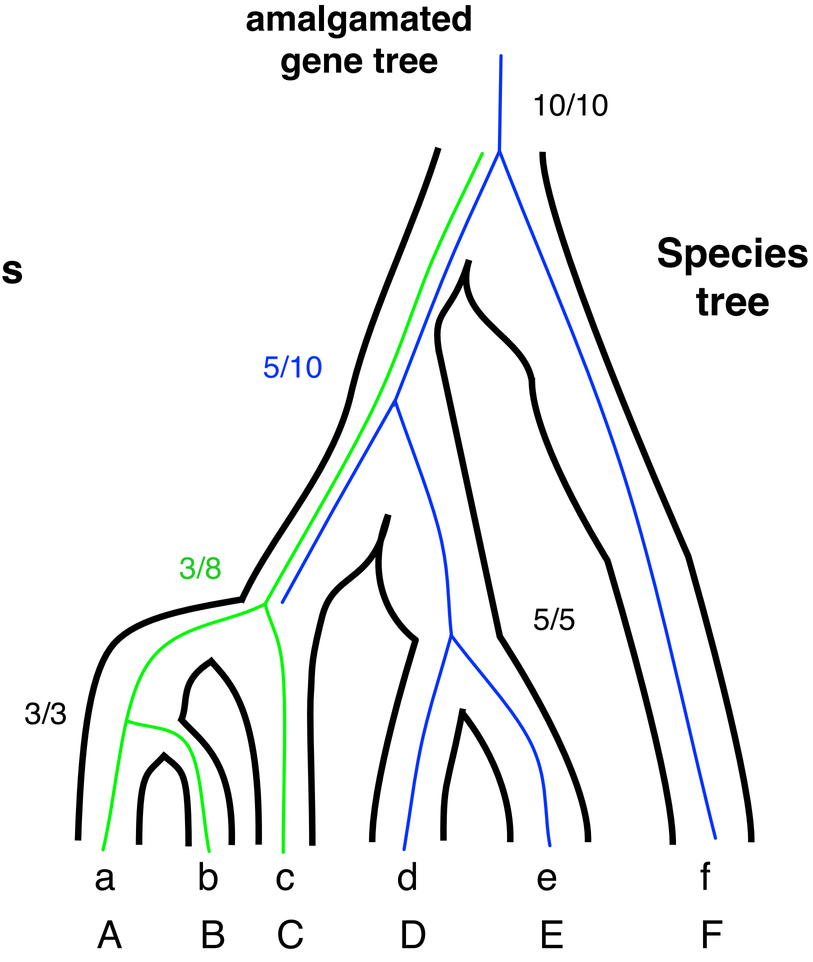


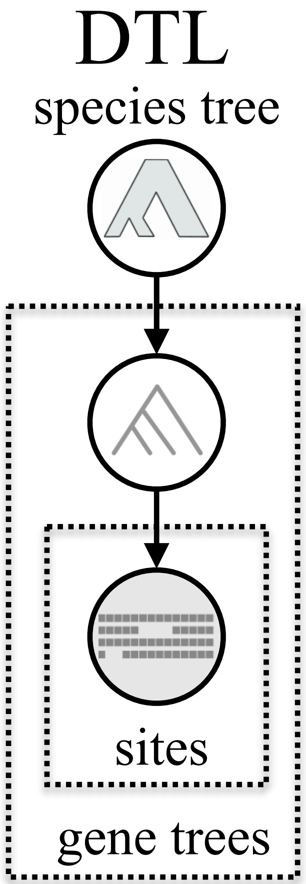
`abcdef/`

```
ALEml S.tree help/rgb.trees.ale
```









joint likelihoods:

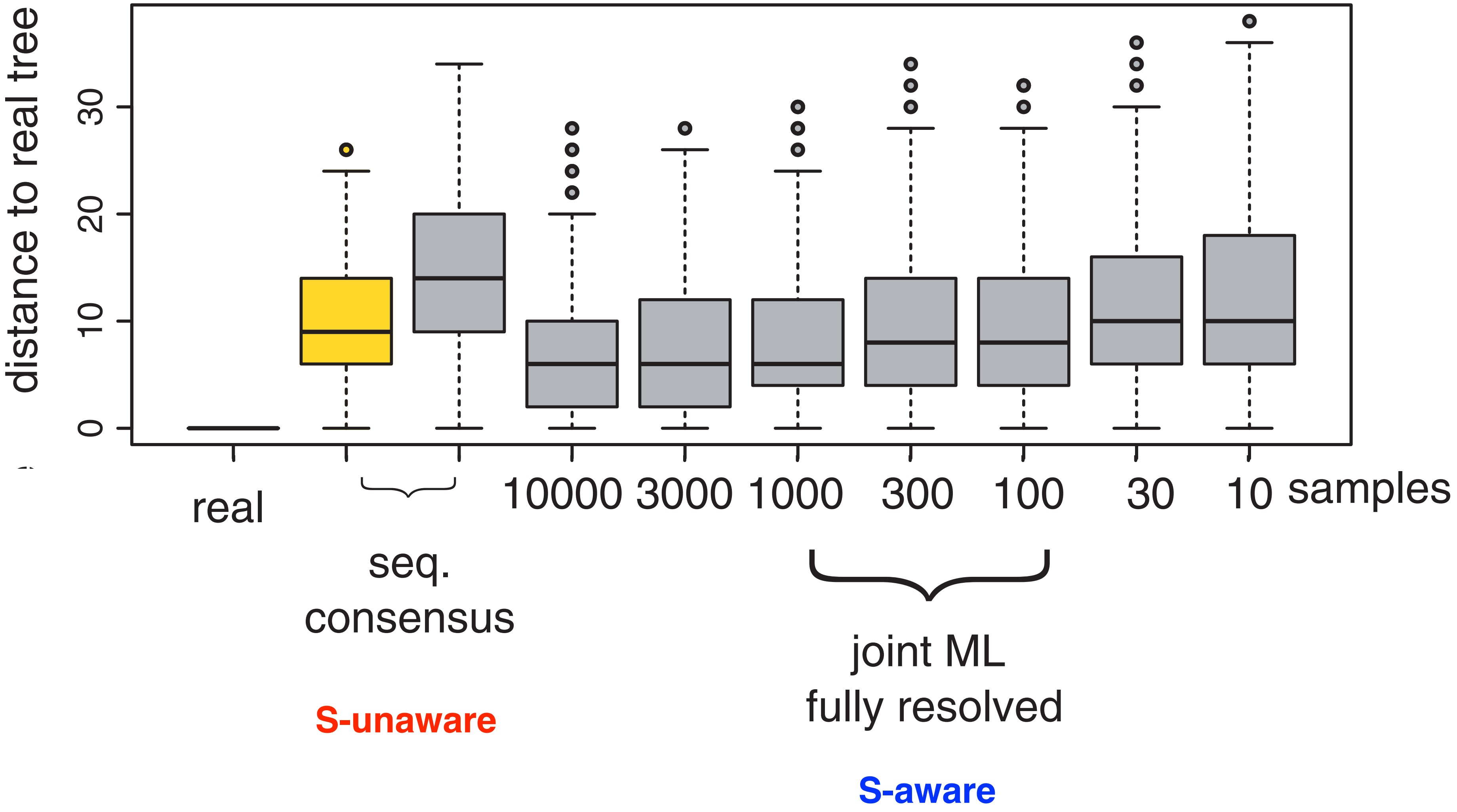
$\frac{5}{10} \times \frac{5}{8} \times P(1 \text{ transfer and } 1 \text{ loss})$

$\frac{5}{10} \times \frac{3}{8} \times P(0 \text{ events})$

Efficiently exploring the space of reconciled gene trees

Based on a sample of trees conditional clade probabilities can be used to estimate posterior probability of any gene tree that can be amalgamated. This is usually a very large number of trees (e.g. for 10^4 samples 10^{12} trees, but up to 10^{40}).

<u>more samples the better</u>

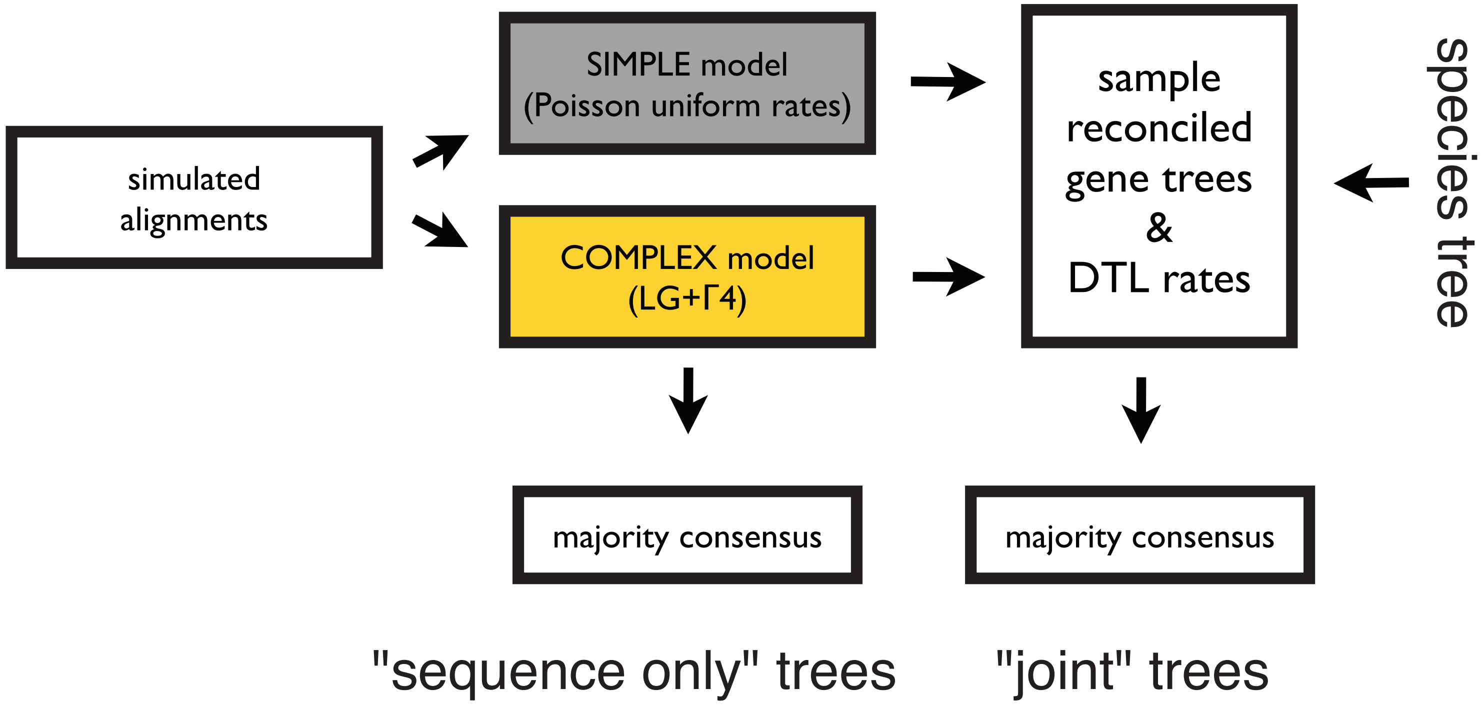


`real_data/simulated/sc_univ_fams`

Real data!

OK .. first realistic data

```
$ cd ~/workshop_materials/lab_data/real_data/simulated
$ cd sc_univ_fams
```



simulated alignments

SIMPLE model (Poisson uniform rates)

COMPLEX model (LG+Γ4)

sample reconciled gene trees & DTL rates

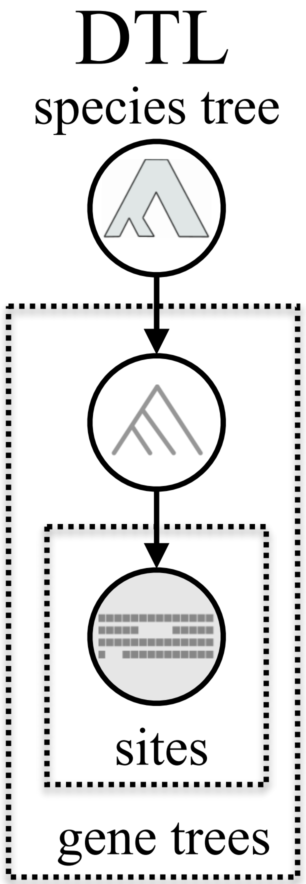
species tree

majority consensus

majority consensus

"sequence only" trees

"joint" trees



`real_data/simulated/sc_univ_fams`

Real data!

OK .. first realistic data

Sample trees using bootstrap and take a look:

```
iqtree2 -m LG -bb 10000 -s HBG486560_sim.fasta -wbtl
less HBG486560_sim.fasta.ufboot
```

Run ALEml_undated on the ML tree

```
ALEobserve HBG486560_sim.fasta.treefile
ALEml_undated ../S.tree HBG486560_sim.fasta.treefile.ale
```

Run ALEml_undated on the **true** tree

```
ALEobserve HBG486560_true.tree
ALEml_undated ../S.tree HBG486560_true.tree.ale
```

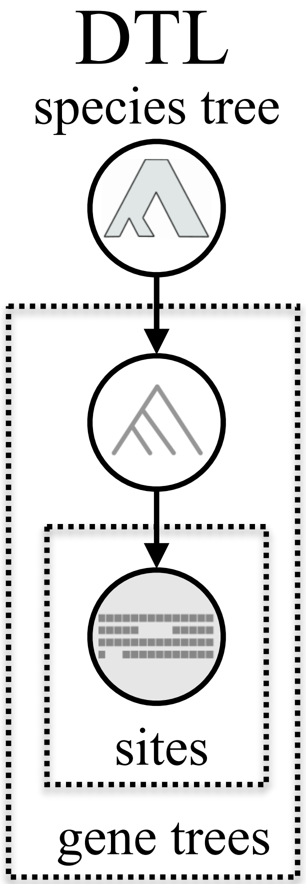
Run ALEml_undated on the **sample of trees**

```
ALEobserve HBG486560_sim.fasta.ufboot
ALEml_undated ../S.tree HBG486560_sim.fasta.ufboot.ale
```

Do the same for HBG747311_sim.fasta..

What do you see?

(Hint: compare the “Total” rows giving the avg. number of events)



`real_data/sc_univ_fams`

Real data!

```
$ cd ~/workshop_materials/lab_data/real_data/
$ cd sc_univ_fams
```

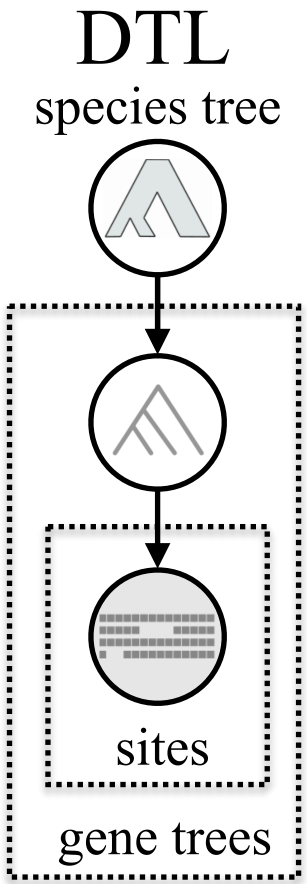
Run ALEml_undated on the ML tree

```
ALEml_undated ../S.tree HBG486560_real.fasta.treefile.ale
```

we don't know the true tree, sorry

Run ALEml_undated on the **sample of trees** from phylobayes

```
ALEml_undated ../S.tree HBG486560_real.ale
```



What do you see?

(Hint: compare the "Total" rows giving the avg. number of events)

`real_data/sc_univ_fams`

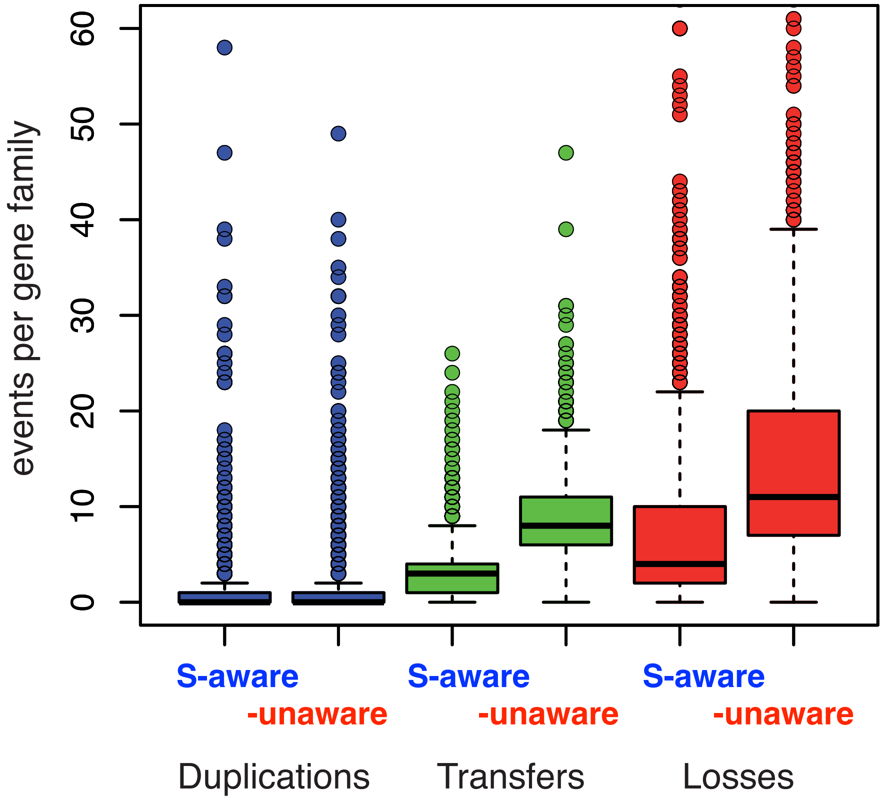
Real data!

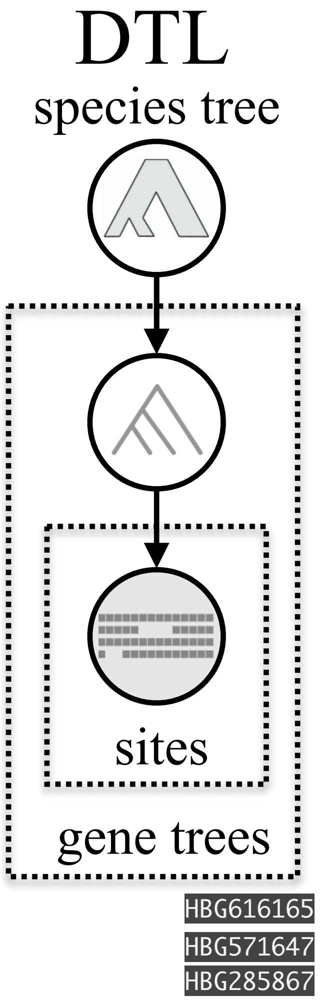
```
ALEml_undated ../S.tree HBG486560_real.fasta.treefile.ale
```

```
# of     Duplications    Transfers        Losses   Speciations
Total    0               6.25             3.96     32.71
```

```
ALEml_undated ../S.tree HBG486560_real.ale
```

```
# of     Duplications    Transfers        Losses   Speciations
Total    0               1.05             0.99     34.94
```





`real_data/sc_univ_fams`

Real data!

```
ALEml_undated ../S.tree HBG486560_real.fasta.treefile.ale
```

```
# of     Duplications       Transfers          Losses   Speciations
Total    0                  6.25               3.96     32.71
```

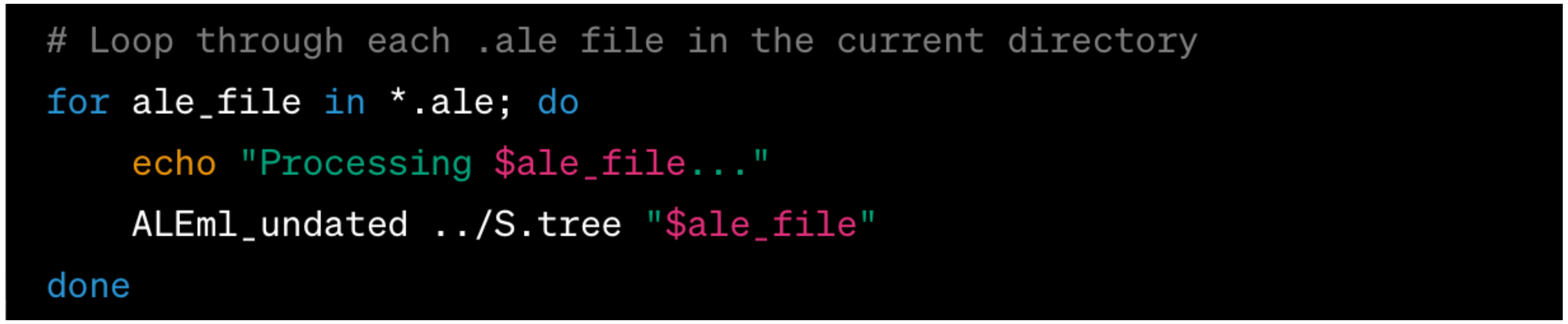
```
ALEml_undated ../S.tree HBG486560_real.ale
```

```
# of     Duplications       Transfers          Losses   Speciations
Total    0                  1.05               0.99     34.94
```

Can you find a true orthologous family?

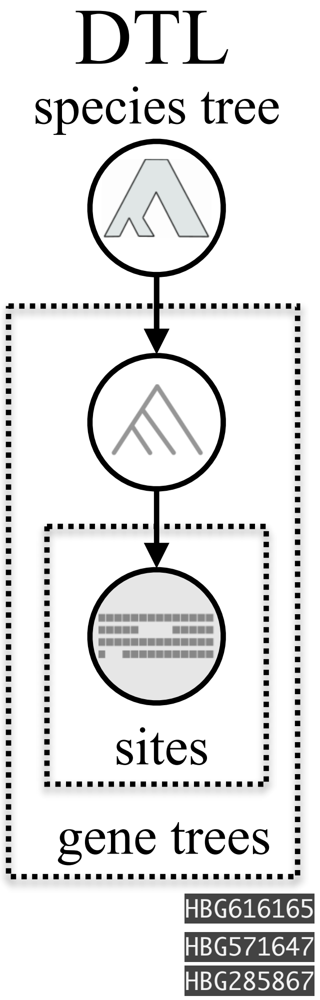
(i.e. a family with 0 Duplication , Transfer and Loss events)

Hint: if you are less familiar with the command line you can ask ChatGPT or Bard how to run the same command on multiple files?



```
# Loop through each .ale file in the current directory
for ale_file in *.ale; do
    echo "Processing $ale_file..."
    ALEml_undated ../S.tree "$ale_file"
done
```

ChatGPT

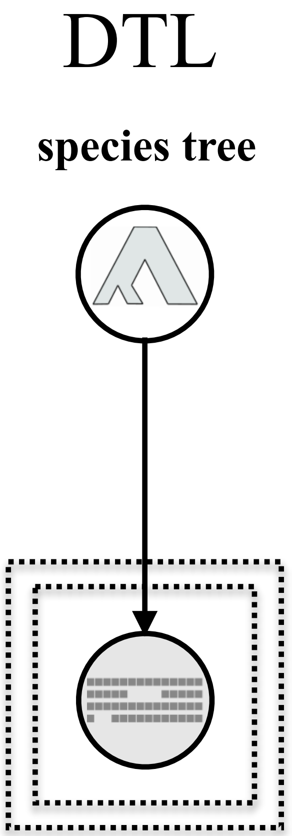


`real_data/general_fams`

Real data!

```
$ cd ~/workshop_materials/lab_data/real_data/simulated
$ cd general_fams
```

Find the rooted species tree with the highest likelihood using DTL by summing the log-likelihood across all .ale files (cf. bash command on previous page) for each candidate species tree S.tree, S_alt1.tree, S_alt2.tree (or your own rerooted version of S.tree made with seaview or FigTree).



```
ALEml_undated ../S.tree $ale_file
```

```
$ wget http://ssolo.web.elte.hu/S_alt1.tree
ALEml_undated S_alt1.tree $ale_file
```

```
$ wget http://ssolo.web.elte.hu/S_alt2.tree
ALEml_undated S_alt2.tree $ale_file
```

Bonus/Home Work:
try our new implementation that can do this and a lot more for you (efficiently using MPI):

https://github.com/BenoitMorel/AleRax.git

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Join us for a postdoc at the interface of computational & evolutionary biology! Use probabilistic models & machine learning to model coevolution, reconstruct the Tree of Life, understand somatic evolution or pursue your own project..

`Model-Based Evolutionary Genomics Unit`
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`https://www.oist.jp/research/research-units/modevolgenom`

`Okinawa Institute of Science and Technology`

gergely.szollosi@oist.jp

Bonus/Home Work:
try our new implementation that can do this and a lot more for you (efficiently using MPI):
https://github.com/BenoitMorel/AleRax.git