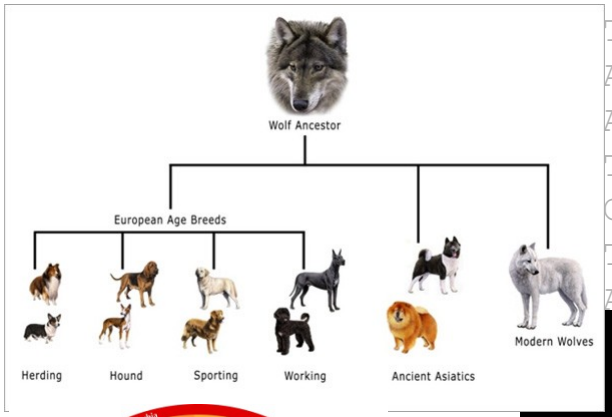
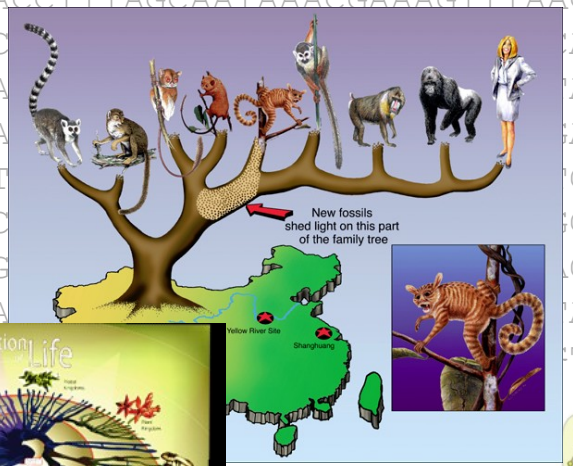
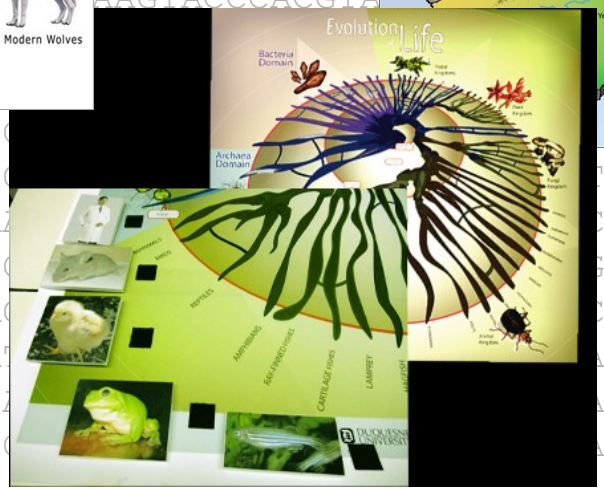
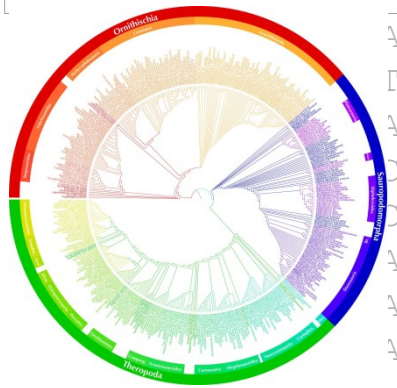
MODULARIZACE VÝUKY EVOLUČNÍ A EKOLOGICKÉ BIOLOGIE
CZ.1.07/2.2.00/15.0204

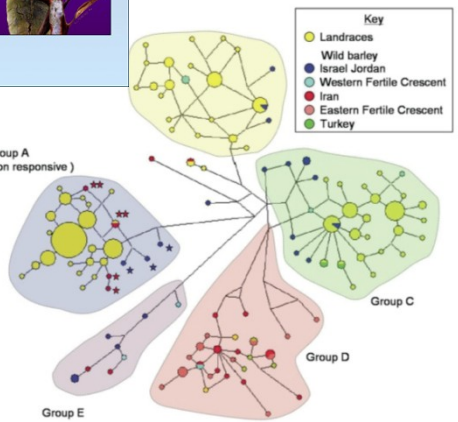
FYLOGENETICKÁ ANALÝZA I.











esf evropský sociální fond v ČR
EVROPSKÁ UNIE
MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY
OP Vzdělávání pro konkurenceschopnost
INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Definice základních pojmů:

fylogenetický strom = fylogenie (*phylogeny*): s kořenem, bez kořene

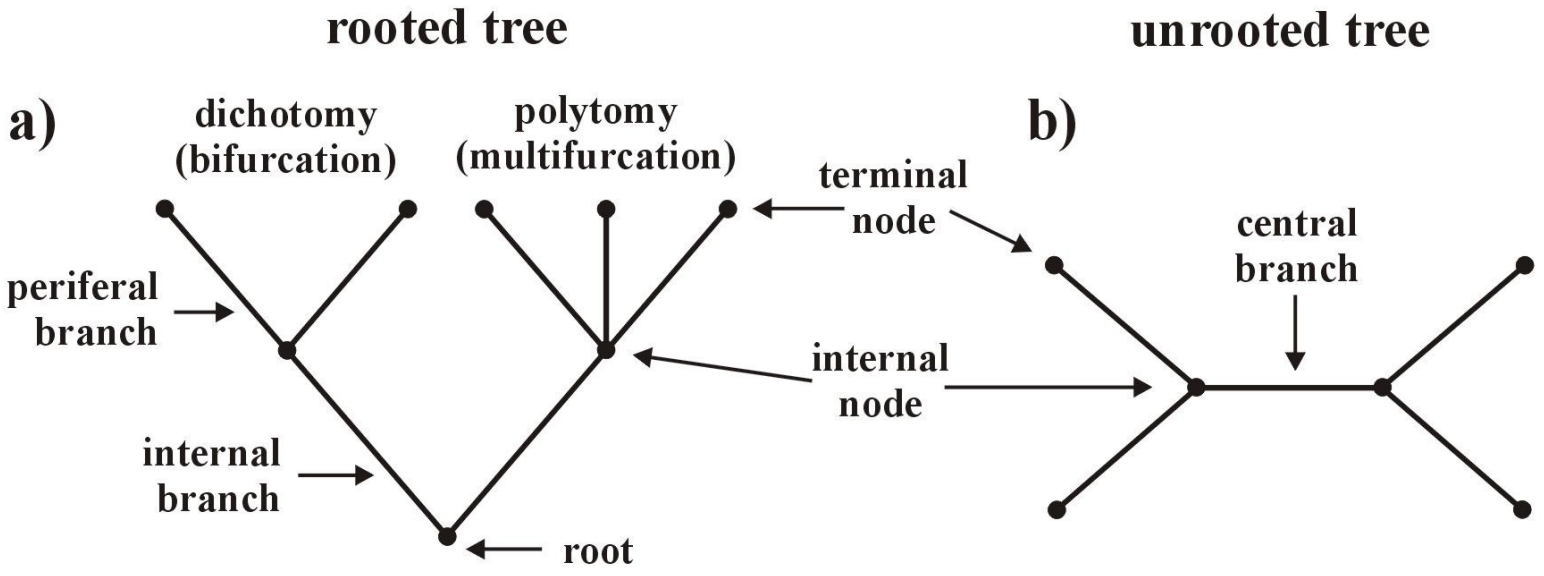
větve (*branches*, *edges*): vnější, vnitřní, centrální

uzly (*nodes*, *vertices*): vnitřní, terminální (externí)

dichotomie, polytomie

OTU, HTU

topologie



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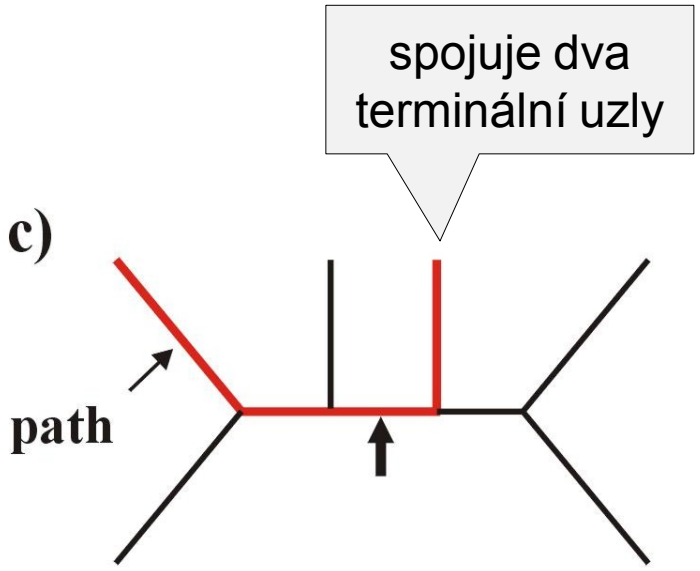
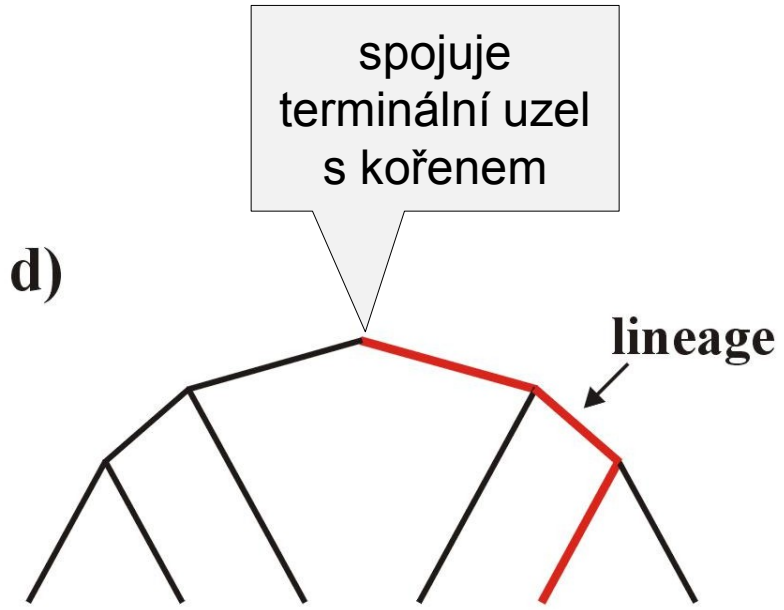
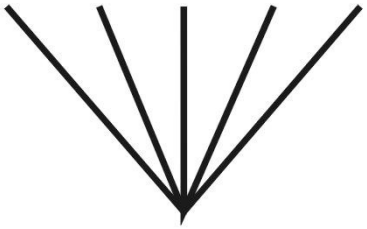


dráha

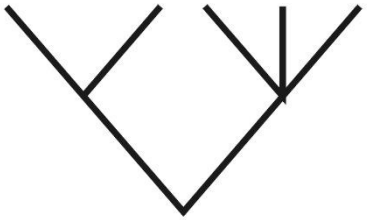


linie

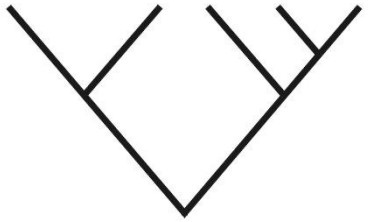
Definice základních pojmů:



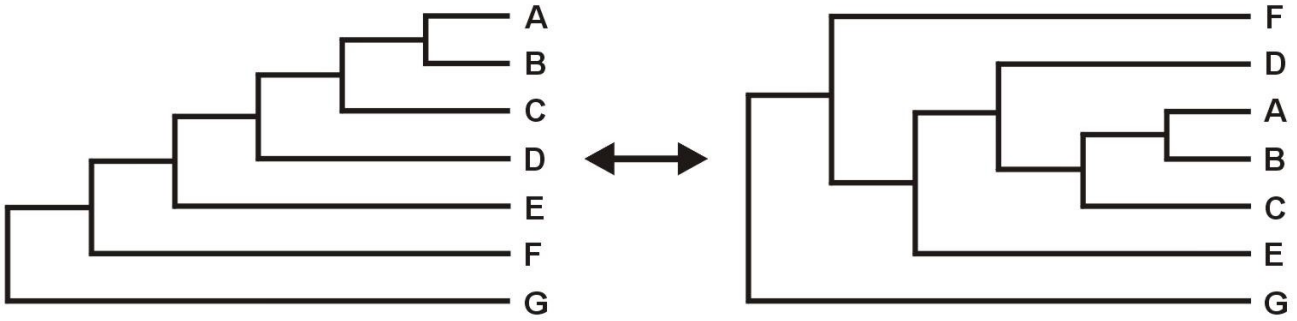
star tree

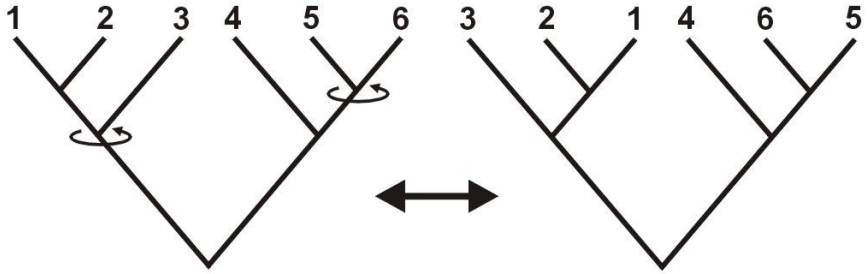


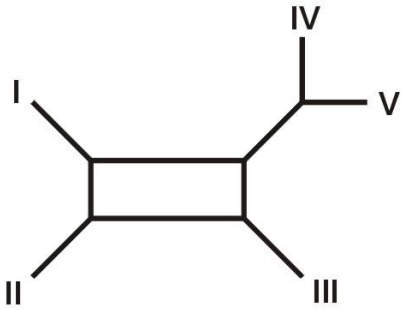
partly resolved



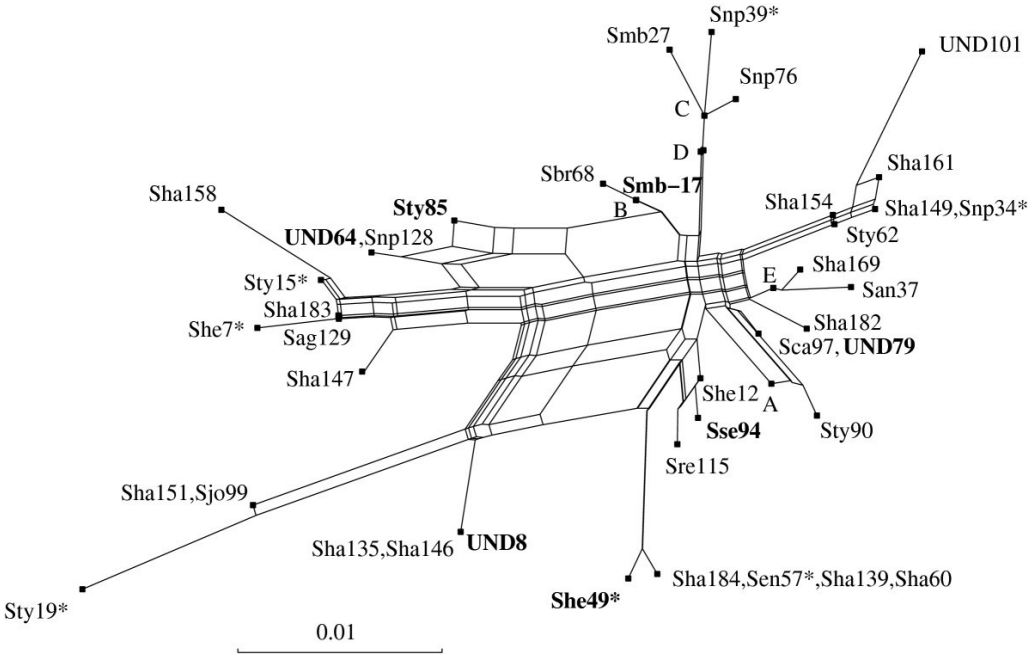
fully resolved

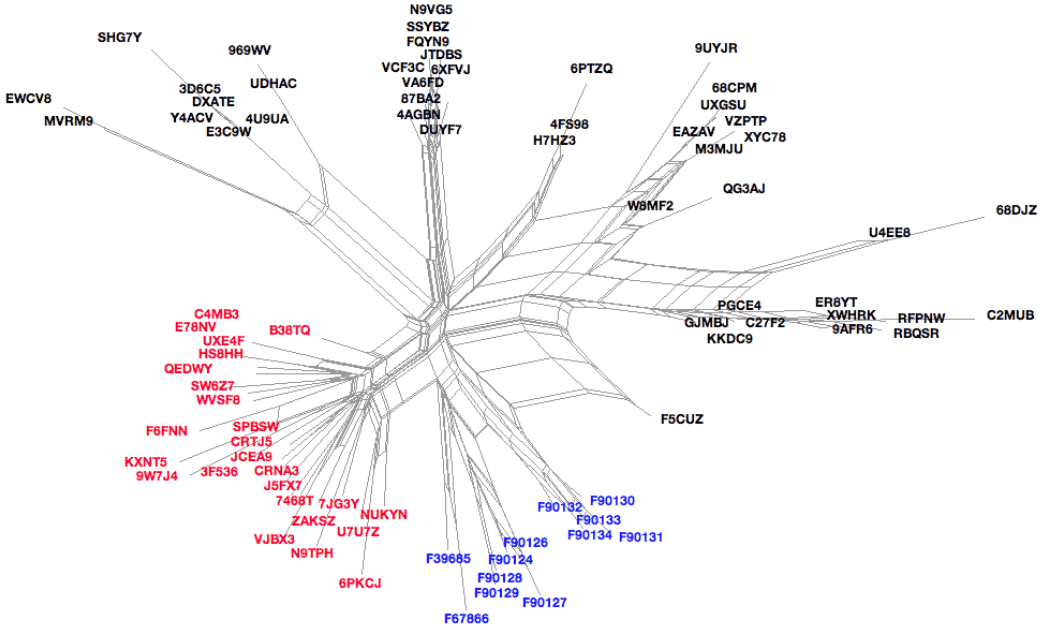




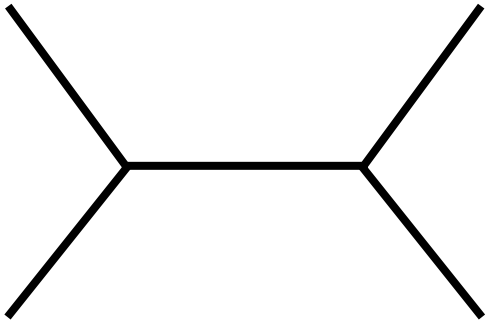


network

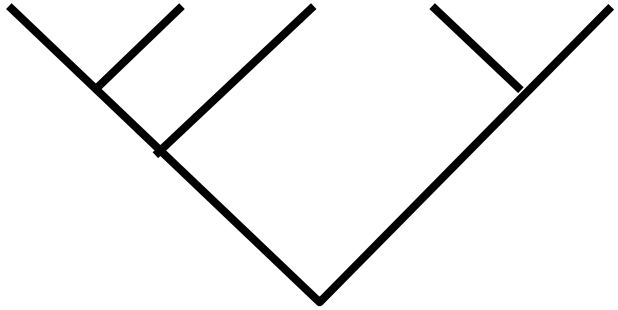

Snp39*
Smb27
UND101
Snp76
C
D
Sha161
Sbr68
Smb−17
Sha158
Sty85
B
Sha154
Sha149,Snp34*
UND64,Snp128
Sty62
Sty15*
Sha169
E
San37
Sha183
Sha182
She7*
Sag129
Sca97, UND79
Sha147
She12
A
Sse94
Sty90
Sre115
Sha151,Sjo99
Sha135,Sha146
UND8
Sty19*
Sha184,Sen57*,Sha139,Sha60
She49*
0.01


N9VG5
SSYBZ
FQYN9
JTDBS
SHG7Y
969WV
VCF3C
6XFVJ
6PTZQ
9UYJR
3D6C5
UDHAC
VA6FD
68CPM
EWCV8
DXATE
87BA2
UXGSU
MVRM9
Y4ACV
4U9UA
4AGBN
VZPTP
4FS98
E3C9W
DUYF7
EAZAV
XYC78
H7HZ3
M3MJU
QG3AJ
W8MF2
68DJZ
U4EE8
PGCE4
ER8YT
C4MB3
XWHRK
C2MUB
GJMBJ
C27F2
RFPNW
E78NV
B38TQ
9AFR6
KKDC9
RBQSR
UXE4F
HS8HH
QEDWY
SW6Z7
WVSF8
F5CUZ
F6FNN
SPBSW
CRTJ5
JCEA9
KXNT5
9W7J4
3F536
CRNA3
J5FX7
7468T
7JG3Y
F90130
F90132
NUKYN
F90133
ZAKSZ
F90134
F90131
U7U7Z
VJBX3
F90126
N9TPH
F39685
F90124
6PKCJ
F90128
F90129
F90127
F67866

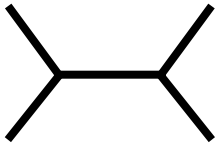
Kolik existuje stromů?



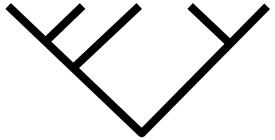
$$\frac{(2n-2)!}{2^{n-2}(n-2)!}$$



$$\frac{(2n-2)!}{2^{n-2}(n-2)!}$$



$$\frac{(2n-3)!}{2^{n-2}(n-2)!}$$



$$\frac{(2n-2)!}{2^{n-1}(n-1)!}$$

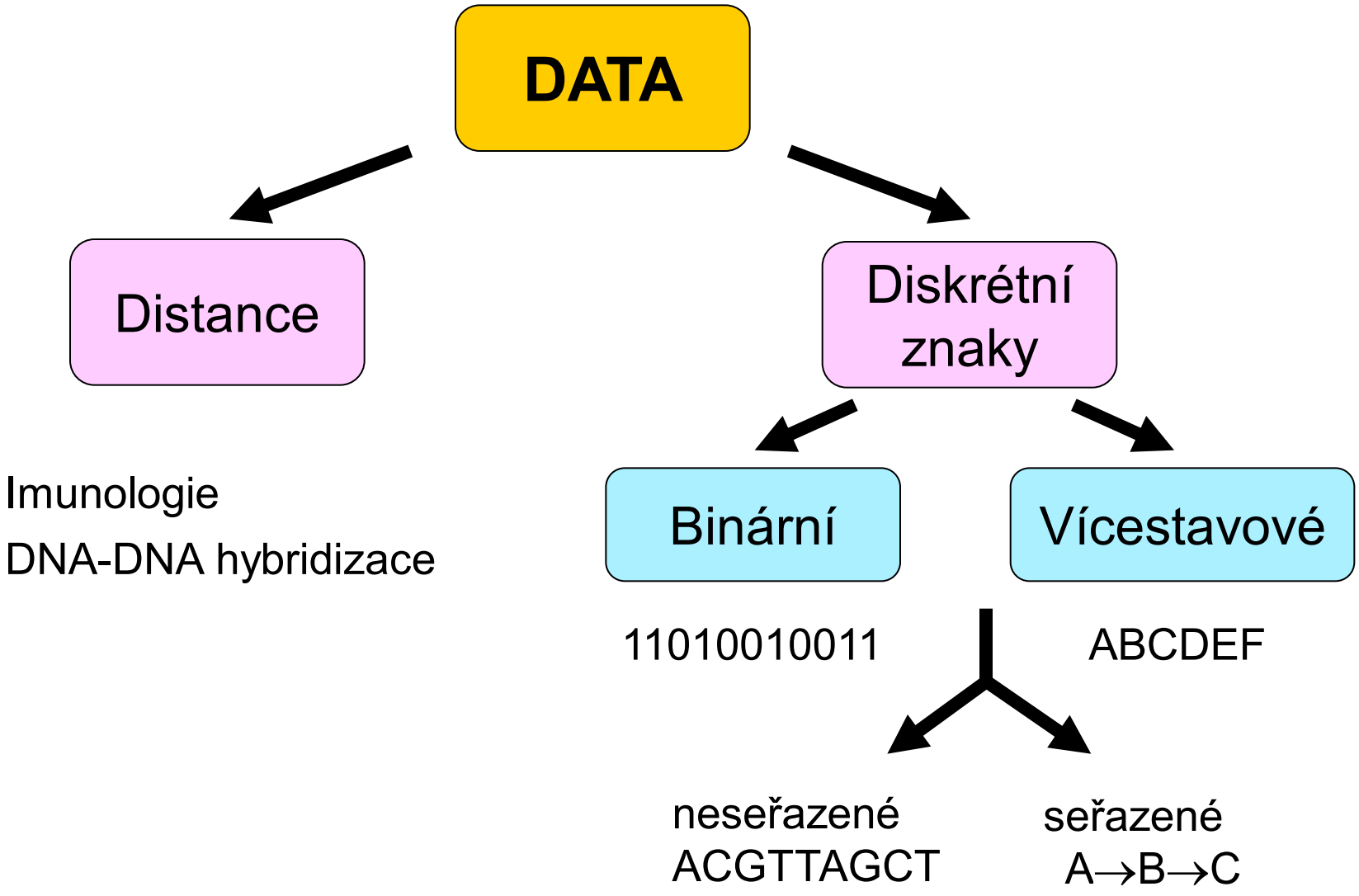
No. Taxons	Unrooted trees	Rooted trees
3	1	3
4	3	15
5	15	105
6	105	945
7	945	10 395
8	10 395	135 135
9	135 135	2 027 025
10	2 027 025	34 459 425
11	34 459 425	654 729 075
12	654 729 075	13 749 310 575
13	13 749 310 575	316 234 143 225
14	316 234 143 225	7 905 853 580 625
15	7 905 853 580 625	213 458 046 676 875
20	213 458 046 676 875	8 [illegible] 375
30	8 200 794 532 [illegible] 637 891 559 375	[illegible] 10^{38}
40	$4{,}9518\times10^{38}$	[illegible] 10^{57}
50	$1{,}00986\times10^{57}$	[illegible] 10^{76}

> Avogadrova konstanta*)

počet elektronů ve viditelném vesmíru (Eddingtonovo číslo)

*) $6{,}022\ 141\ 79\times10^{23}\ \mathrm{mol}^{-1}$

Jaké typy dat můžeme použít?



Typy dat

Nukleotidové a proteinové sekvence:

H_sapiens MTPMRKINPLMKLINHSFIDLPTPSNISAWWNFGS

báze = stav znaku

P_troglod ATGACCCCGACACGCAAAATTAACCCACTAATAAA

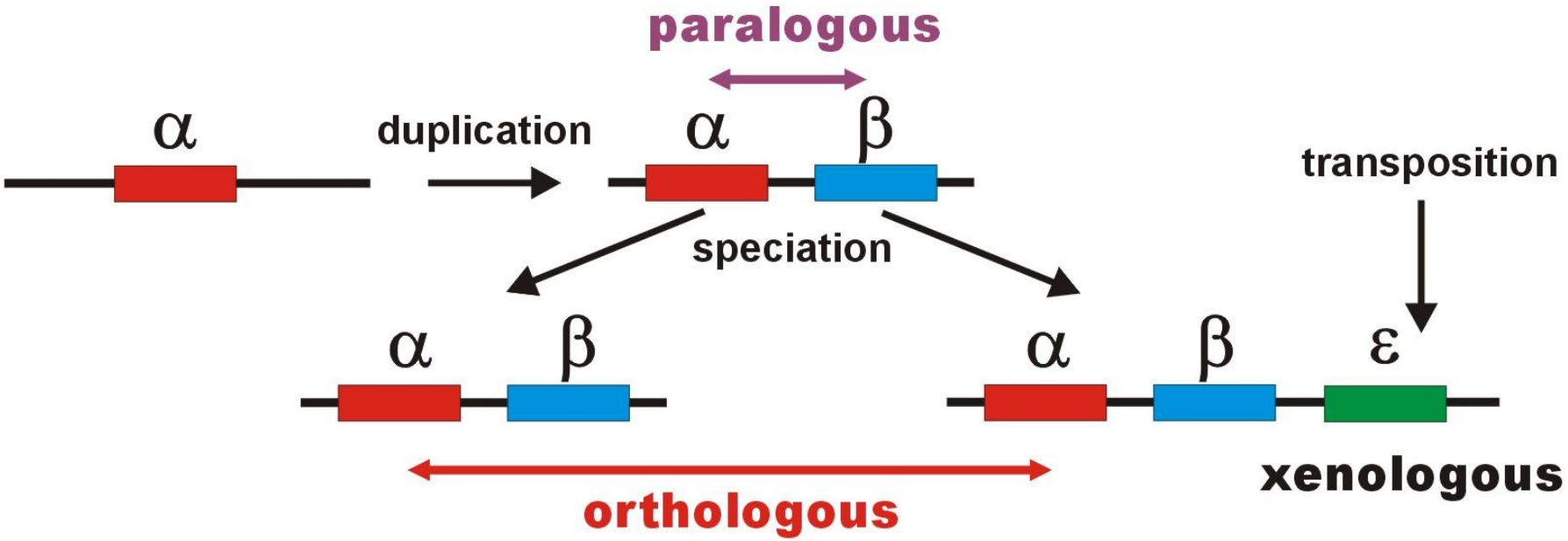
pozice (site) = znak

Typy dat

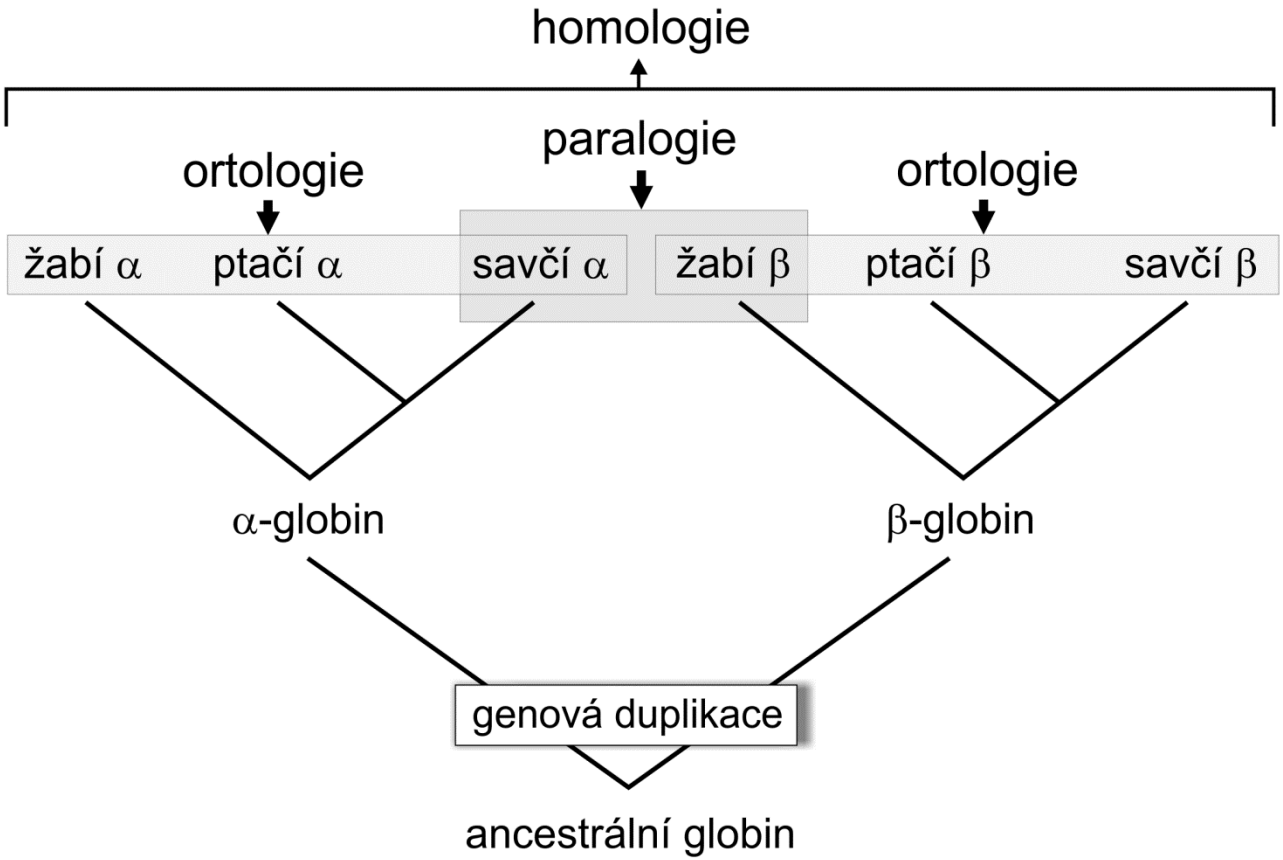
retroelementy: SINE (*Alu*, B1, B2), LINE

mikrosatelity, SNP

Problém homologie sekvencí



Problém homologie sekvencí



Pozor, ani jednotlivá místa v sekvenci DNA nejsou vzájemně zcela nezávislá!

Práce se sekvencemi

DNA databáze:

EMBL (European Molecular Biology Laboratory) – European Bioinformatics Institute, Hinxton, UK: *http://www.ebi.ac.uk/embl/*

GenBank – NCBI (National Center for Biotechnology Information), Bethesda, Maryland, USA: *http://www.ncbi.nlm.nih.gov/Genbank/*

DDBJ (DNA Data Bank of Japan) – National Institute of Genetics, Mishima, Japan: *http://www.ddbj.nig.ac.jp/*

Správa databází: většinou balíky programů Sybase nebo ORACLE

výstupy: ASCII (*American Standard Code for Information Interchange*)

Práce se sekvencemi

Proteinové databáze:

SWISS-PROT – University of Geneve & Swis Institute of Bioinformatics:
http://www.expasy.ch/sprot/ a *http://www.ebi.ac.uk/swissprot/*

PIR (Protein Information Resource) – NBRF (National Biomedical Research Foundation, Washington, D.C., USA) & Tokyo University & JIPID (Japanese International Protein Information Database, Tokyo) & MIPS (Martinsried Institute for Protein Sequences, Martinsried, Germany): *http://www-nbrf.georgetown.edu/*

PRF/SEQDB (Protein Resource Foundation) – Ósaka, Japan:
http://www.prf.or.jp/en/os.htm

PDB (Protein Data Bank) – University of New Jersey, San Diego & Super-computer Center, University of California & National Institute of Standards and Technology:
http://www.rcsb.org/pdb/

Formáty souborů:

FASTA:

```
>H_sapiens
ATGACCCCAATACGCAAAATTAACCCCCTAATAAAATTAATTAACCACTCATTCATCGACCTCCCCACCC
CATCCAACATCTCCGCATGATGAAACTTCGGCTCACTCCTTGGCGCCTGCCTGATCCTCCAAATCACCAC
AGGACTATTCCTAGCCATACACTACTCACCAGACGCCTCAACCGCCTTTTCATCAATCGCCCACATCACT
CGAGACGTAAATTATGGCTGAATCATCCGCTACCTTCACGCCAATGGCGCCTCAATATTCTTTATCTGCC
TCTTCCTACACATCGGGCGAGGCCTATATTACGGATCATTTCTCTACTCAGAAACCTGAAACATCGGCAT
...
>P_troglod
ATGACCCCGACACGCAAAATTAACCCACTAATAAAATTAATTAATCACTCATTTATCGACCTCCCCACCC
CATCCAACATTTCCGCATGATGGAACTTCGGCTCACTTCTCGGCGCCTGCCTAATCCTTCAAATTACCAC
AGGATTATTCCTAGCTATACACTACTCACCAGACGCCTCAACCGCCTTCTCGTCGATCGCCCACATCACC
CGAGACGTAAACTATGGTTGGATCATCCGCTACCTCCACGCTAACGGCGCCTCAATATTTTTTATCTGCC
TCTTCCTACACATCGGCCGAGGTCTATATTACGGCTCATTTCTCTACCTAGAAACCTGAAACATTGGCAT
...
>P_paniscus
ATGACCCCAACACGCAAAATCAACCCACTAATAAAATTAATTAATCACTCATTTATCGACCTCCCCACCC
CATCCAATATTTCCACATGATGAAACTTCGGCTCACTTCTCGGCGCCTGCCTAATCCTTCAAATCACCAC
AGGACTATTCCTAGCTATACACTACTCACCAGACGCCTCAACCGCCTTCTCATCGATCGCCCACATTACC
CGAGACGTAAACTATGGTTGAATCATCCGCTACCTTCACGCTAACGGCGCCTCAATACTTTTCATCTGCC
TCTTCCTACACGTCGGTCGAGGCCTATATTACGGCTCATTTCTCTACCTAGAAACCTGAAACATTGGCAT
...
```

Formáty souborů:

GenBank:

```
ORIGIN
        1 tgaaatgaag atattctctt ctcaagacat caagaagaag gaactactcc ccaccaccag
       61 cacccaaagc tggcattcta attaaactac ttcttgtgta cataaattta catagtacaa
      121 tagtacattt atgtatatcg tacattaaac tattttcccc aagcatataa gcaagtacat
      181 ttaatcaatg atataggcca taaaacaatt atcaacataa actgatacaa accatgaata
      241 ttatactaat acatcaaatt aatgctttaa agacatatct gtgttatctg acatacacca
      301 tacagtcata aactcttctc ttccatatga ctatcccctt ccccatttgg tctattaatc
      361 taccatcctc cgtgaaacca acaacccgcc caccaatgcc cctcttctcg ctccgggccc
      421 attaaacttg ggggtagcta aactgaaact ttatcagaca tctggttctt acttcagggc
      481 catcaaatgc gttatcgccc atacgttccc cttaaataag acatctcgat ggtatcgggt
      541 ctaatcagcc catgaccaac ataactgtgg tgtcatgcat ttggtatttt tttattttgg
      601 cctactttca tcaacatagc cgtcaaggca tgaaaggaca gcacacagtc tagacgcacc
      661 tacggtgaag aatcattagt ccgcaaaacc caatcaccta aggctaatta ttcatgcttg
      721 ttagacataa atgctactca ataccaaatt ttaactctcc aaaccccccа acccctcct
      781 cttaatgcca aaccccaaaa acactaagaa cttgaaagac atatattatt aactatcaaa
      841 ccctatgtcc tgatcgattc tagtagttcc caaaatatga ctcatatttt agtacttgta
      901 aaaattttac aaaatcatgc tccgtgaacc aaaactctaa tcacactcta ttacgcaata
      961 aatattaaca agttaatgta gcttaataac aaagcaaagc actgaaaatg cttagatgga
     1021 taattttatc cca
//
```

Formáty souborů:

PHYLIP (“interleaved” format):

```
6 1120
H_sapiens     ATGACCCCAA TACGCAAAAT TAACCCCCTA ATAAAATTAA TTAACCACTC
P_troglod     ATGACCCCGA CACGCAAAAT TAACCCACTA ATAAAATTAA TTAATCACTC
P_paniscus    ATGACCCCAA CACGCAAAAT CAACCCACTA ATAAAATTAA TTAATCACTC
G_gorilla     ATGACCCCTA TACGCAAAAC TAACCCACTA GCAAAACTAA TTAACCACTC
P_pygmaeus    ATGACCCCAA TACGCAAAAC CAACCCACTA ATAAAATTAA TTAACCACTC
H_lar         ATGACCCCCC TGCGCAAAAC TAACCCACTA ATAAAACTAA TCAACCACTC

              ATTCATCGAC CTCCCCACCC CATCCAACAT CTCCGCATGA TGAAACTTCG
              ATTTATCGAC CTCCCCACCC CATCCAACAT TTCCGCATGA TGGAACTTCG
              ATTTATCGAC CTCCCCACCC CATCCAATAT TTCCACATGA TGAAACTTCG
              ATTCATTGAC CTCCCTACCC CGTCCAACAT CTCCACATGA TGAAACTTCG
              ACTCATCGAC CTCCCCACCC CATCAAACAT CTCTGCATGA TGGAACTTCG
              ACTTATCGAC CTTCCAGCCC CATCCAACAT TTCTATATGA TGAAACTTTG
```

Formáty souborů:

NEXUS (PAUP*, “interleaved”):

```
#NEXUS
begin data;
dimensions ntax=6 nchar=1120;
format datatype=DNA interleave datatype=DNA missing=? gap=-;
matrix
P_troglod   ATGACCCCGACACGCAAAATTAACCCACTAATAAAATTAATTAATCACTC
P_paniscus  ATGACCCCAACACGCAAAATCAACCCACTAATAAAATTAATTAATCACTC
H_sapiens   ATGACCCCAATACGCAAAATTAACCCCCTAATAAAATTAATTAACCACTC
G_gorilla   ATGACCCCTATACGCAAAACTAACCCACTAGCAAAACTAATTAACCACTC
P_pygmaeus  ATGACCCCAATACGCAAAACCAACCCACTAATAAAATTAATTAACCACTC
H_lar       ATGACCCCCCTGCGCAAAACTAACCCACTAATAAAACTAATCAACCACTC

P_troglod   ATTTATCGACCTCCCCACCCCATCCAACATTTCCGCATGATGGAACTTCG
P_paniscus  ATTTATCGACCTCCCCACCCCATCCAATATTTCCACATGATGAAACTTCG
H_sapiens   ATTCATCGACCTCCCCACCCCATCCAACATCTCCGCATGATGAAACTTCG
G_gorilla   ATTCATTGACCTCCCTACCCCGTCCAACATCTCCACATGATGAAACTTCG
P_pygmaeus  ACTCATCGACCTCCCCACCCCATCAAACATCTCTGCATGATGGAACTTCG
H_lar       ACTTATCGACCTTCCAGCCCCATCCAACATTTCTATATGATGAAACTTTG

end;
```

Formáty souborů:

Clustal X:

```
P_troglod   ATGACCCCGACACGCAAAATTAACCCACTAATAAAATTAATTAATCACTCATTTATCGAC
P_paniscus  ATGACCCCAACACGCAAAATCAACCCACTAATAAAATTAATTAATCACTCATTTATCGAC
H_sapiens   ATGACCCCAATACGCAAAATTAACCCCCTAATAAAATTAATTAACCACTCATTCATCGAC
G_gorilla   ATGACCCCTATACGCAAAACTAACCCACTAGCAAAACTAATTAACCACTCATTCATTGAC
P_pygmaeus  ATGACCCCAATACGCAAAACCAACCCACTAATAAAATTAATTAACCACTCACTCATCGAC
H_lar       ATGACCCCCCTGCGCAAAACTAACCCACTAATAAAACTAATCAACCACTCACTTATCGAC
            ********    *******  ***** ***  **** **** ** ****** * ** ***

P_troglod   CTCCCCACCCCATCCAACATTTCCGCATGATGGAACTTCGGCTCACTTCTCGGCGCCTGC
P_paniscus  CTCCCCACCCCATCCAATATTTCCACATGATGAAACTTCGGCTCACTTCTCGGCGCCTGC
H_sapiens   CTCCCCACCCCATCCAACATCTCCGCATGATGAAACTTCGGCTCACTCCTTGGCGCCTGC
G_gorilla   CTCCCTACCCCGTCCAACATCTCCACATGATGAAACTTCGGCTCACTCCTTGGTGCCTGC
P_pygmaeus  CTCCCCACCCCATCAAACATCTCTGCATGATGGAACTTCGGCTCACTTCTAGGCGCCTGC
H_lar       CTTCCAGCCCCATCCAACATTTCTATATGATGAAACTTTGGTTCACTCCTAGGCGCCTGC
            ** **  **** ** ** ** **   ****** ***** ** ***** ** ** ******
```

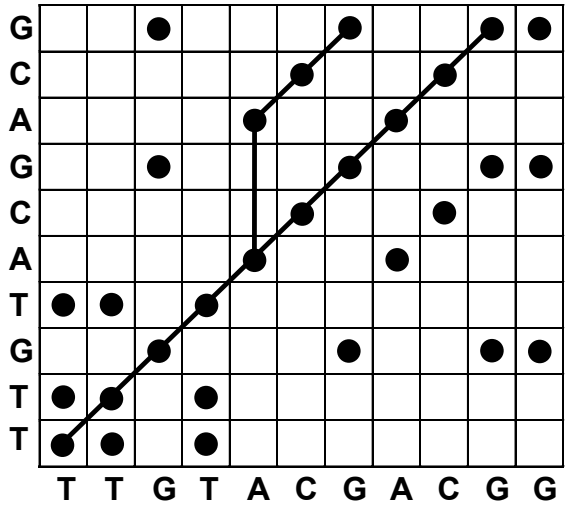
BLAST

GenBank

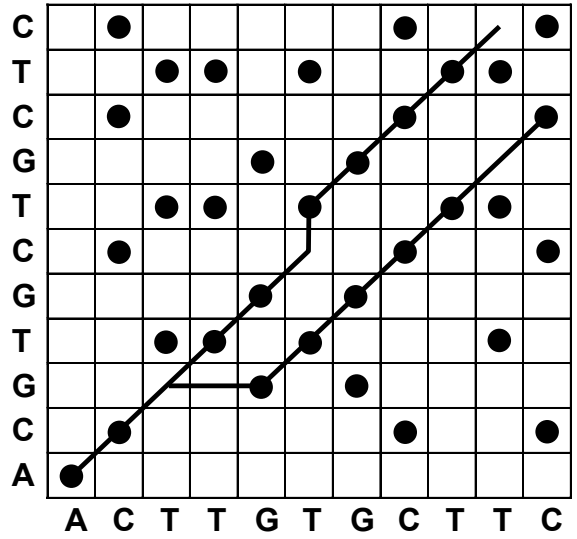
ClustalX

Seřazení sekvencí (alignment):

```
Sekvence 1    TTGTACGACGG
Sekvence 2    TTGTACGACG

TTGTACGACGG   TTGT---ACGACGG
||||||||||    ||||   |||
TTGTACGACG    TTGTACGACG
```




```
Sekvence 1    ACTTGTGCTTC
Sekvence 2    ACGTGCTGCTC

              ACTTG-TGCTTC
Path 1        ||  ||  ||||
              ACGTGCTGCTC

              ACTTGTGCTTC
Path 2        ||   |||||  |
              AC--GTGCTGCTC
```



Seřazení sekvencí (alignment):

Penalizace mezer (*gap penalty*):

$GP = g + hl$

g - gap penalty
h – gap extension penalty
l – gap length

g = penalizace za výskyt mezery (1×)

h = extenze za každou „pomlčku“

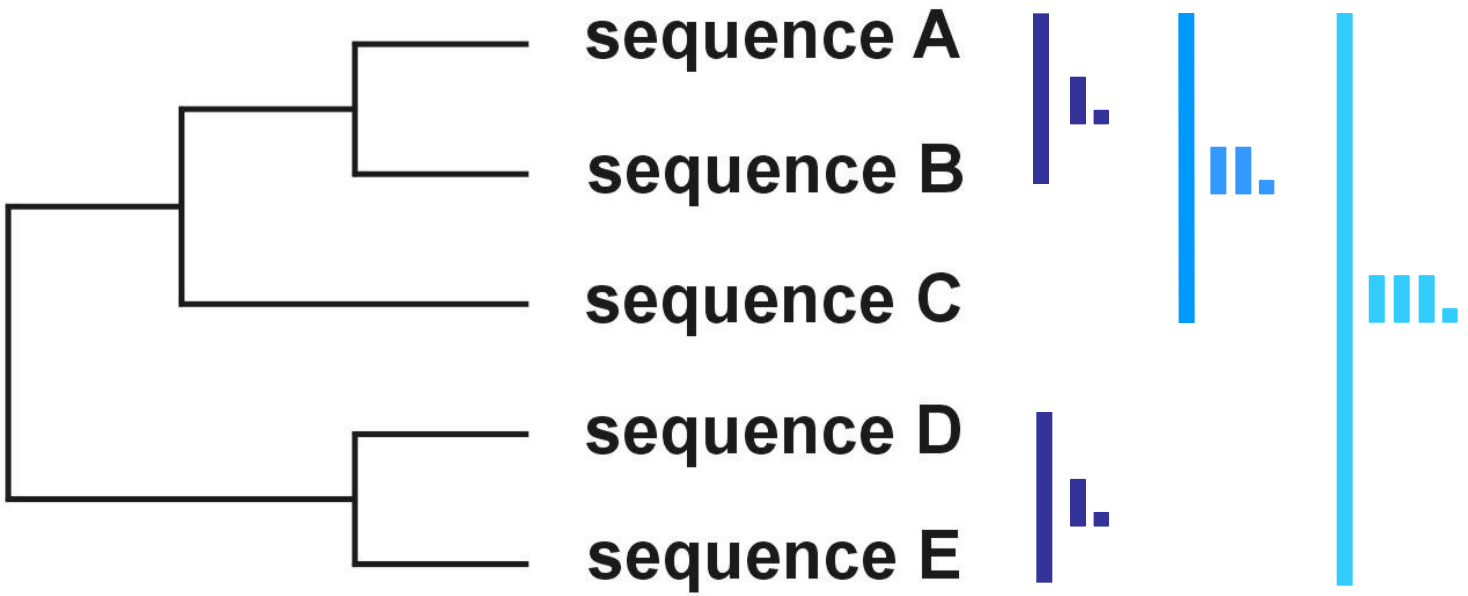
l = délka mezery (= počet „pomlček“)

Př.: GC– – – – –TTAA
l = 5, *g* = *x*, *h* = 5*x*

Progresivní seřazení - ClustalX

3 fáze:

1. Seřazení dvojic sekvencí → párové distance
2. Konstrukce „guide tree“ (NJ)
3. Seřazení všech sekvencí podle stromu

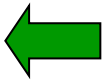


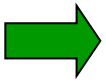
Problém progresivního seřazení

6 druhů:

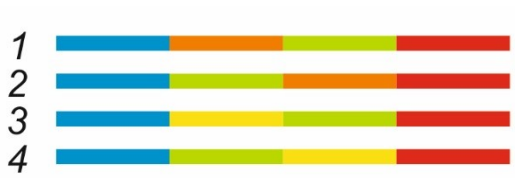
gorila	AGGTT	tučňák	A-GTT
kůň	AG-TT	kuře	A-GTT
panda	AG-TT	pštros	AGGTT

AGGTT	gorila	AGGTT	AGGTT
AG-TT	kůň	AG-TT	A-GTT
AG-TT	panda	AG-TT	A-GTT
AG-TT	tučňák	A-GTT	A-GTT
AG-TT	kuře	A-GTT	A-GTT
AGGTT	pštros	AGGTT	AGGTT

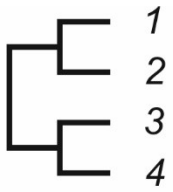




Existují i metody bez seřazení:

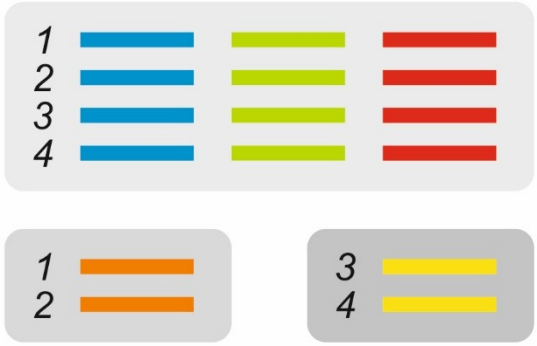


homologní sekvence

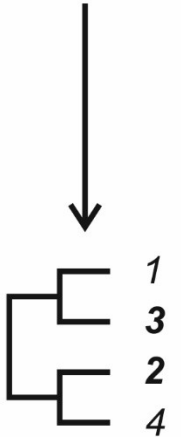


referenční strom

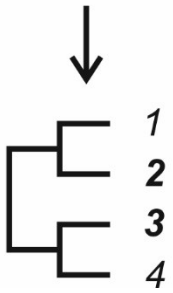
seřazení všech sekvencí



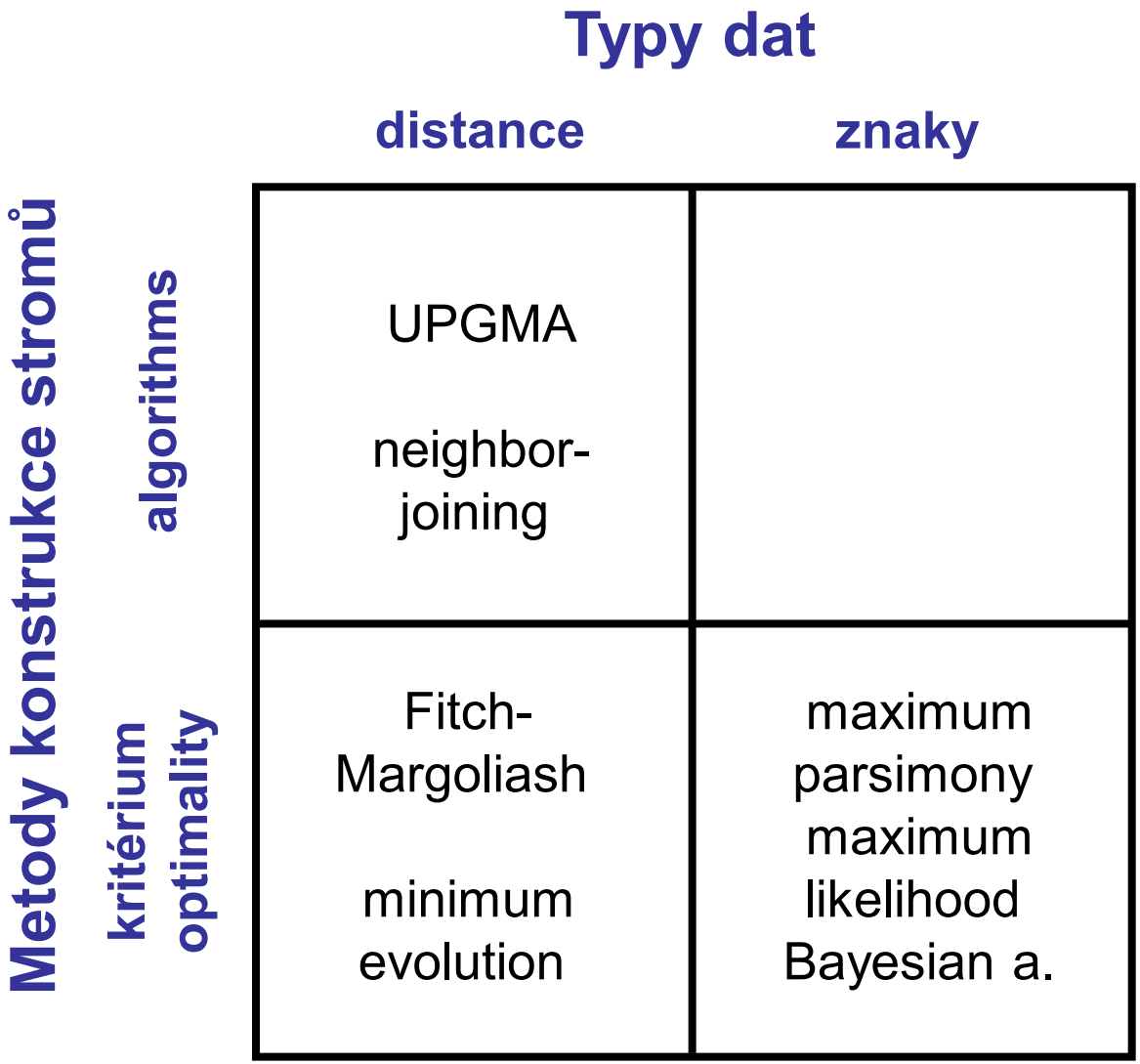
metoda bez seřazení sekvencí



fylogenetický strom



Rozdělení metod



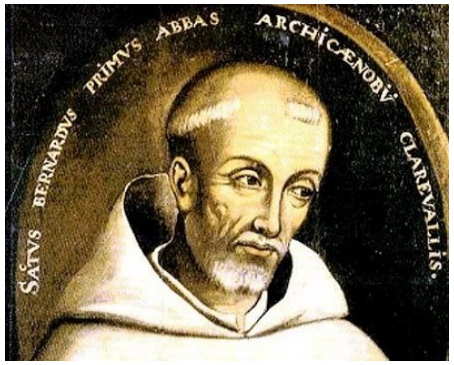
Jak hodnotit jednotlivé metody?

výkonnost (efficiency):	jak rychlá je metoda?
síla (power):	kolik znaků je třeba?
konzistence (consistency):	vede zvyšující se počet znaků ke správnému stromu?
robustnost (robustness):	jak metoda funguje při neplatnosti předpokladů?
falzifikovatelnost (falsifiability):	umožňuje testování platnosti předpokladů?

MAXIMÁLNÍ ÚSPORNOST (*maximum parsimony*, MP)

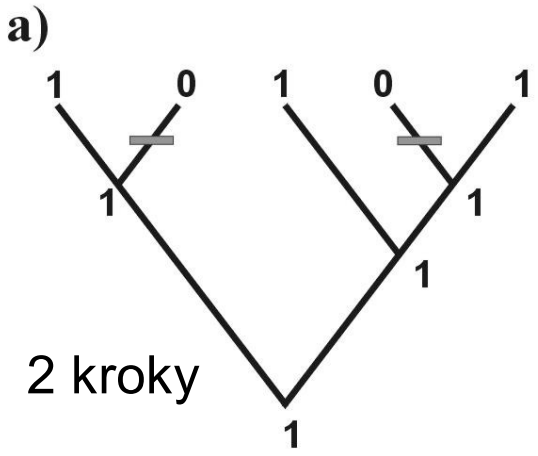
William of Ockham (c. 1287 – 1347)

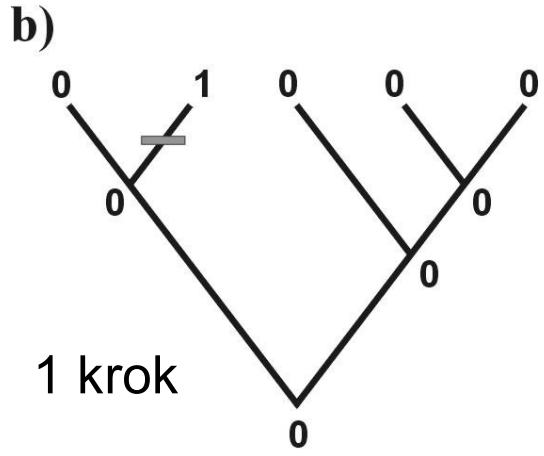
Occamova břitva

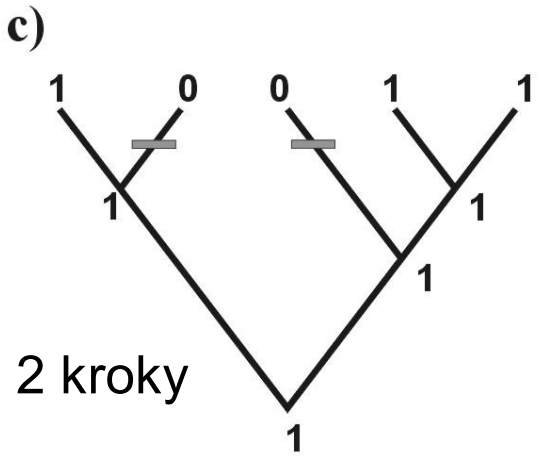


	I	II	III
A	1	0	1
B	0	0	1
C	1	0	0
D	0	1	0
E	1	0	1

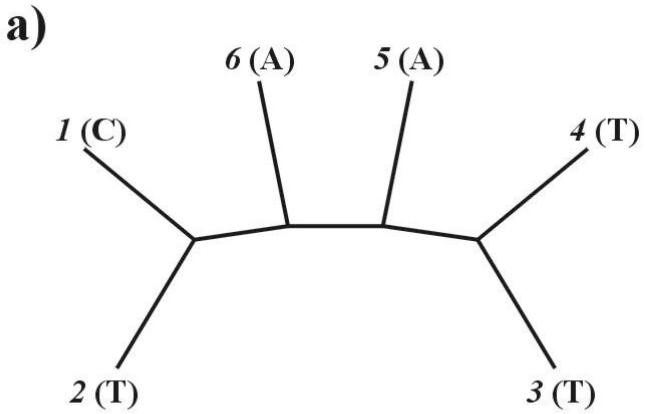
minimální počet kroků = 3
skutečný počet kroků = 5
⇒ 2 extra kroky → homoplasie





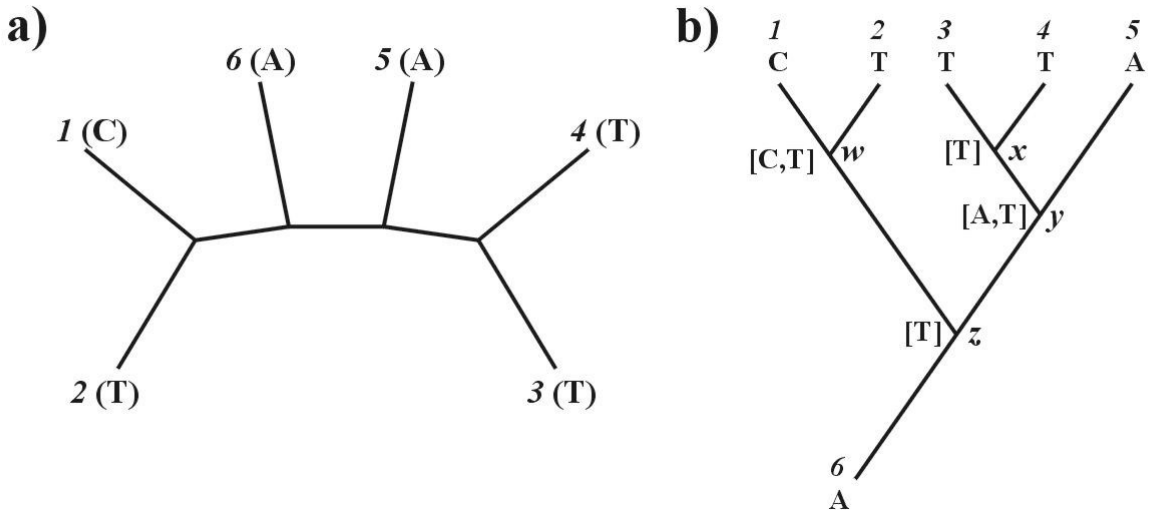


Odhad počtu kroků: Fitchův algoritmus



1. arbitrární kořen

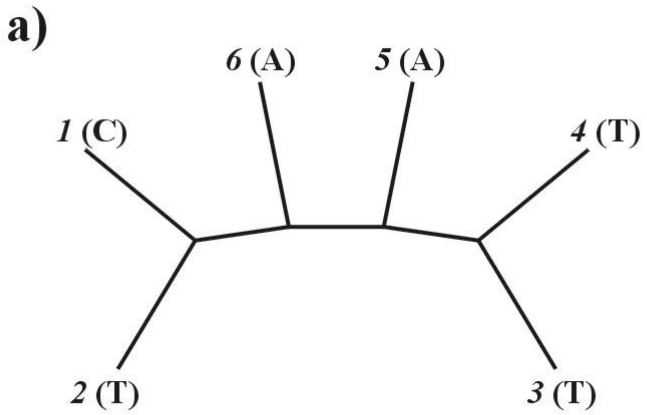
Odhad počtu kroků: Fitchův algoritmus

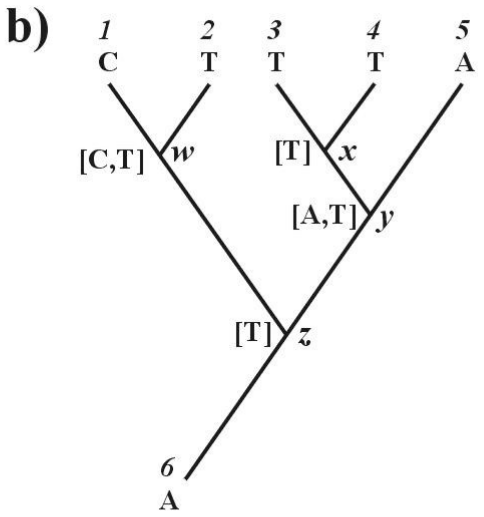


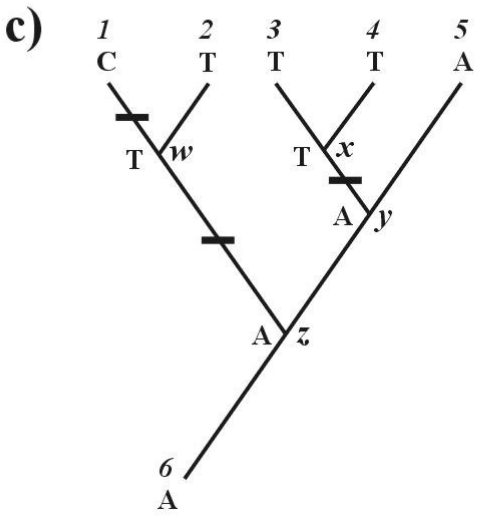
1. arbitrární kořen

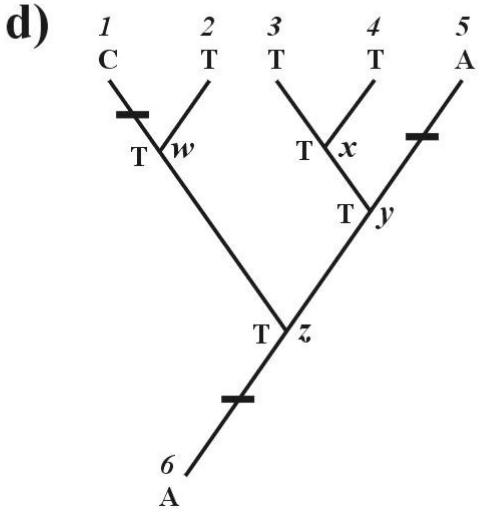
2. Shora dolů:
   w = C, nebo T
   x = T
   y = A, nebo T
   z = T

Odhad počtu kroků: Fitchův algoritmus





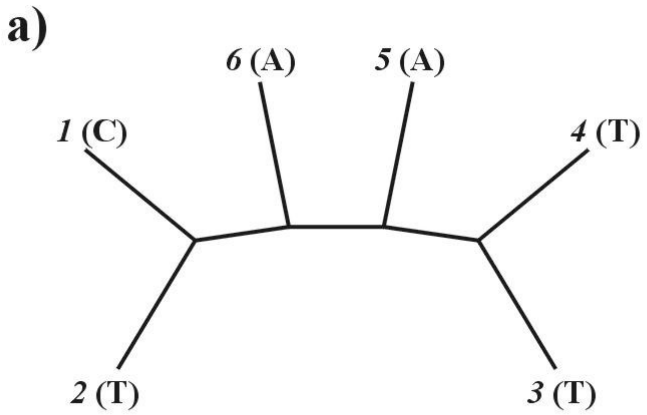


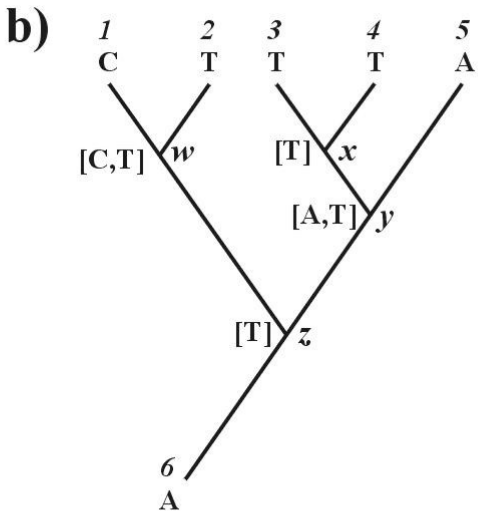


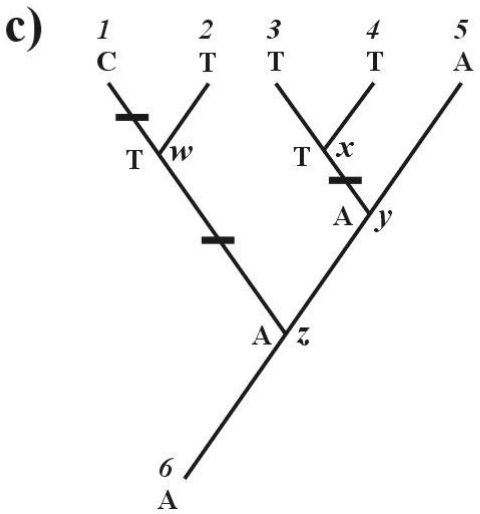
1. arbitrární kořen
2. Shora dolů:
   w = C, nebo T
   x = T
   y = A, nebo T
   z = T
3. Zdola nahoru:
   z = T, nebo A

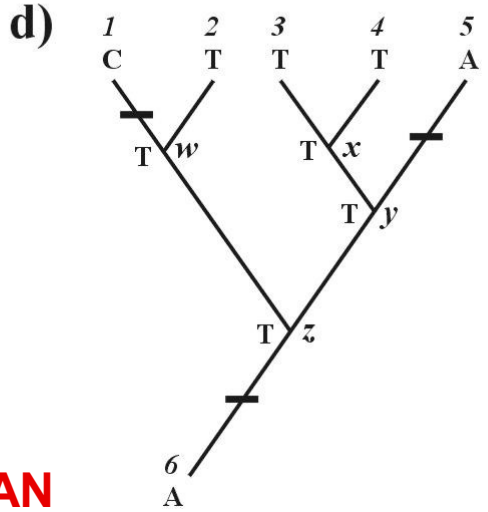
celková délka = 3

Odhad počtu kroků: Fitchův algoritmus









1. arbitrární kořen
2. Shora dolů:
   w = C, nebo T
   x = T
   y = A, nebo T
   z = T
3. Zdola nahoru:
   z = T, nebo A

celková délka = 3

DELTRAN
(DELayed TRANsformation)

ACCTRAN
(ACCelerated TRANsformation)

Problém homoplasie:

parsimony-informative and non-informative characters (sites)
- invariant sites (symplesiomorphies)
- singletons (autapomorphies)

index konzistence (consistency i., CI)
retenční index (retention i., RI)
upravený CI (rescaled CI, RC)
index homoplasie (homoplasy i., HI)

$$CI = \frac{m}{s} \qquad RI = \frac{g - s}{g - m}$$

RC = CI × RI
HI = 1 - CI

m = min. no. of possible steps
s = min. no. needed for explaining the tree
g = max. no. of steps for any tree

Metody parsimonie:

Fitchova: $X \rightarrow Y$ a $Y \rightarrow X$
neseřazené znaky ($A \rightarrow T$ nebo $A \rightarrow G$ etc.)

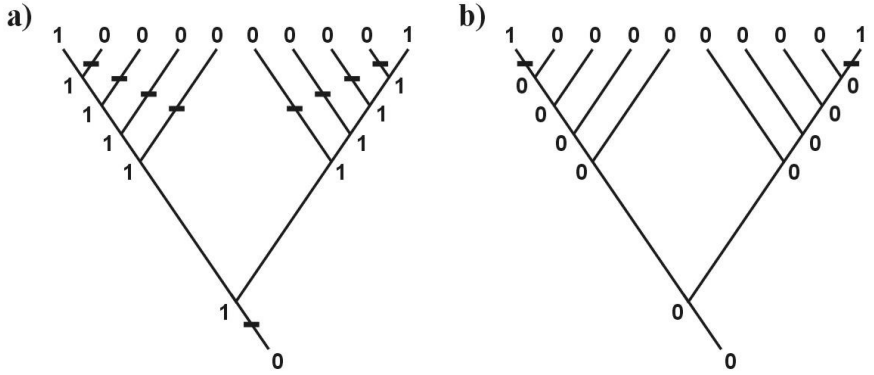
Wagnerova: $X \rightarrow Y$ a $Y \rightarrow X$
seřazené znaky ($1 \rightarrow 2 \rightarrow 3$)

Dollova: $X \rightarrow Y$ a $Y \rightarrow X$, potom nelze $X \rightarrow Y$

… *restriction-site and restriction-fragment data*

Caminova-Sokalova: $X \rightarrow Y$,
ne $Y \rightarrow X$

… SINE, LINE



vážená (*weighed*, *transversion*): “*relaxed Dollo criterion*”

generalizovaná: matice nákladů (*cost matrix*) = kroková matice (*step matrix*)

Wagnerova

a)

	a	b	c	d
a	-	1	2	3
b	1	-	1	2
c	2	1	-	1
d	3	2	1	-

Fitchova

b)

	a	b	c	d
a	-	1	1	1
b	1	-	1	1
c	1	1	-	1
d	1	1	1	-

c)

	a	b	c	d
a	-	*M* *)	2*M*	3*M*
b	1	-	*M*	2*M*
c	2	1	-	*M*
d	3	2	1	-

Dollova

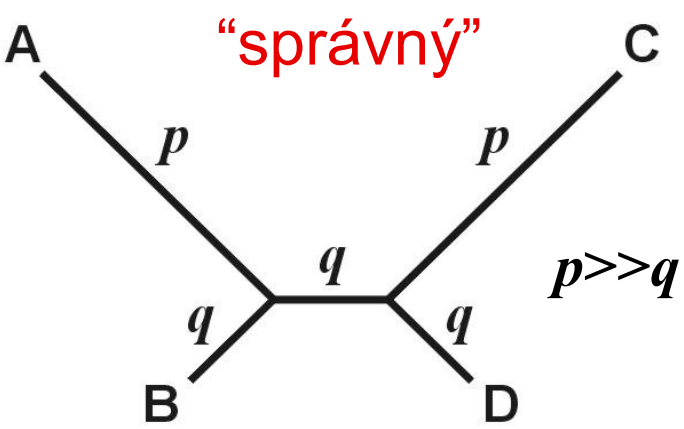
d)

	A	C	G	T
A	-	5	1	5
C	5	-	5	1
G	1	5	-	5
T	5	1	5	-

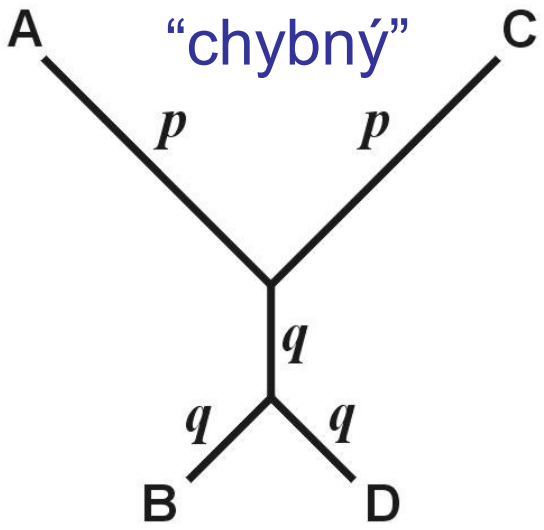
vážená (transverzní)

*) *M* je libovolně velké číslo zaručující, že bude povolena pouze jedna transformace do každého odvozeného stavu.

Parsimonie a konzistence

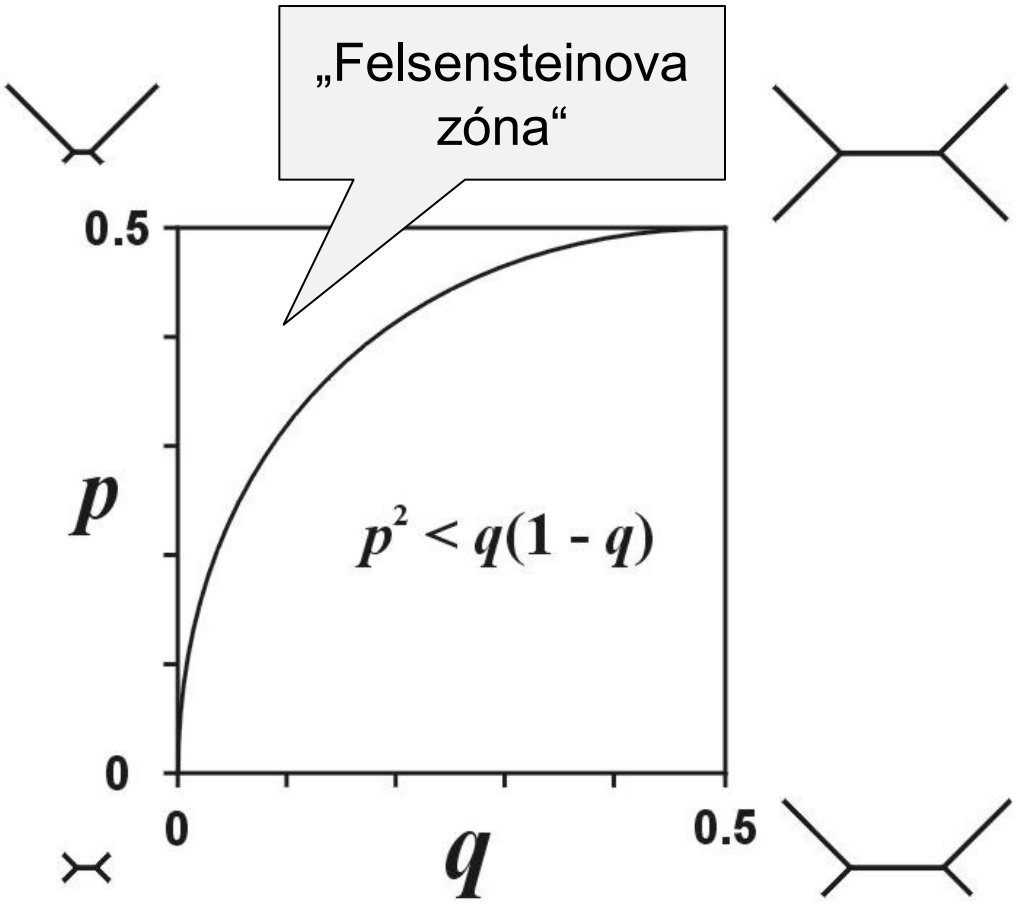


((A,B),(C,D))



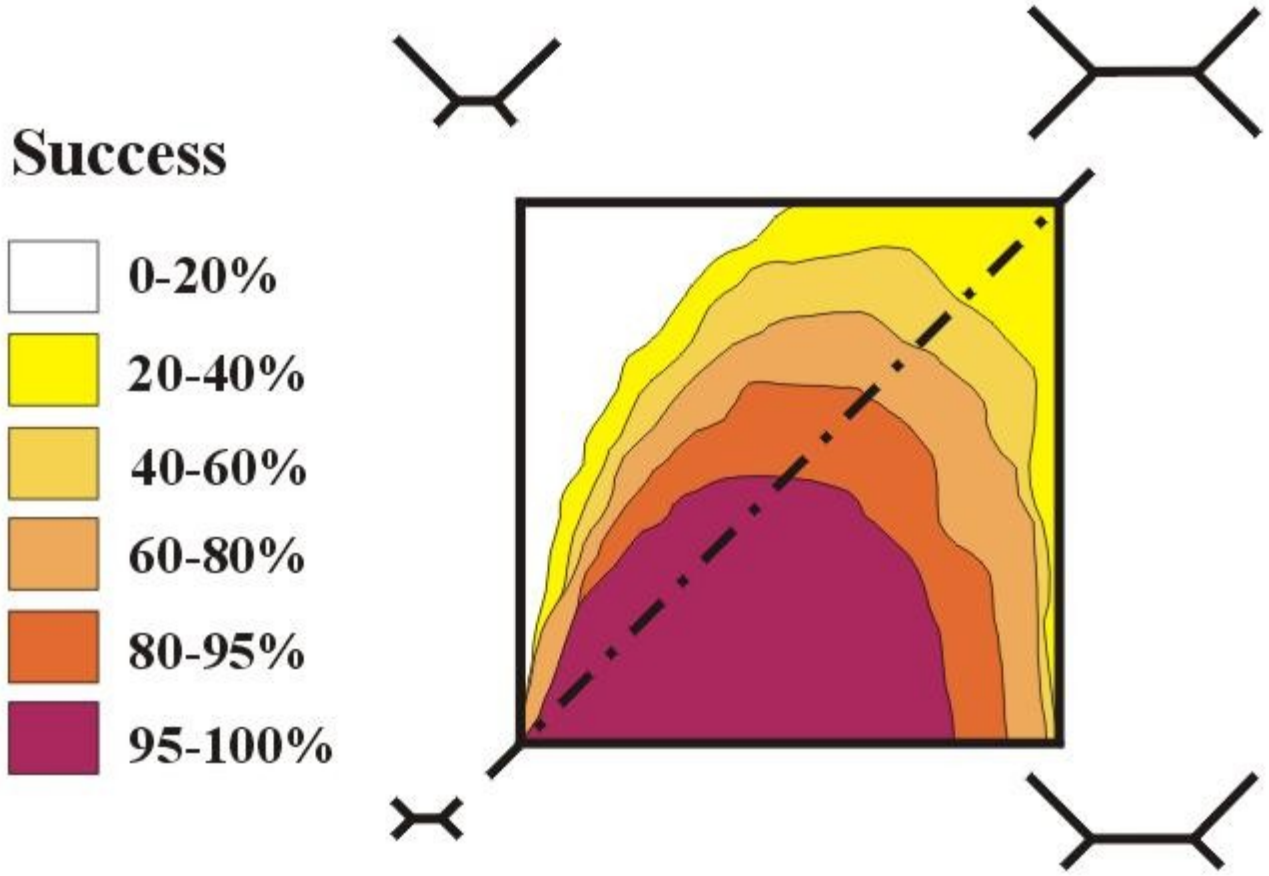
((A,C),(B,D))

Parsimonie a konzistence

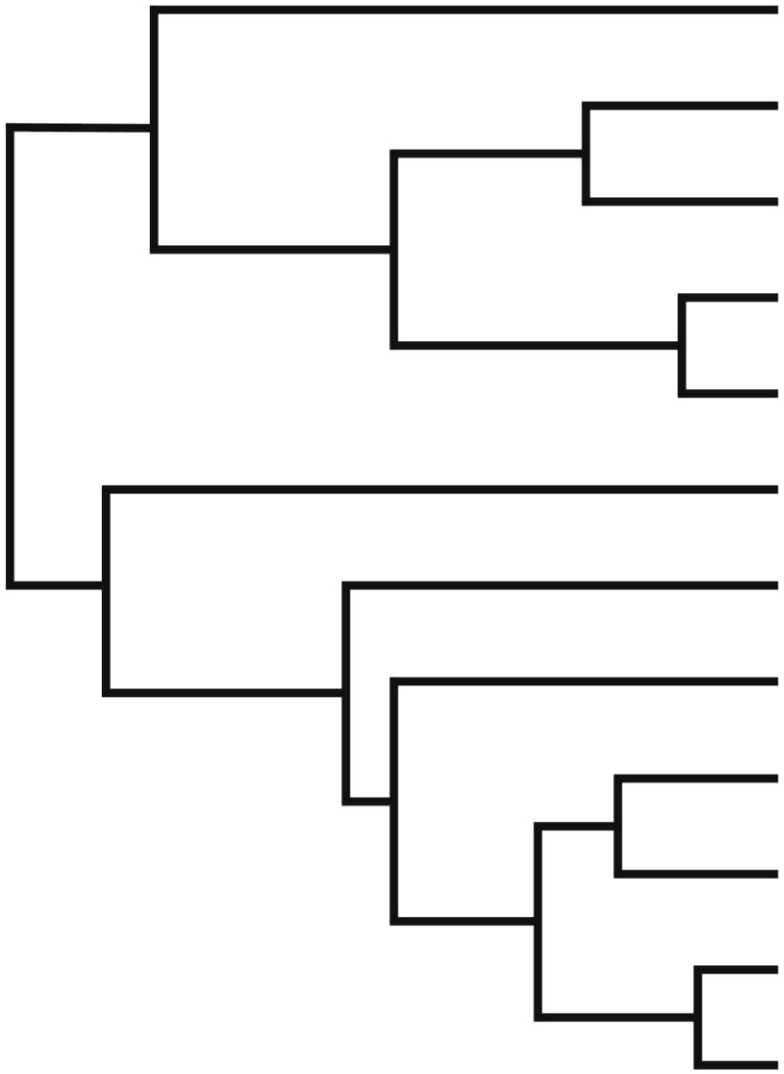


Ve Felsensteinově zóně je parsimonie nekonzistentní

Parsimonie a konzistence

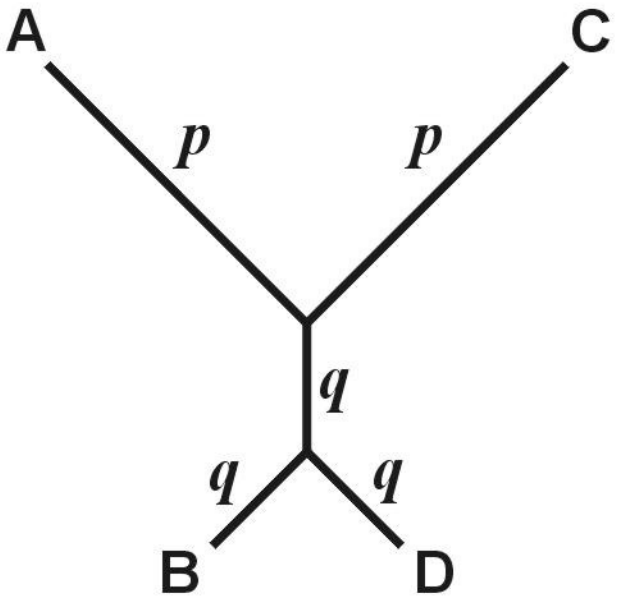


Parsimonie a konzistence



dlouhé větve

„přitažlivost dlouhých větví“
(*long-branch attraction*, LBA)



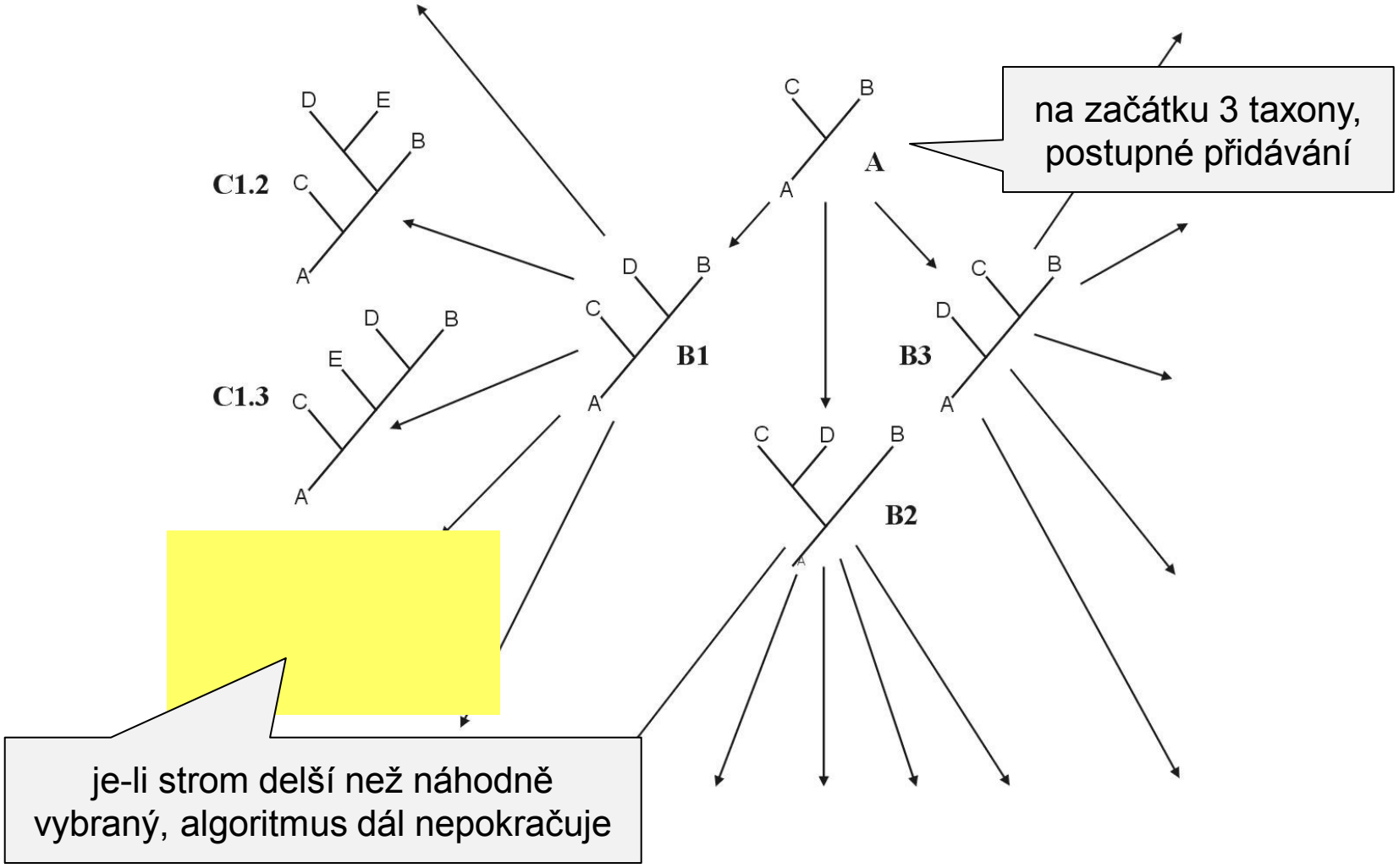
Hledání optimálního stromu

1. Exaktní metody:

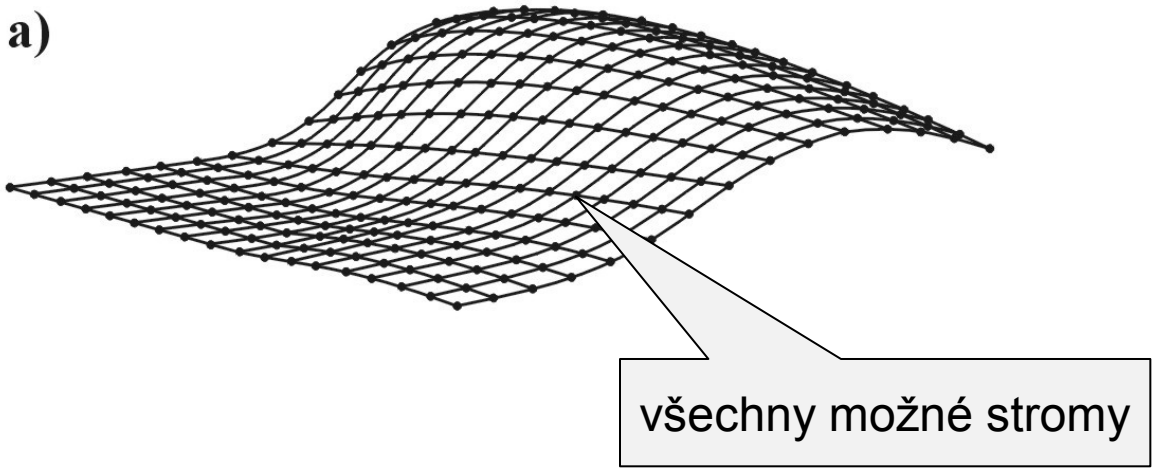
   a) vyčerpávající hledání (*exhaustive search*)

   b) *branch-and-bound*

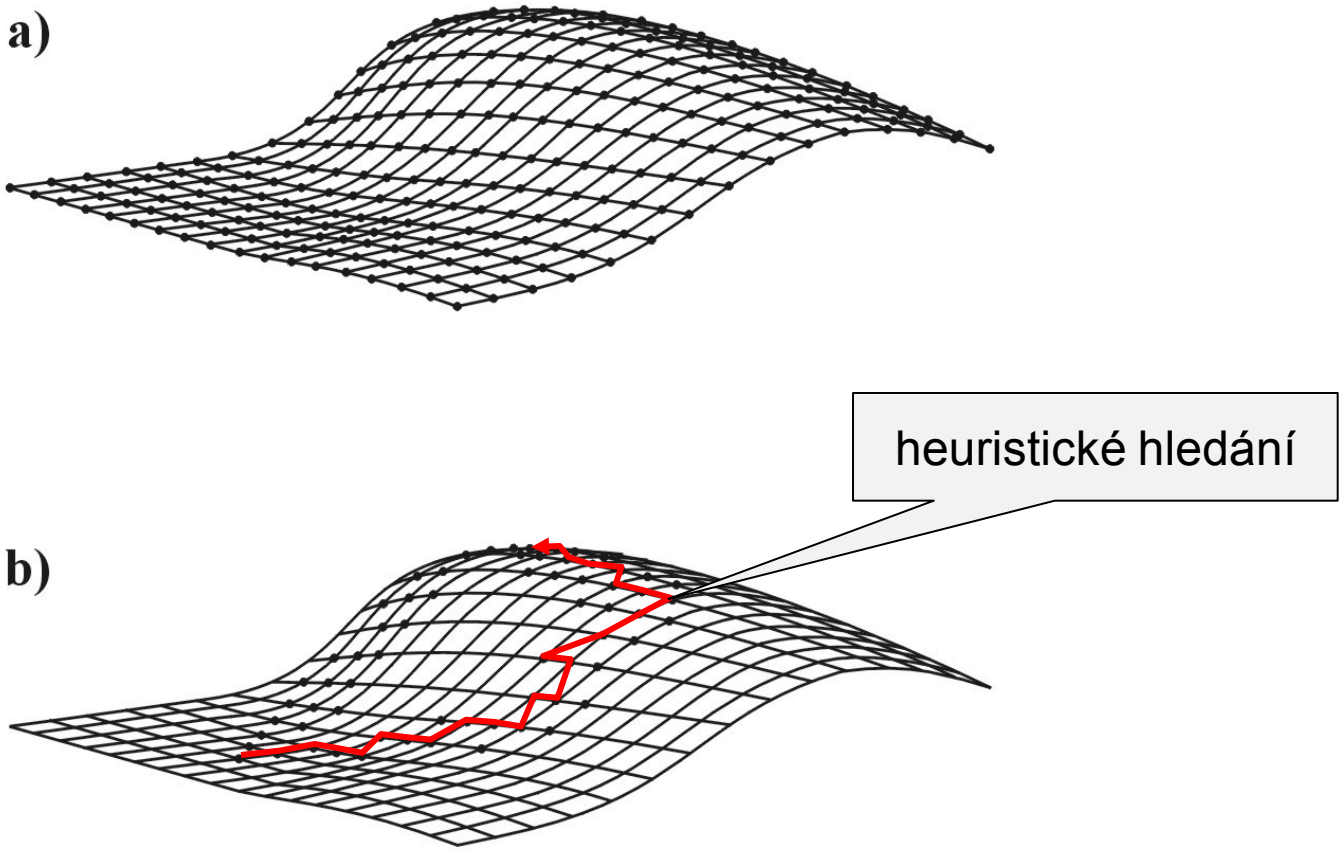
branch-and-bound



2. Heuristické hledání



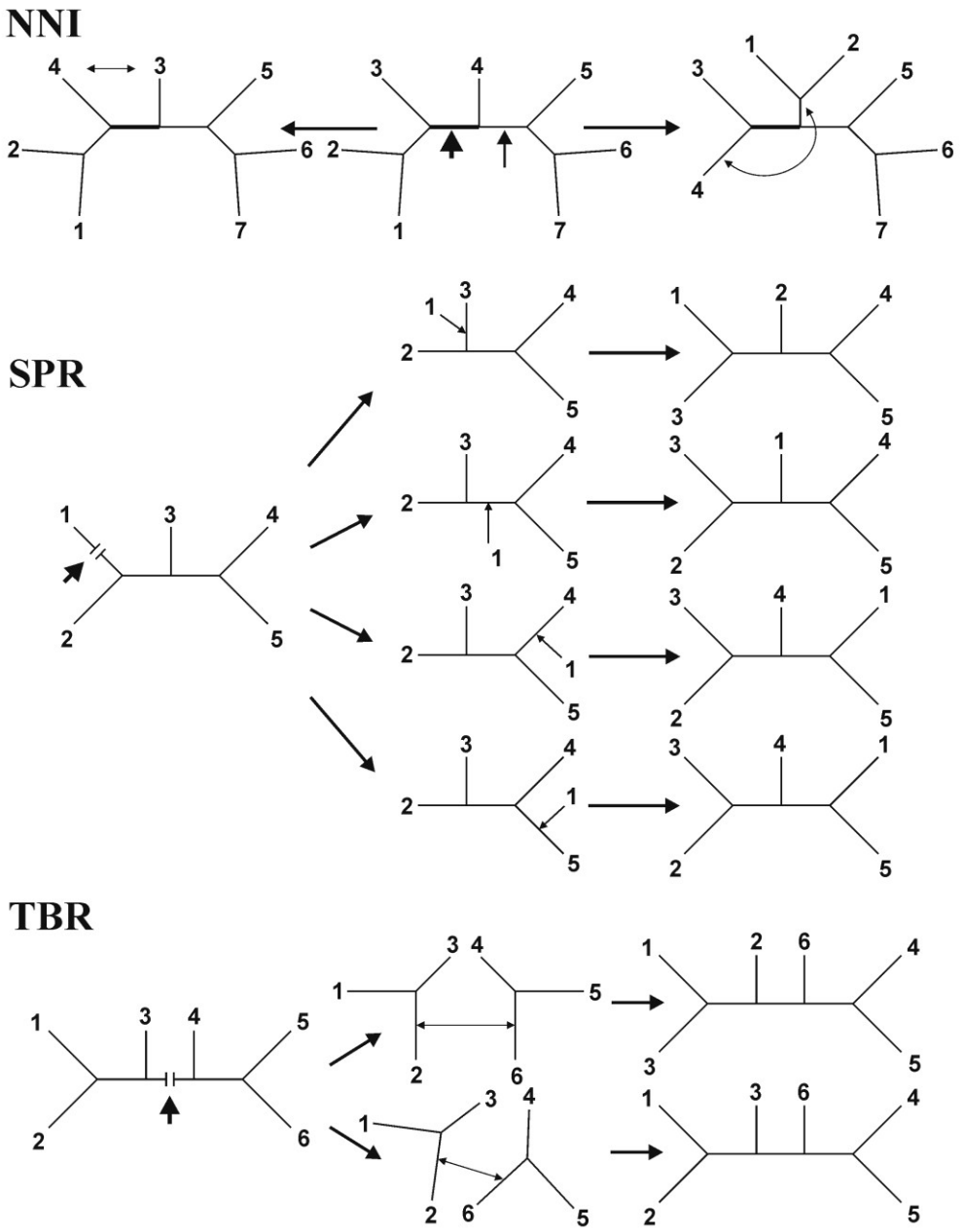
stepwise addition
star decomposition
branch swapping



nearest-neighbor interchanges (NNI)

subtree prunning and regrafting (SPR)

tree bisection and reconnection (TBR)



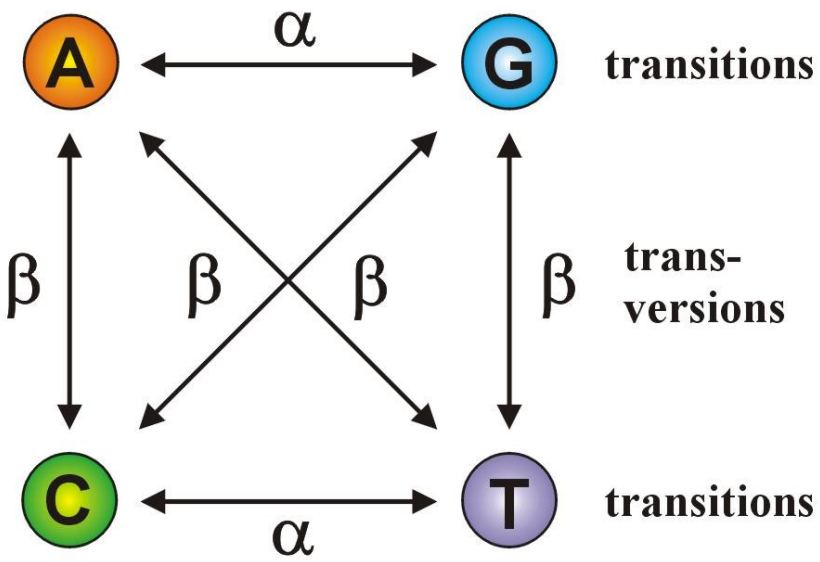
Evoluční modely a distanční metody

		Báze po substituci			
		A	C	G	T
Původní báze	A	$-\frac{3}{4}$	$\frac{1}{4}$	$\frac{1}{4}$	$\frac{1}{4}$
	C	$\frac{1}{4}$	$-\frac{3}{4}$	$\frac{1}{4}$	$\frac{1}{4}$
	G	$\frac{1}{4}$	$\frac{1}{4}$	$-\frac{3}{4}$	$\frac{1}{4}$
	T	$\frac{1}{4}$	$\frac{1}{4}$	$\frac{1}{4}$	$-\frac{3}{4}$

$$\mathbf{Q} = \begin{pmatrix} - & \alpha & \alpha & \alpha \\ \alpha & - & \alpha & \alpha \\ \alpha & \alpha & - & \alpha \\ \alpha & \alpha & \alpha & - \end{pmatrix}$$

Jukes-Cantor (JC): stejné frekvence bází
stejné frekvence substitucí

Kimura 2-parameter (K2P): transice ≠ transverze



$$Q = \begin{pmatrix} - & \beta & \alpha & \beta \\ \beta & - & \beta & \alpha \\ \alpha & \beta & - & \beta \\ \beta & \alpha & \beta & - \end{pmatrix}$$

Jestliže $\alpha = \beta$, K2P = JC

Felsenstein (F81): různé frekvence bází

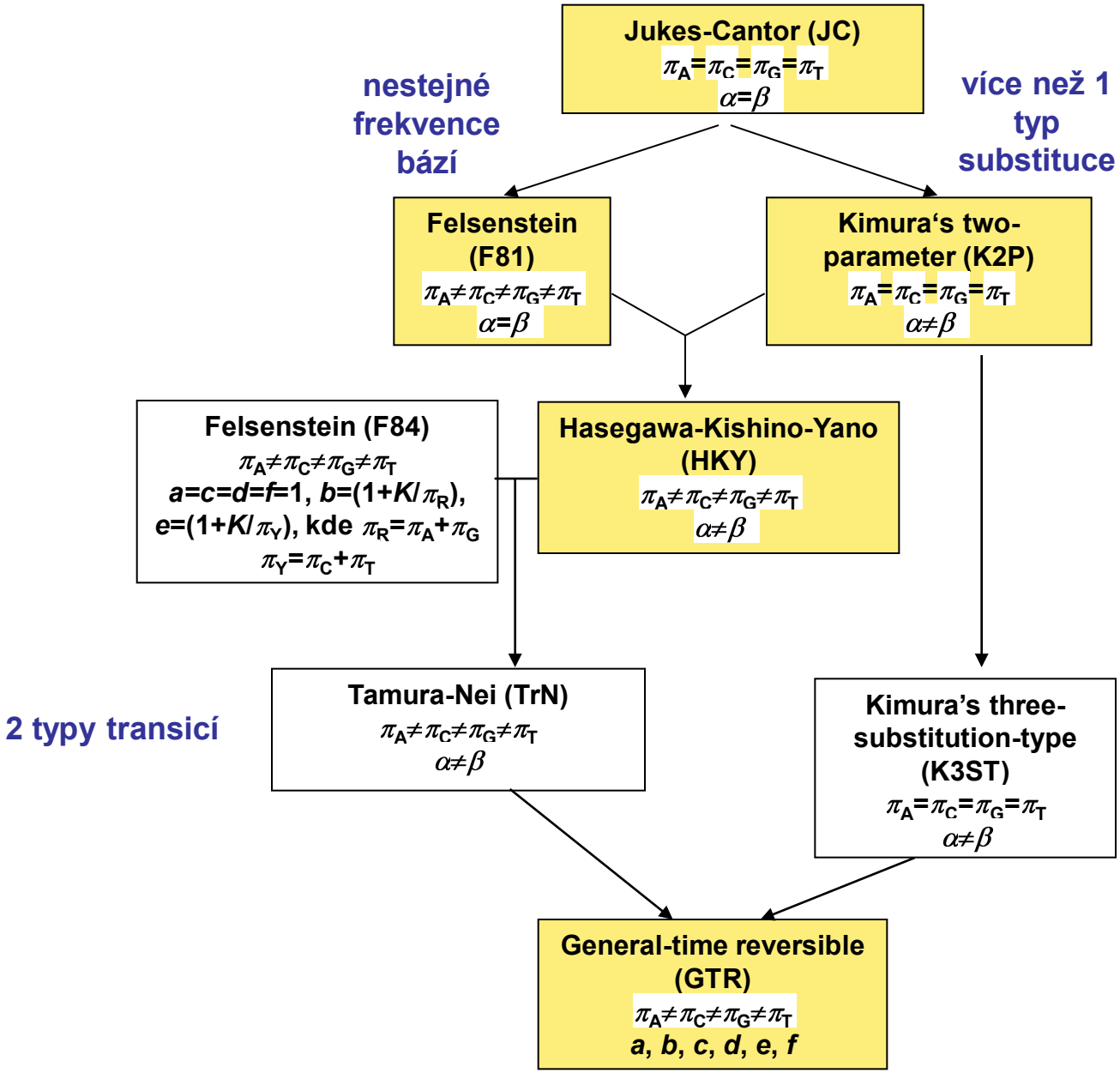
$$Q = \begin{pmatrix} - & \pi_C & \pi_G & \pi_T \\ \pi_A & - & \pi_G & \pi_T \\ \pi_A & \pi_C & - & \pi_T \\ \pi_A & \pi_C & \pi_G & - \end{pmatrix}$$

Jestliže $\pi A = \pi C = \pi G = \pi T$, F81 = JC

Hasegawa-Kishino-Yano (HKY): různé frekvence bází
transice ≠ transverze

$$Q = \begin{pmatrix} - & \pi_C\beta & \pi_G\alpha & \pi_T\beta \\ \pi_A\beta & - & \pi_G\beta & \pi_T\alpha \\ \pi_A\alpha & \pi_C\beta & - & \pi_T\beta \\ \pi_A\beta & \pi_C\alpha & \pi_G\beta & - \end{pmatrix}$$

General time-reversible (GTR, REV): různé frekvence bází
různé frekvence jednotlivých typů substitucí


Jukes-Cantor (JC)
$\pi_A=\pi_C=\pi_G=\pi_T$
$\alpha=\beta$
nestejné frekvence bází
více než 1 typ substituce
Felsenstein (F81)
$\pi_A\neq\pi_C\neq\pi_G\neq\pi_T$
$\alpha=\beta$
Kimura‘s two-parameter (K2P)
$\pi_A=\pi_C=\pi_G=\pi_T$
$\alpha\neq\beta$
Felsenstein (F84)
$\pi_A\neq\pi_C\neq\pi_G\neq\pi_T$
$a=c=d=f=1$, $b=(1+K/\pi_R)$, $e=(1+K/\pi_Y)$, kde $\pi_R=\pi_A+\pi_G$
$\pi_Y=\pi_C+\pi_T$
Hasegawa-Kishino-Yano (HKY)
$\pi_A\neq\pi_C\neq\pi_G\neq\pi_T$
$\alpha\neq\beta$
2 typy transicí
Tamura-Nei (TrN)
$\pi_A\neq\pi_C\neq\pi_G\neq\pi_T$
$\alpha\neq\beta$
Kimura’s three-substitution-type (K3ST)
$\pi_A=\pi_C=\pi_G=\pi_T$
$\alpha\neq\beta$
General-time reversible (GTR)
$\pi_A\neq\pi_C\neq\pi_G\neq\pi_T$
a, b, c, d, e, f

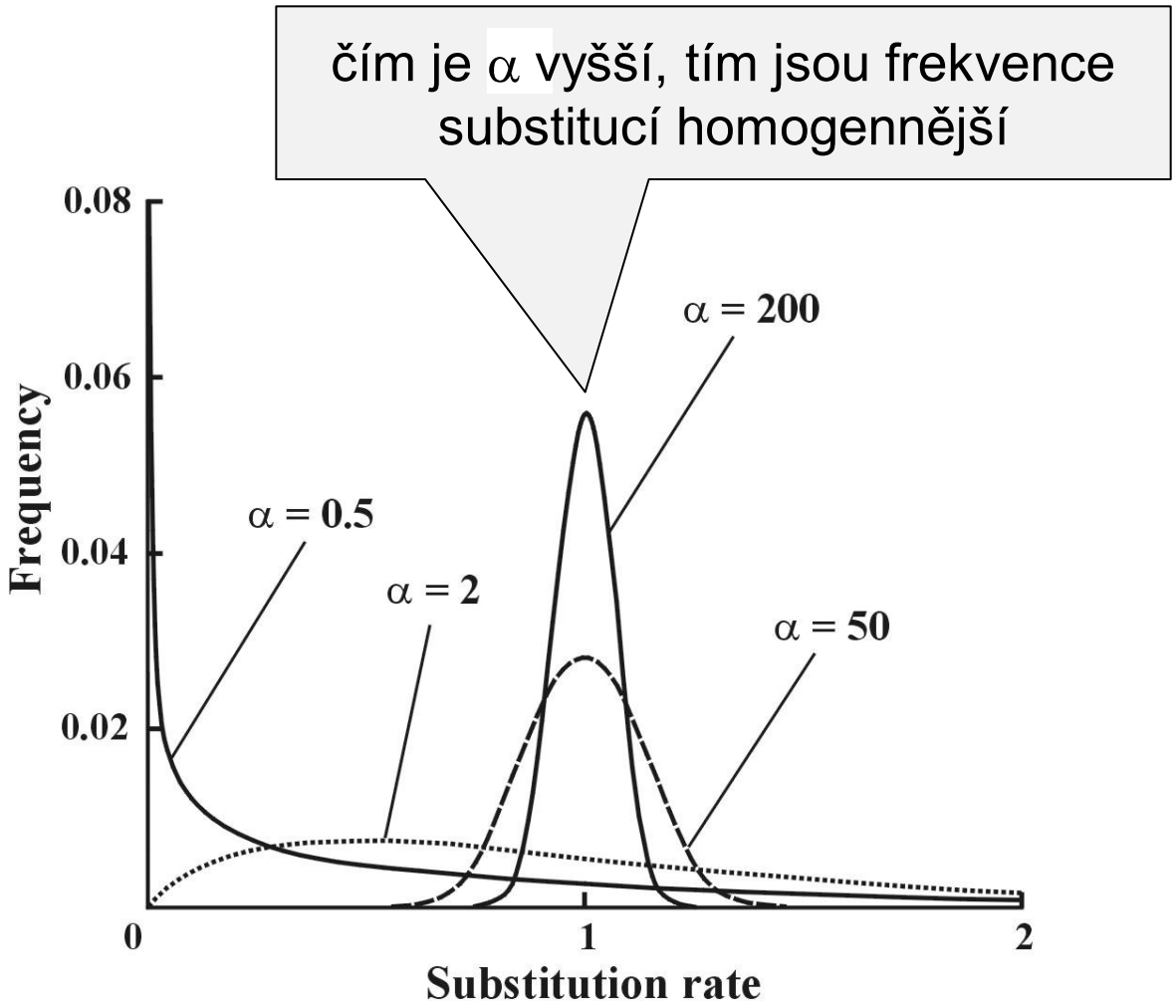
Heterogenita substitučních rychlostí v různých částech sekvence

Gama (Γ) rozdělení:

parametr tvaru α

diskrétní gama model

invariantní pozice
→ GTR+ Γ+I



Porovnání modelů:

Likelihood ratio test (LRT):

zahnízděné modely (*nested models*)

$LR = 2(\ln L2 - \ln L1)$

χ^2 rozdělení, p2 – p1 stupňů volnosti

Akaike information criterion (AIC):

nonnested models

$AIC = -2\ln L + 2p$, kde p = počet volných parametrů

lepší model $\rightarrow$ nižší *AIC*

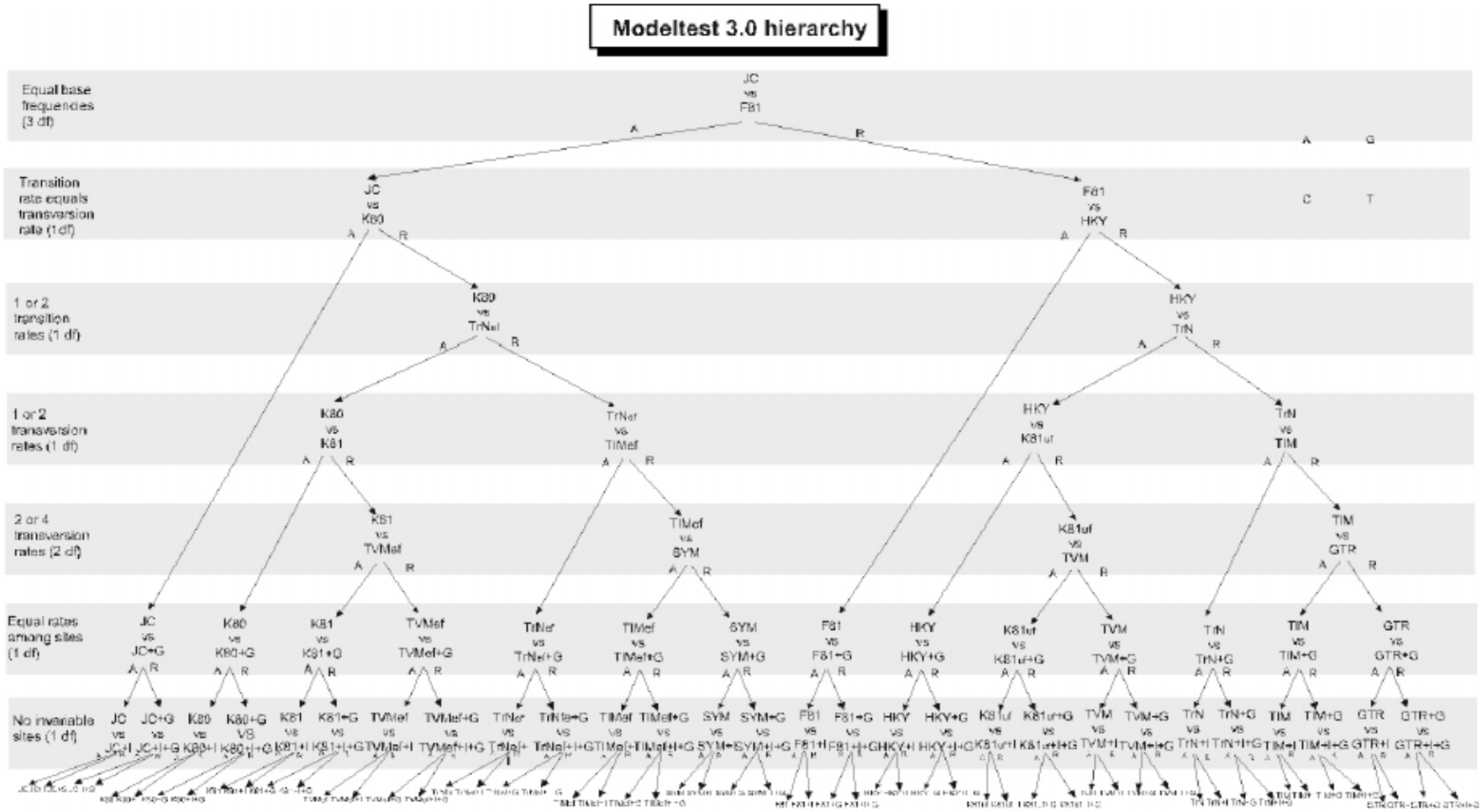
Bayesian information criterion (BIC):

nonested models

$BIC = -2\ln L + p\ln N$, kde N = velikost vzorku

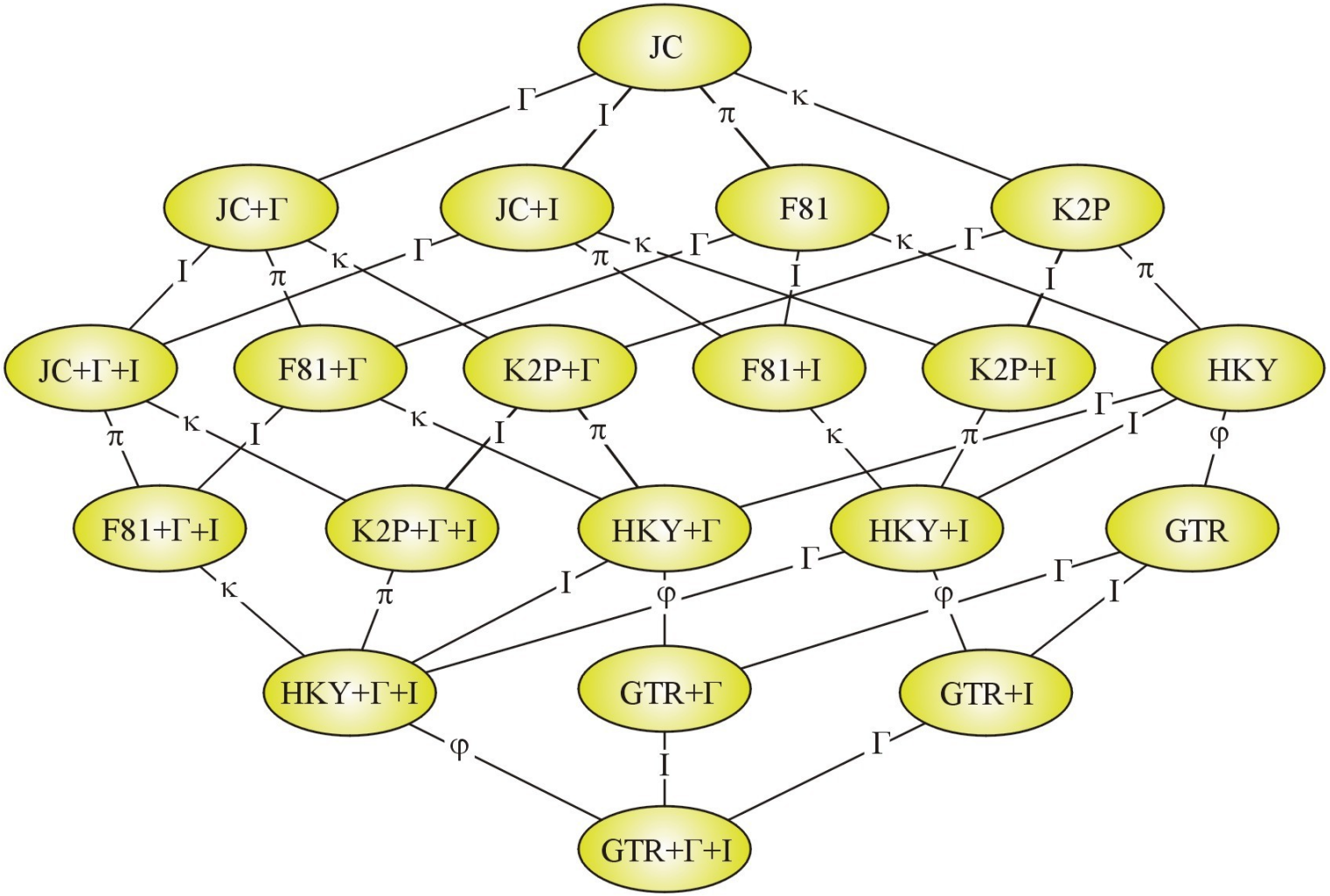
Porovnání modelů:

hierarchický LRT – ModelTest (Crandall and Posada)

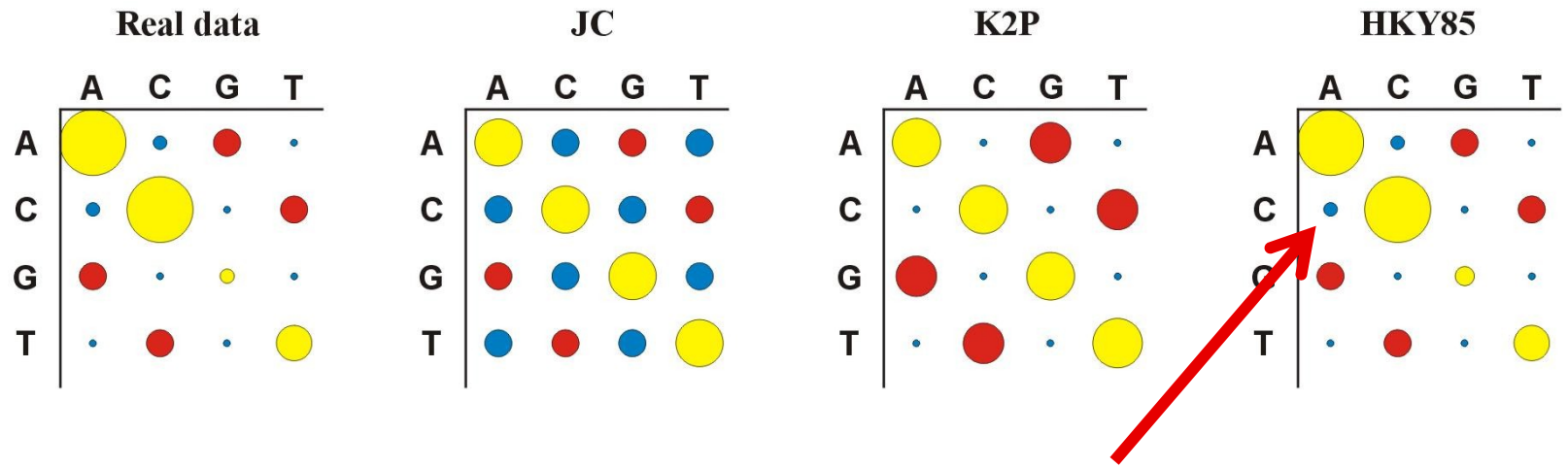


Porovnání modelů:

dynamický LRT:



Porovnání modelů:



Více parametrů $\Rightarrow$ více realismu, ale …

… také více neurčitosti, protože jsou odhadovány ze stejného množství dat

Distance

počítány pro každý pár taxonů, z matice distancí (nebo podobností)
konstruován strom

distanční metody založeny na předpokladu, že pokud bychom znali skutečné distance mezi všemi studovanými taxony, mohli bychom velmi jednoduše rekonstruovat správnou fylogenii

výhoda: velmi rychlé a jednoduché (lze i na kalkulačce)

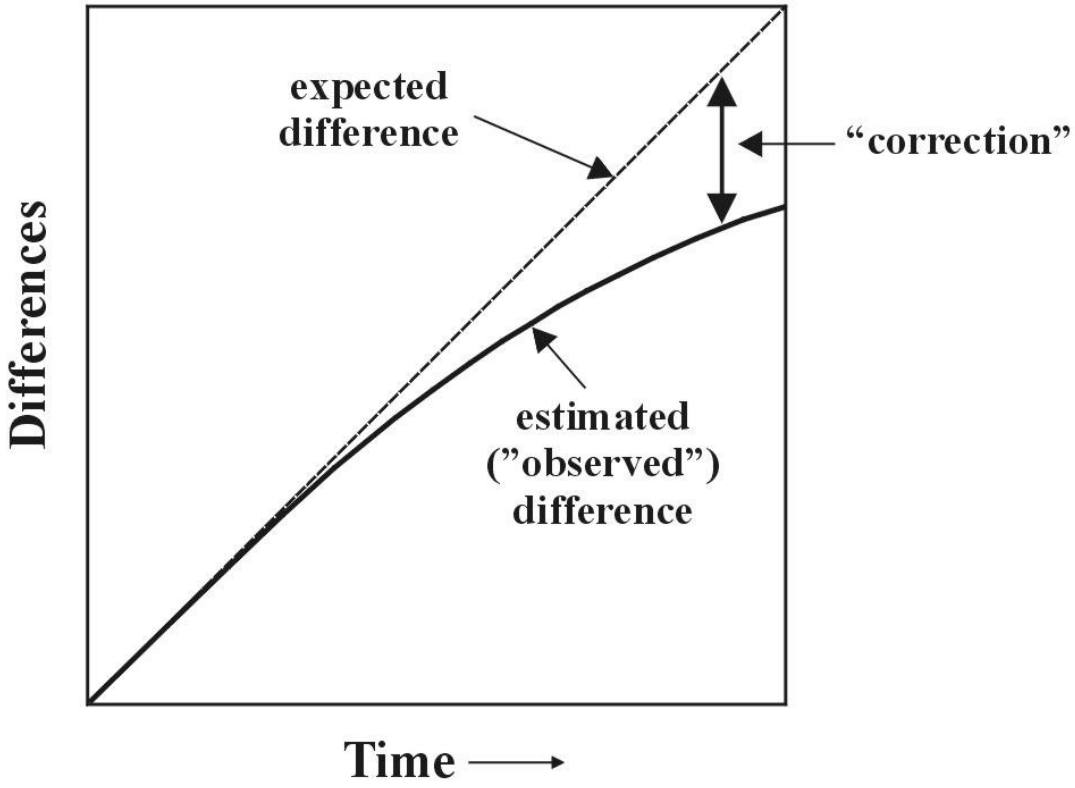
	1				10				20				30
sekvence 1:	A	C	C	C	G	T	T	A	A	G	C	T	T
sekvence 2:	A	C	C	C	G	T	T	A	G	G	C	T	T

sekvence 1:	A	A	C	G	T	A	C	T	T	G	G	A	T
sekvence 2:	A	A	T	G	T	A	C	G	T	G	G	A	T

sekvence 1:	C	G	A	T	C	G	A	T					
sekvence 2:	C	G	A	T	C	G	A	T					

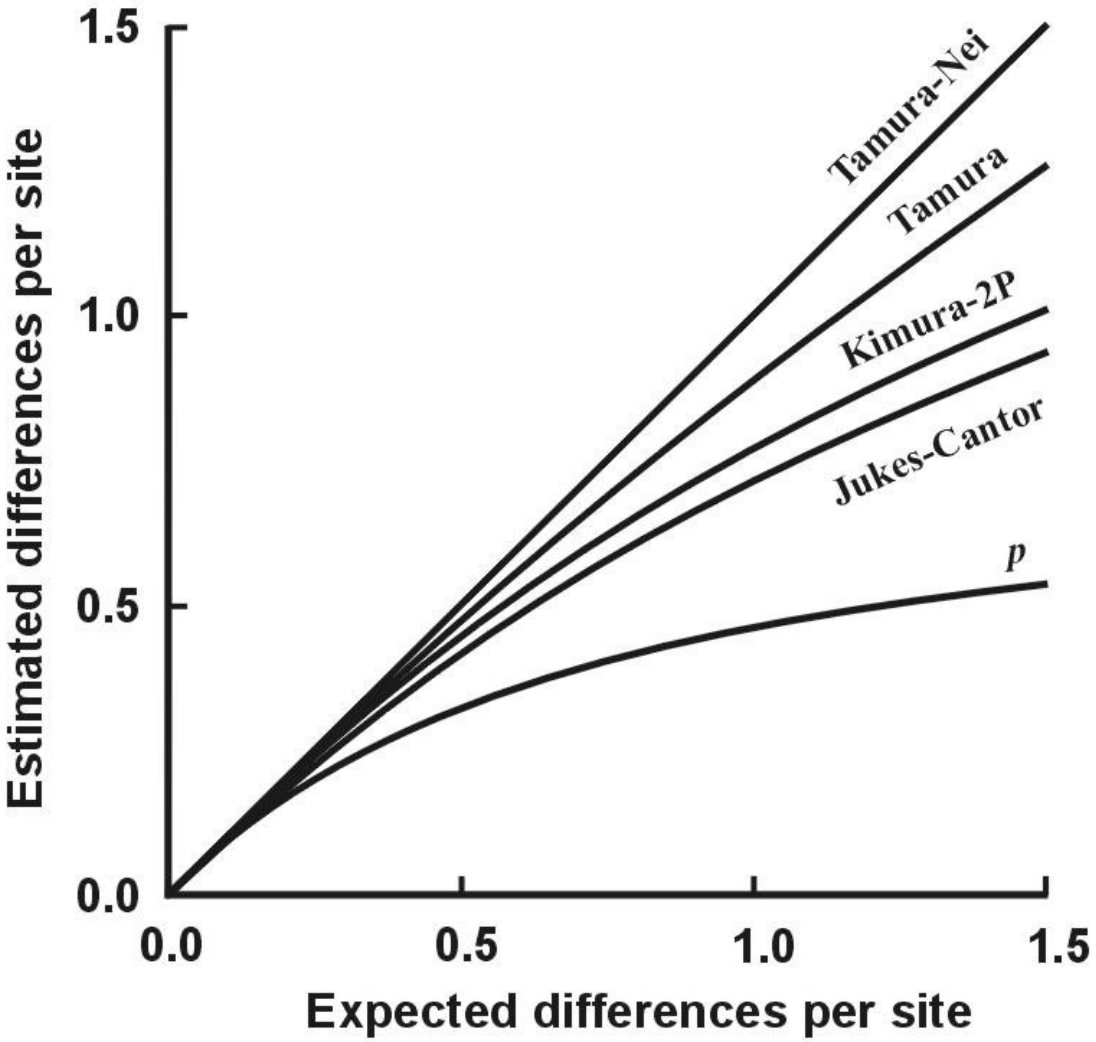
p-distance: $p = k/n = 3/30 = 0{,}10$

problém saturace:



Distance pro některé modely:

JC	$d_{xy} = -\frac{3}{4}\ln\left(1 - \frac{4}{3}D\right)$	$D = 1 - (a + f + k + p)$
F81	$d_{xy} = -B\ln\left(1 - \frac{D}{B}\right)$	D = jako JC $B = 1 - (\pi_A^2 + \pi_C^2 + \pi_G^2 + \pi_T^2)$
K2P	$d_{xy} = \frac{1}{2}\ln\left(\frac{1}{1-2P-Q}\right) + \frac{1}{4}\ln\left(\frac{1}{1-2Q}\right)$	rozdíly typu transicí: $P = c + h + i + n$ rozdíly typu transverzí: $Q = b + d + e + g + j + l + m + o$
F84	$d_{xy} = -2A\ln\left(1 - \frac{P}{2A} - \frac{(A-B)Q}{2AC}\right) - 2(A-B-C)\ln\left(1 - \frac{Q}{2C}\right)$	$\pi_Y = \pi_C + \pi_T$, $\pi_R = \pi_A + \pi_G$, $A = \pi_C\pi_T/\pi_Y + \pi_A\pi_G/\pi_R$, $B = \pi_C\pi_T + \pi_A\pi_G$, $C = \pi_R\pi_Y$, P a Q jako K2P
GTR	$d_{xy} = \text{stopa}\left(-\Pi\ln\Pi^{-1}\mathbf{F}_{xy}\right)$	Π = diagonální matice průměrných četností bází v sekvencích X a Y


1.5
1.0
0.5
0.0
0.0
0.5
1.0
1.5
Estimated differences per site
Expected differences per site
Tamura-Nei
Tamura
Kimura-2P
Jukes-Cantor
p

Shluková analýza - UPGMA

	šimp.	bonobo	gorila	člověk	orang.
šimpanz (Š)	--				
bonobo (B)	0,0118	--			
gorila (G)	0,0427	0,0416	--		
člověk (Č)	0,0382	0,0327	0,0371	--	
orangutan (O)	0,0953	0,0916	0,0965	0,0928	--

1. Najdi min *d*(*ij*)
2. Vypočítej novou matici: *d*(ŠB-*k*) = [*d*(B-*k*)+*d*(Š-*k*)]/2
3. Opakuj 1 a 2.

	ŠB	gorila	člověk	orang.
ŠB	--			
gorila (G)	0,0422	--		
člověk (Č)	0,0355	0,0371	--	
orangutan (O)	0,0935	0,0965	0,0928	--

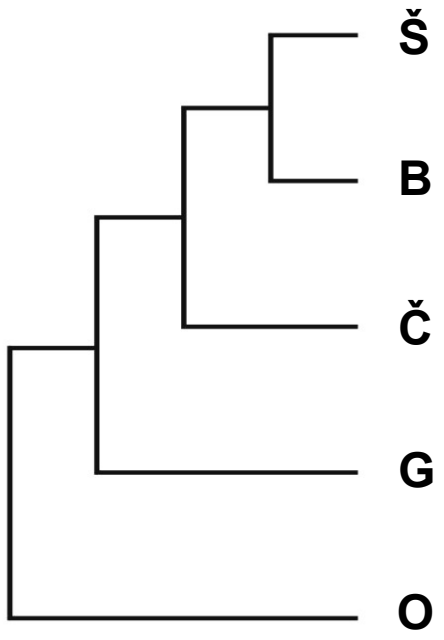
UPGMA (*unweighted pair-group method using arithmetic means*):

d[(BŠČ)G] = {d(BG)+d(ŠG)+d(ČG)}/3

WPGMA: d[(BŠČ)G] = {d[(BŠ)G] + d(ČG)}/2

single-linkage (metoda nejbližšího souseda)

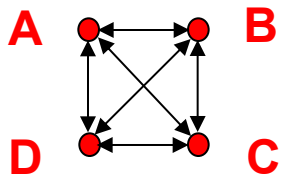
complete-linkage (m. nejvzdálenějšího souseda)



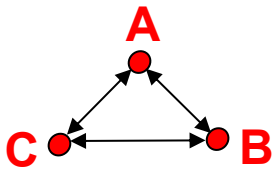
UPGMA a konzistence

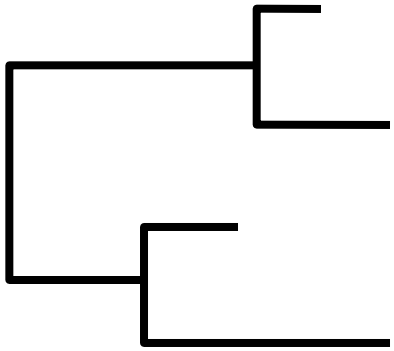
aditivní distance: $d_{AB} + d_{CD} \leq \max (d_{AC} + d_{BD}, d_{AD} + d_{BC})$

tj. vzdálenost mezi 2 taxony je rovna součtu větví, které je spojují

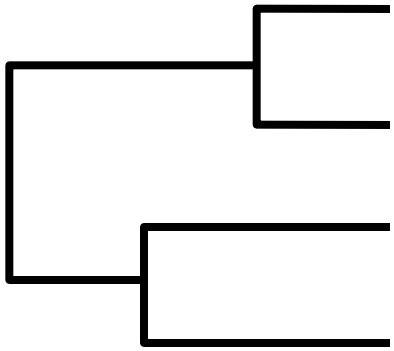


ultrametrické distance: $d_{AC} \leq \max (d_{AB}, d_{BC})$



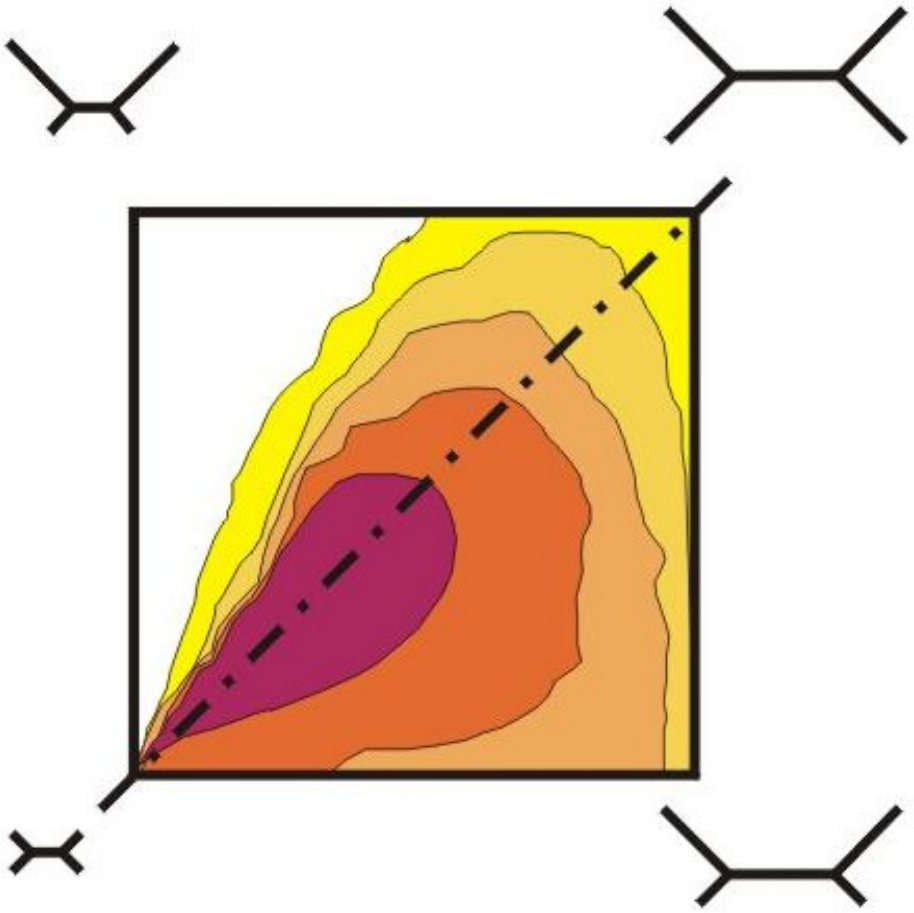


aditivní strom



ultrametrický strom

UPGMA a konzistence



Spojení sousedů (neighbor-joining, NJ)

Algoritmická metoda

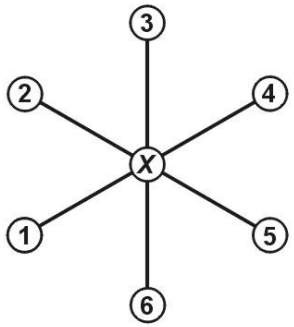
Princip minimální evoluce $\rightarrow$ minimalizuje součet délek větví *S*

Každý pár uzlů adjustován na základě divergence od ostatních

Konstrukce jediného aditivního stromu

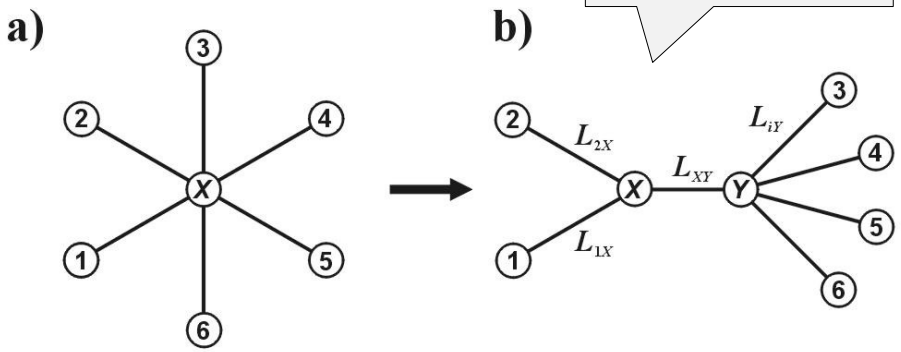
hvězdicový strom

a)



hvězdicový strom

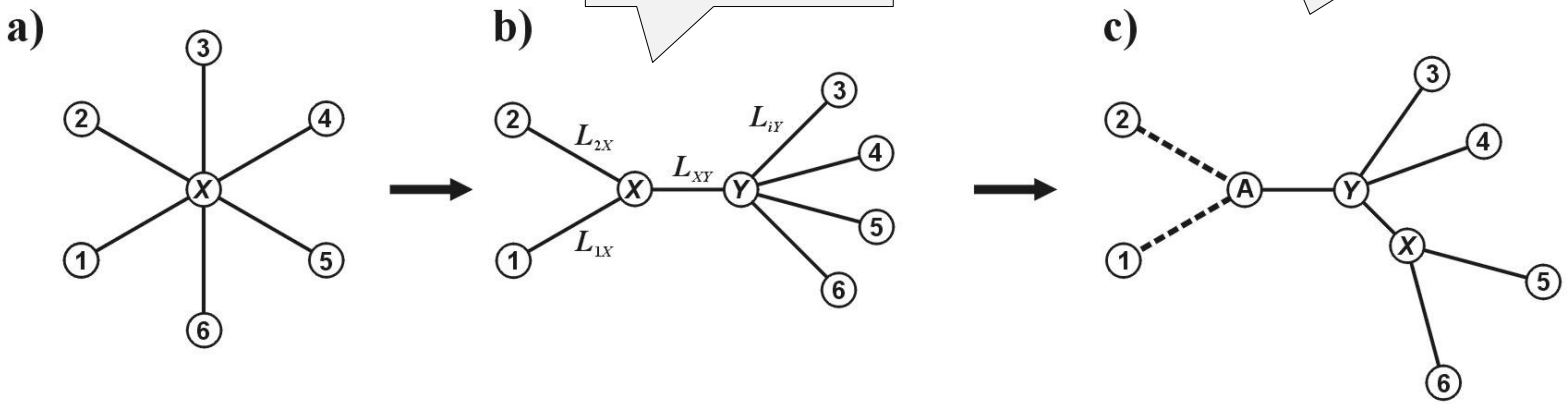
nalezení nejbližších sousedů

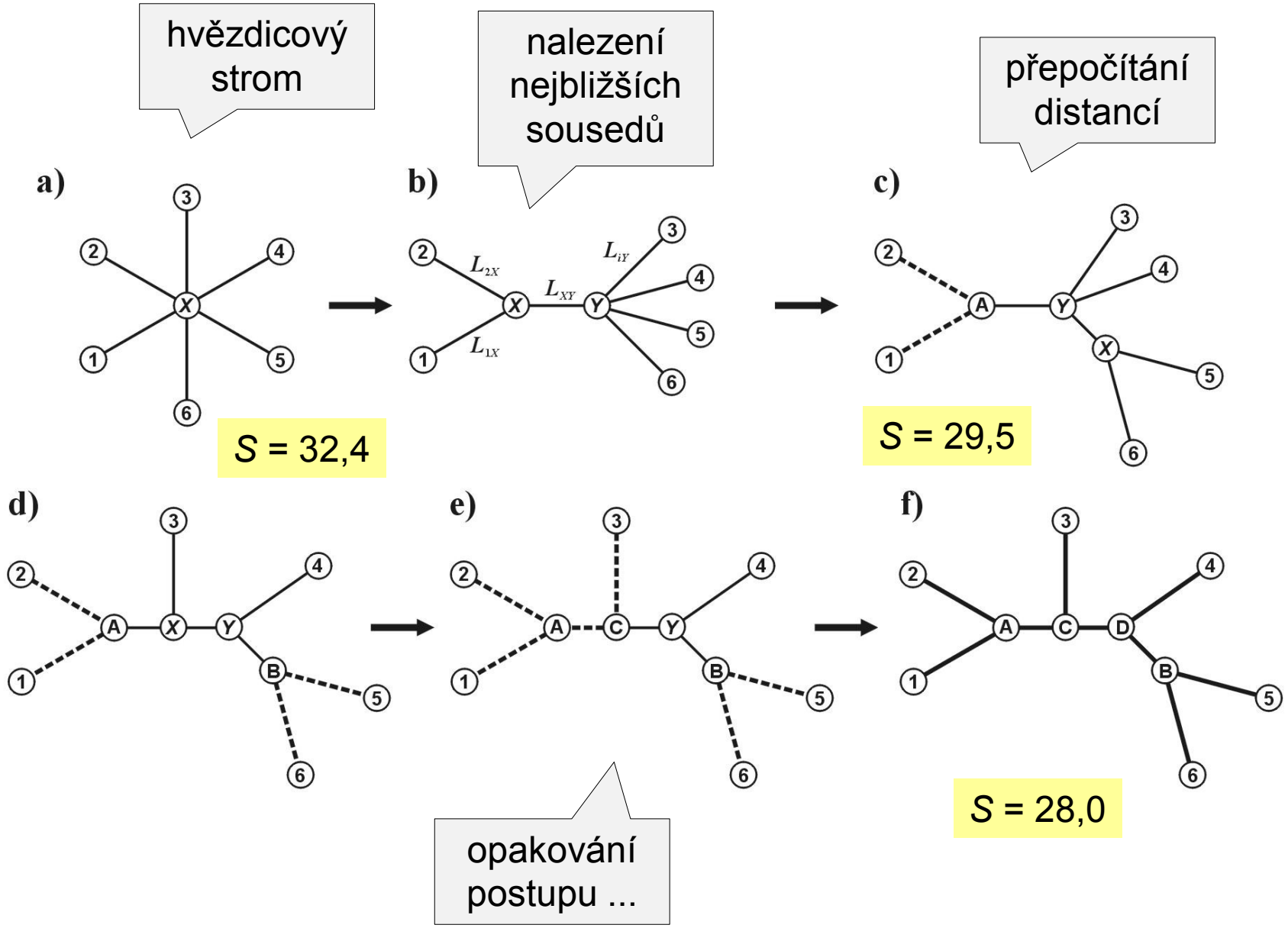


hvězdicový strom

nalezení nejbližších sousedů

přepočítání distancí




hvězdicový strom
nalezení nejbližších sousedů
přepočítání distancí
a)
b)
c)
L_{2X}
L_{XY}
L_{iY}
L_{1X}
S = 32,4
S = 29,5
d)
e)
f)
opakování postupu ...
S = 28,0

Nevýhody distančních dat:

1. ztráta části informace během transformace
2. jakmile data transformována na distance, nelze se vrátit zpět
   (odlišné sekvence mohou dát stejné distance)
3. nelze sledovat evoluci na různých částech sekvence
4. obtížná biologická interpretace délek větví
5. nelze kombinovat různé distanční matice