Mind the gap: Modelling evolution with indels

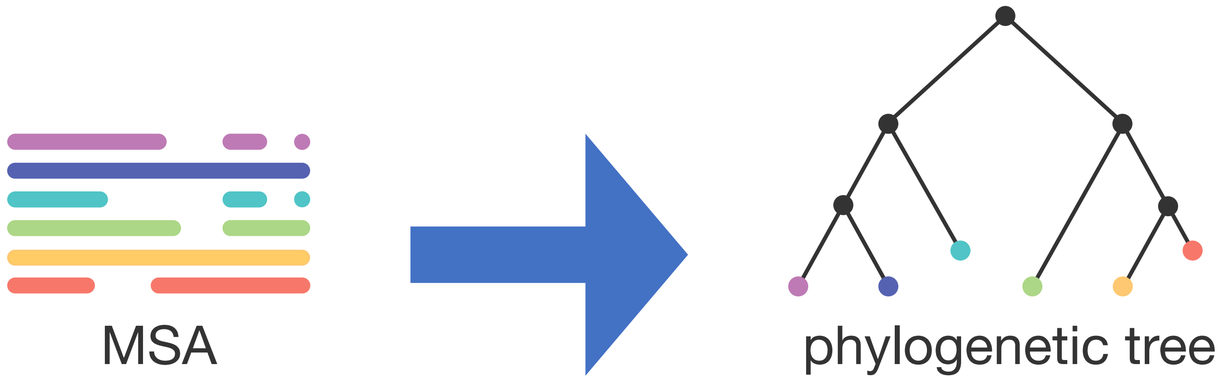
TAMING THE BEAST 2023

Jūlija Pečerska

17.08.23

PHYLOGENETIC PIPELINES

EXPECTATION



PHYLOGENETIC PIPELINES

REALITY

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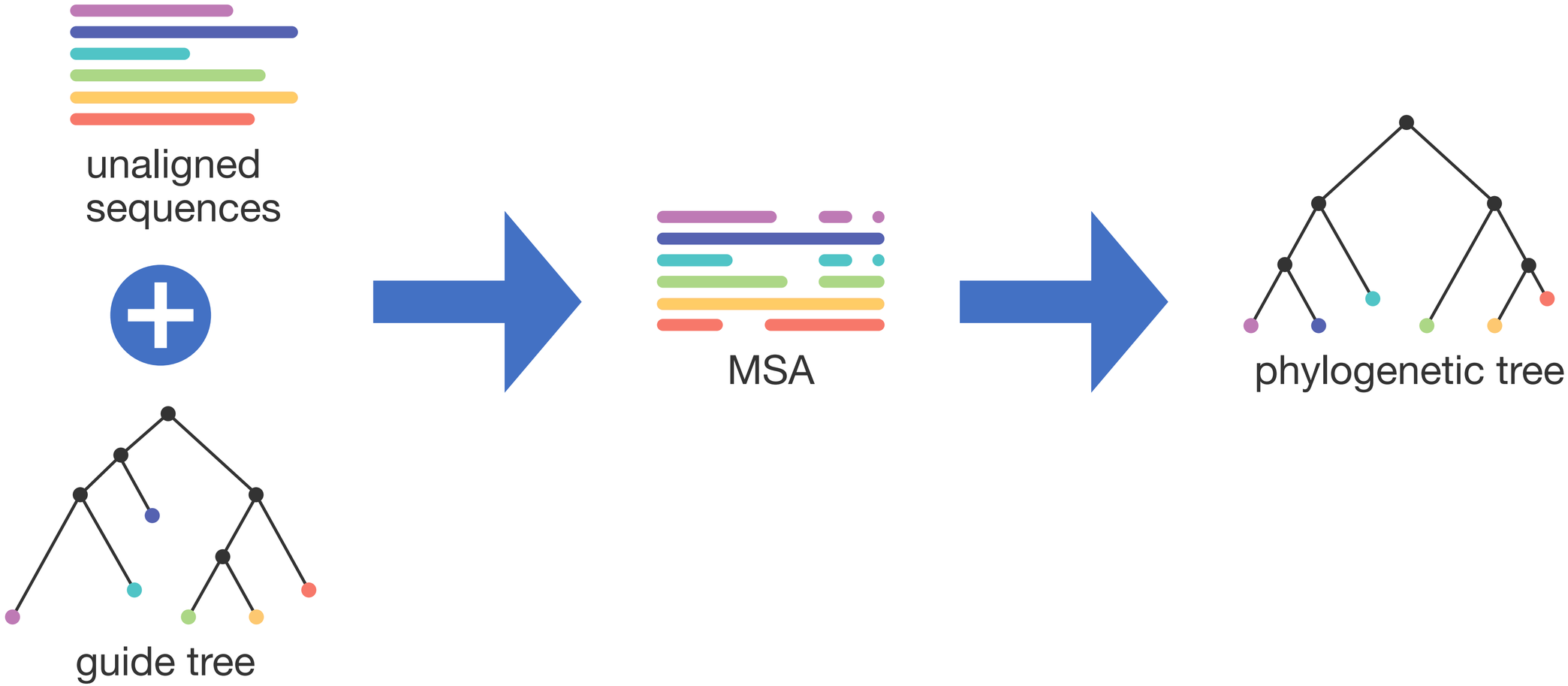

PHYLOGENETIC PIPELINES

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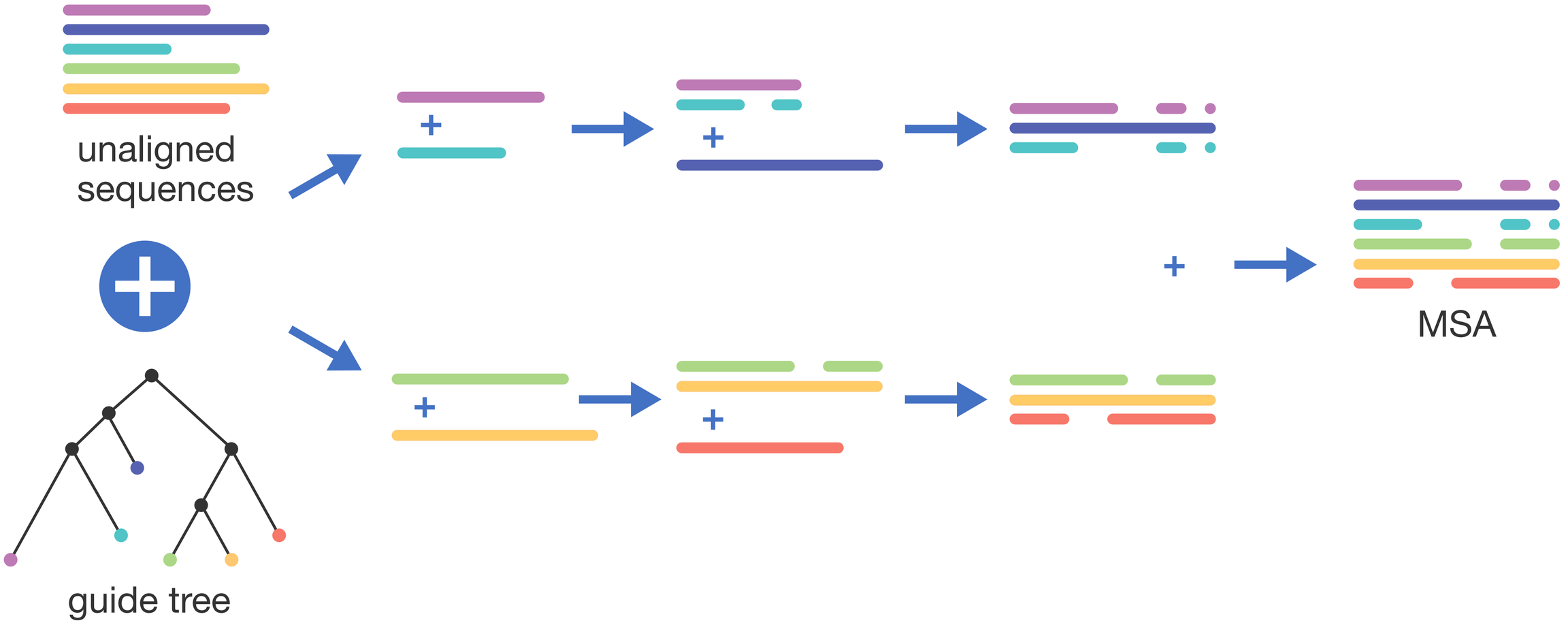

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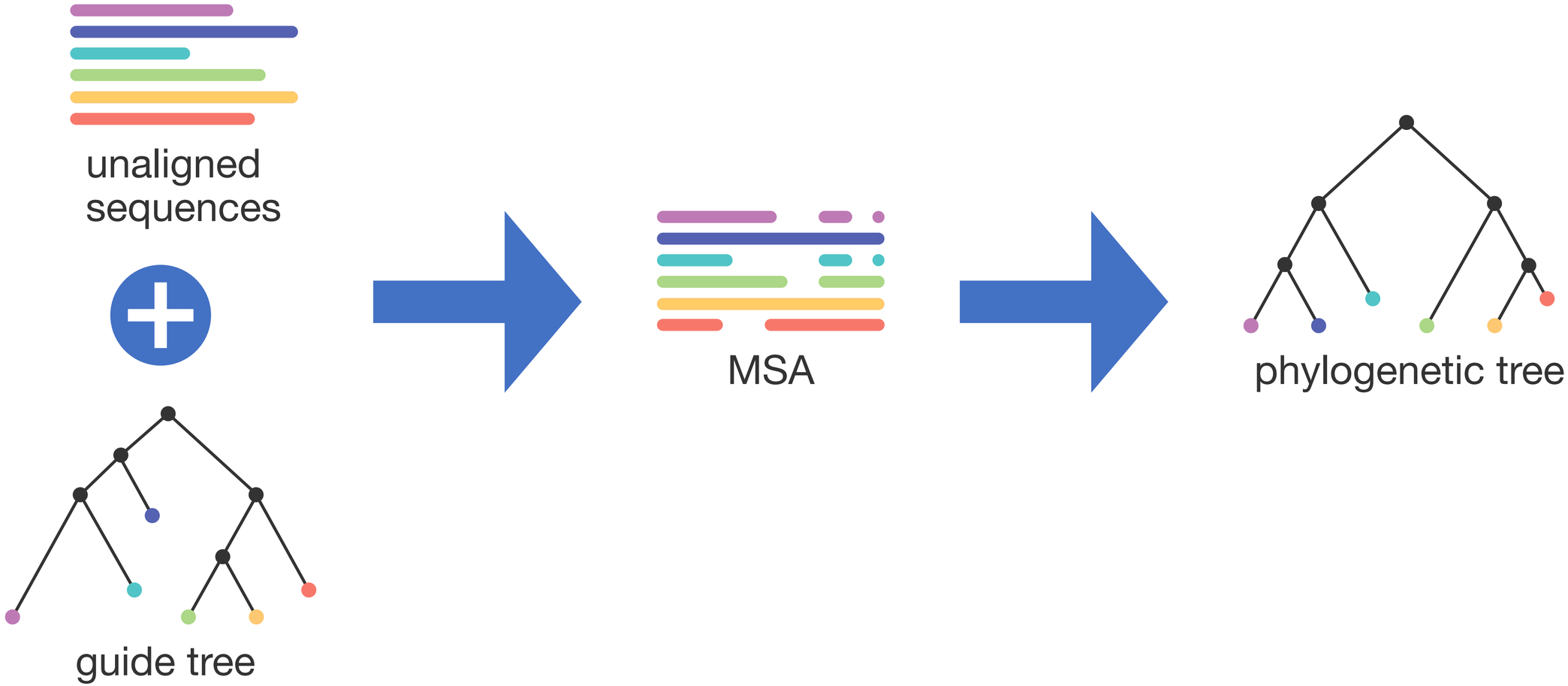
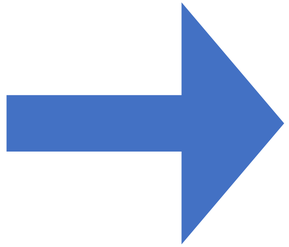
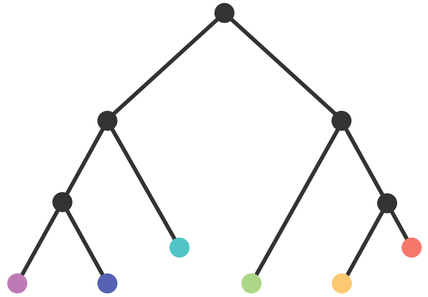


PHYLOGENETIC PIPELINES

REALITY

MSA





phylogenetic tree

PHYLOGENETIC PIPELINES

REALITY

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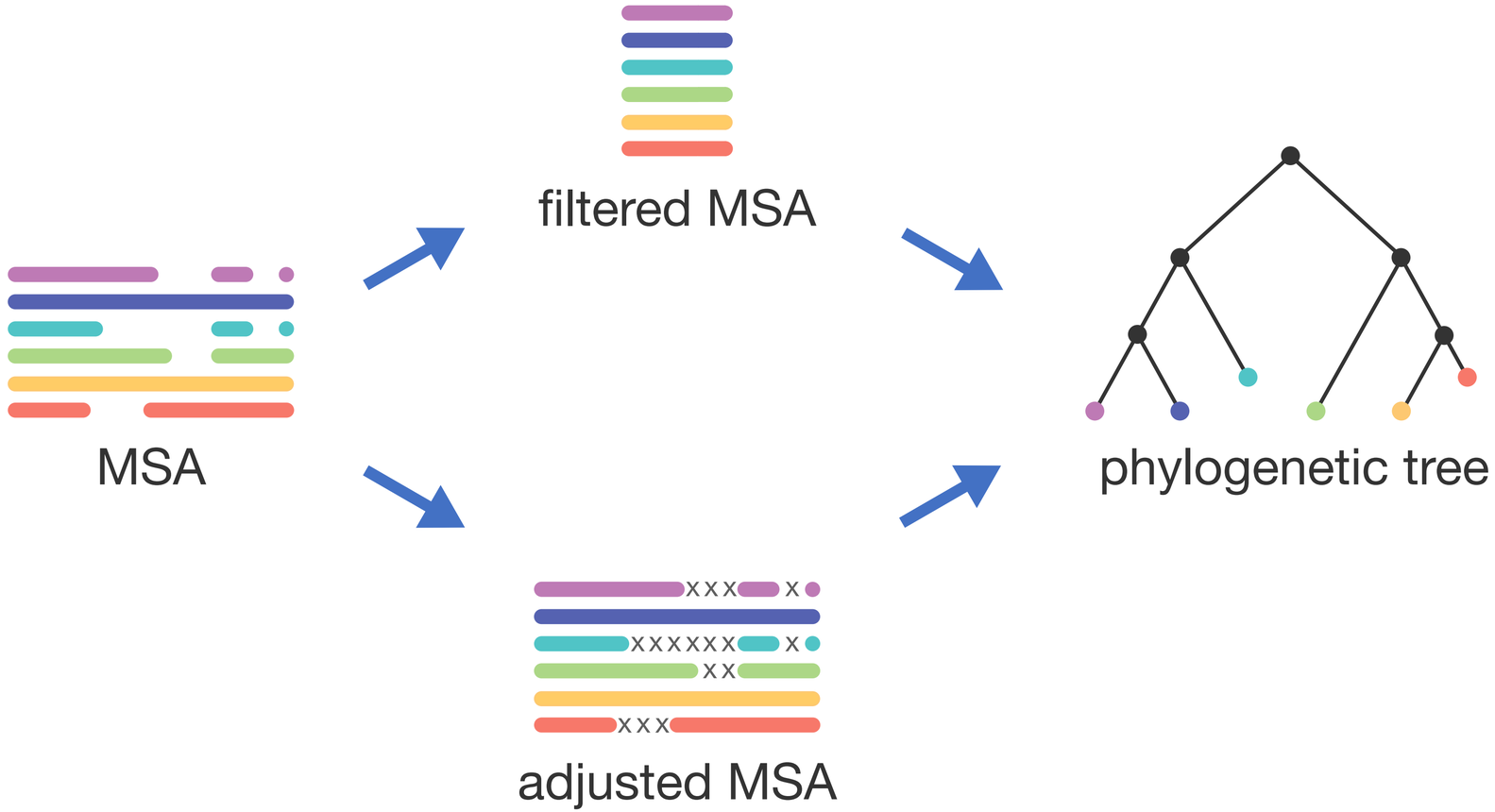
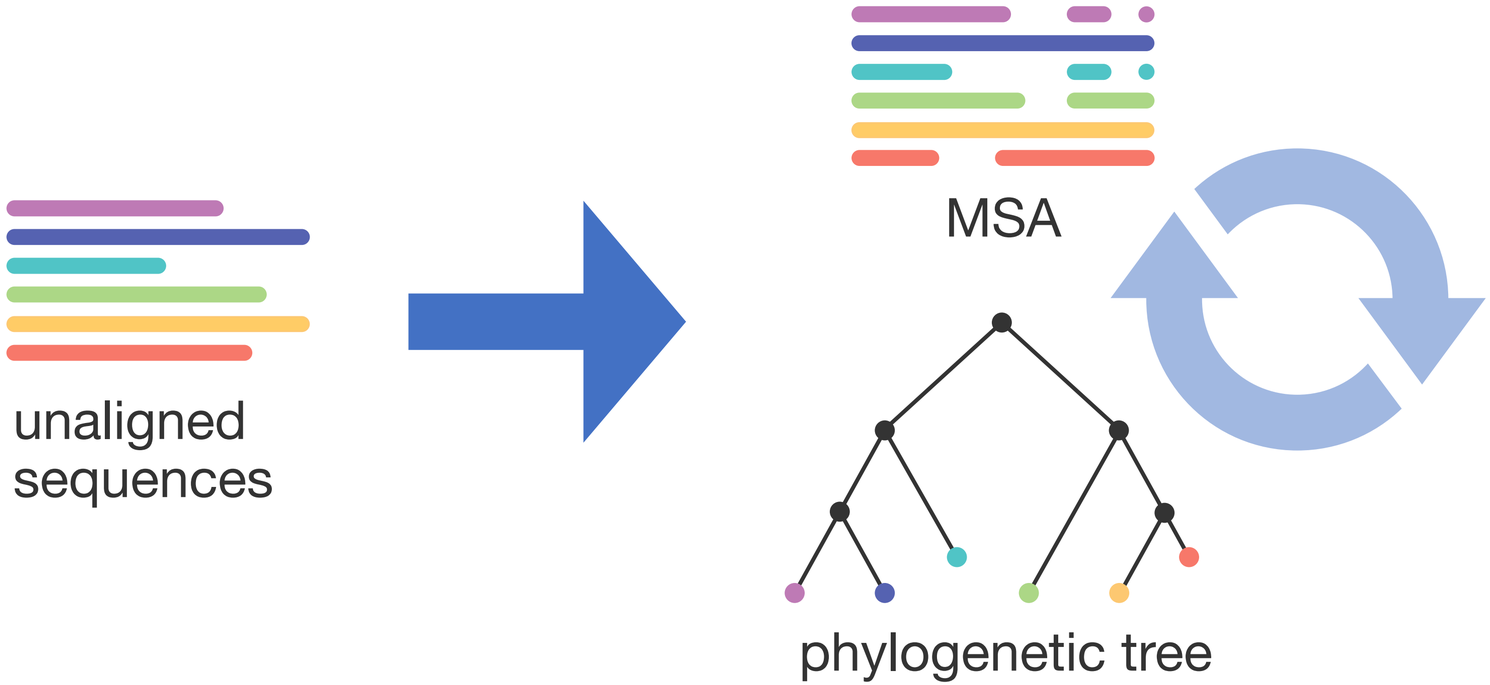


PHYLOGENETIC PIPELINES

EXPECTATION 2.0



REMINDER: SUBSTITUTION MODELS

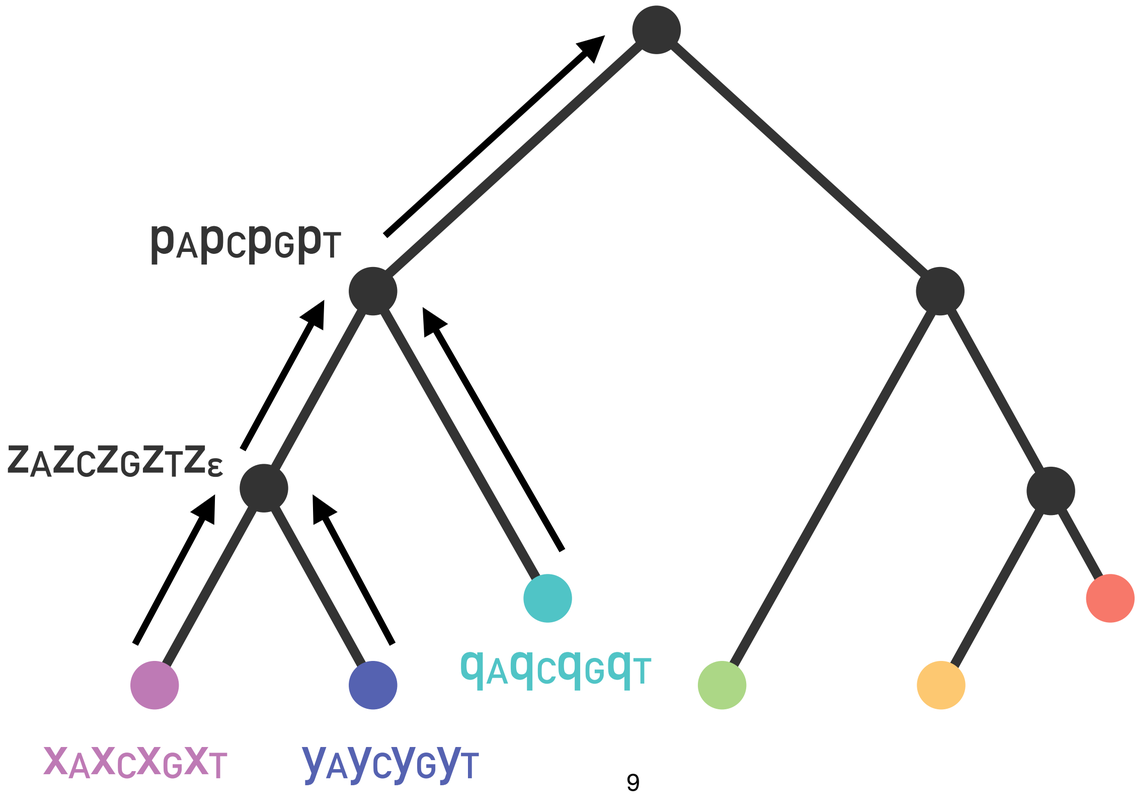
CONTINUOUS TIME MARKOV CHAINS

- Q — substitution rate matrix
- $\mathrm{P}(t)$ — transition probability matrix
- $\mathrm{P}(t) = e^{t\mathrm{Q}}$
  - $\mathrm{P}(t+s) = e^{(t+s)\mathrm{Q}} = e^{t\mathrm{Q}}e^{s\mathrm{Q}} = \mathrm{P}(t)\mathrm{P}(s)$

	T	C	A	G
T	…	$a\pi_{\mathrm{C}}$	$b\pi_{\mathrm{A}}$	$c\pi_{\mathrm{G}}$
C	$a\pi_{\mathrm{T}}$	…	$d\pi_{\mathrm{A}}$	$e\pi_{\mathrm{G}}$
A	$b\pi_{\mathrm{T}}$	$d\pi_{\mathrm{C}}$	…	$f\pi_{\mathrm{G}}$
G	$c\pi_{\mathrm{T}}$	$e\pi_{\mathrm{C}}$	$f\pi_{\mathrm{A}}$	…

REMINDER: PHYLOGENETIC LIKELIHOOD

USING FELSENSTEIN'S PRUNING ALGORITHM



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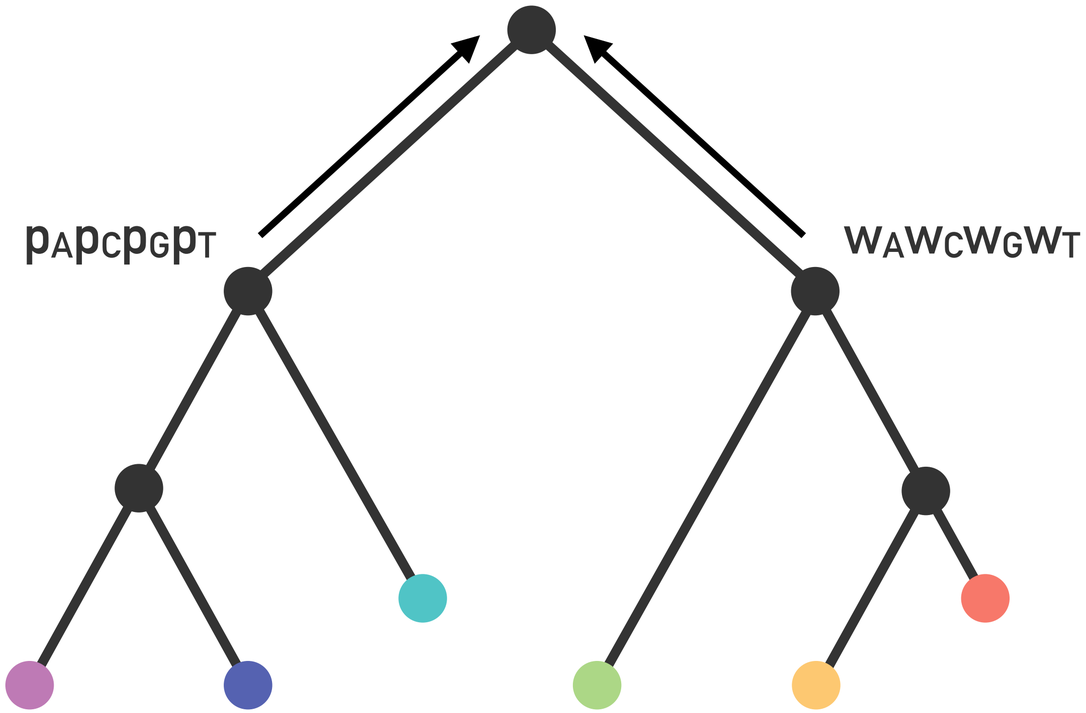

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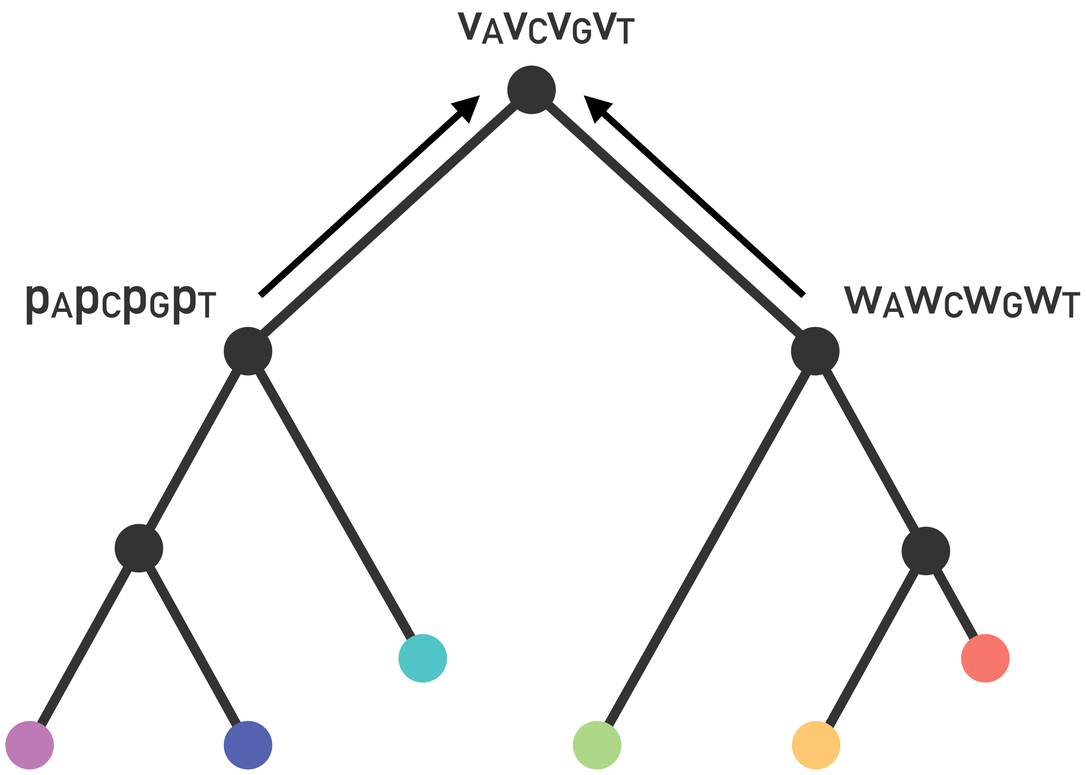
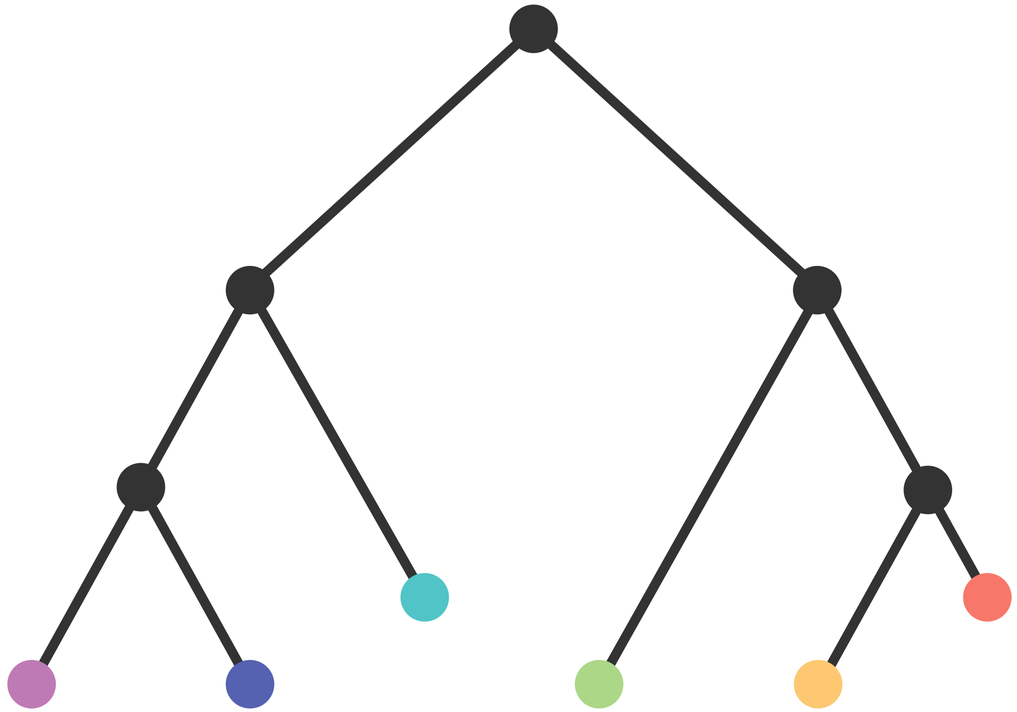


REMINDER: PHYLOGENETIC LIKELIHOOD

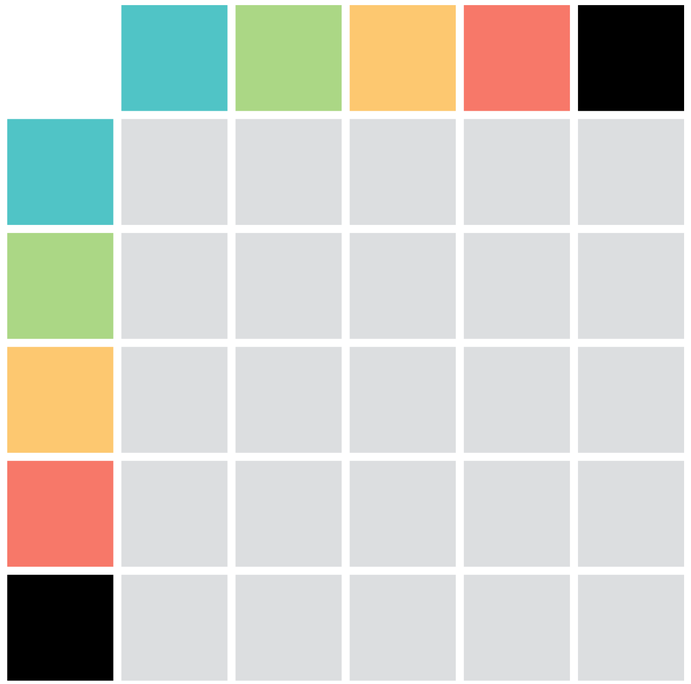
USING FELSENSTEIN'S PRUNING ALGORITHM

Likelihood = $f(v_A v_C v_G v_T)$



MODELLING INDELS

WHY NOT WITH MARKOV CHAINS?



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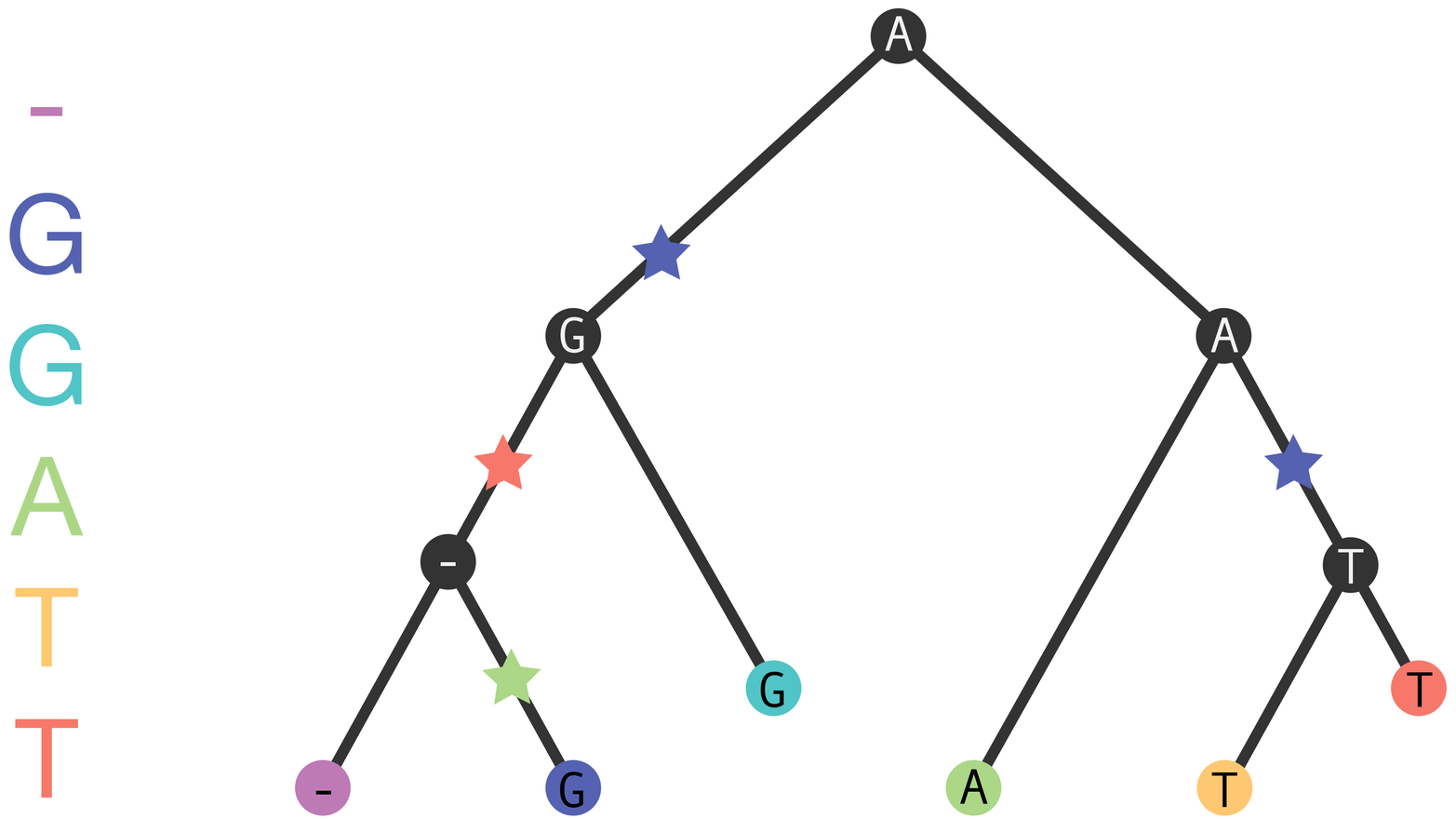

ANOTHER FUNKY INDEL SCENARIO

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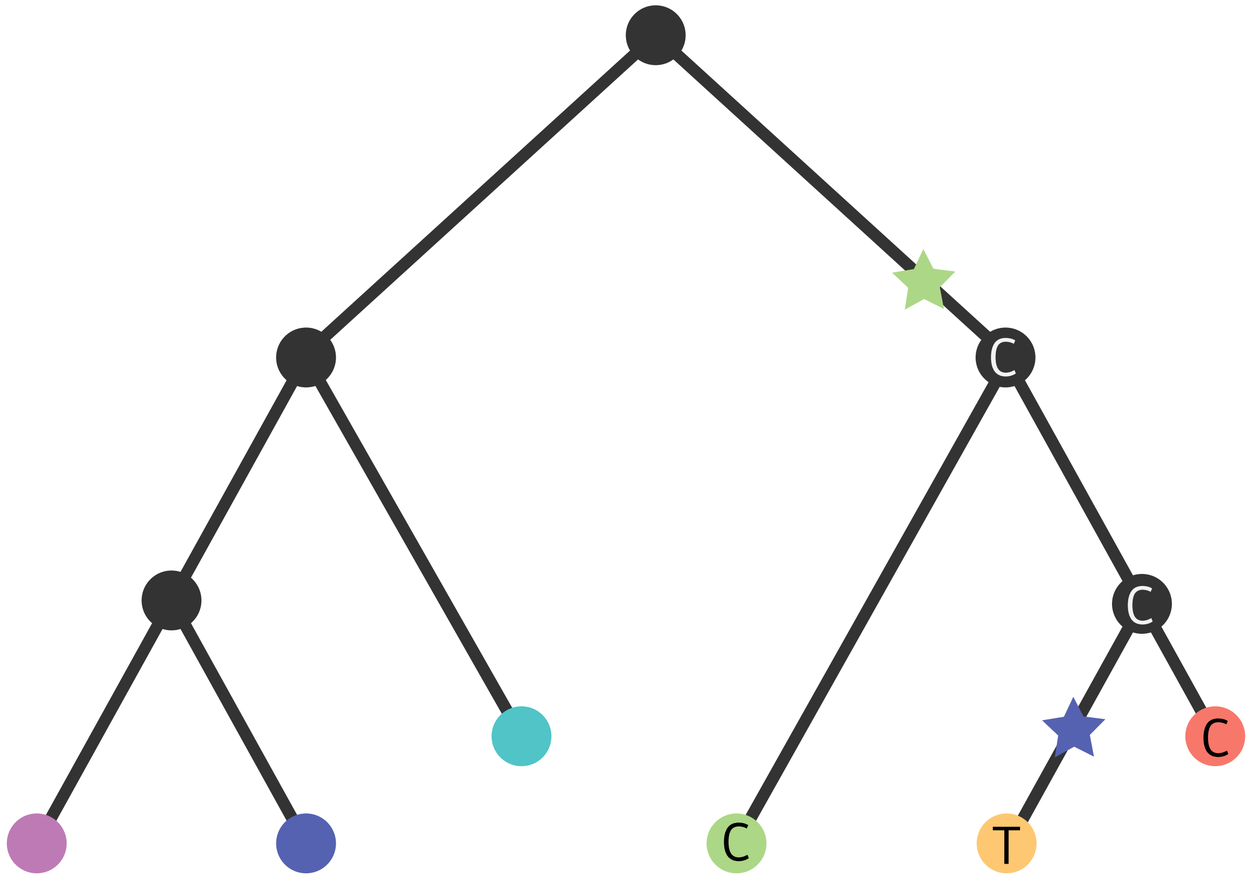
C



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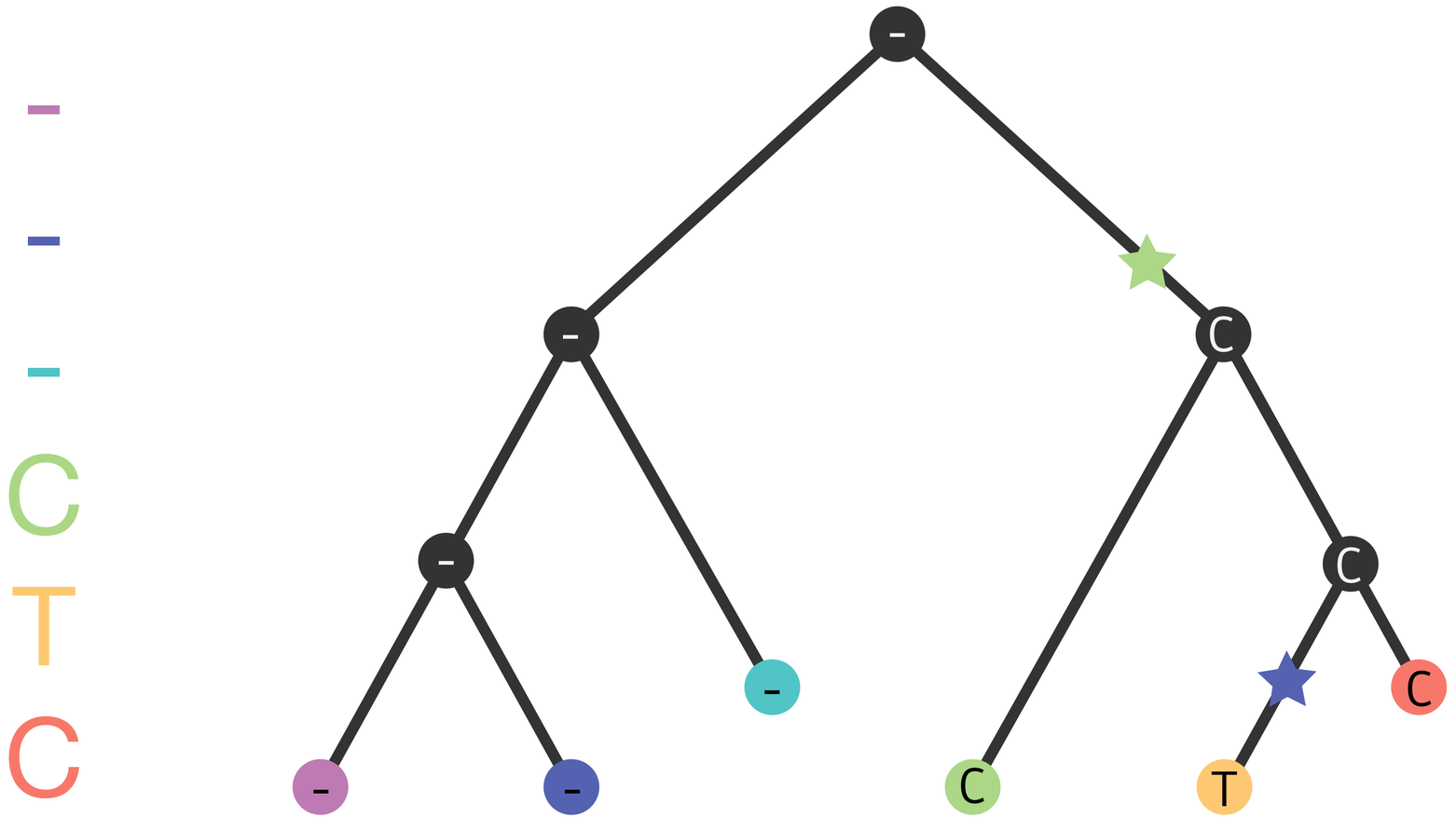

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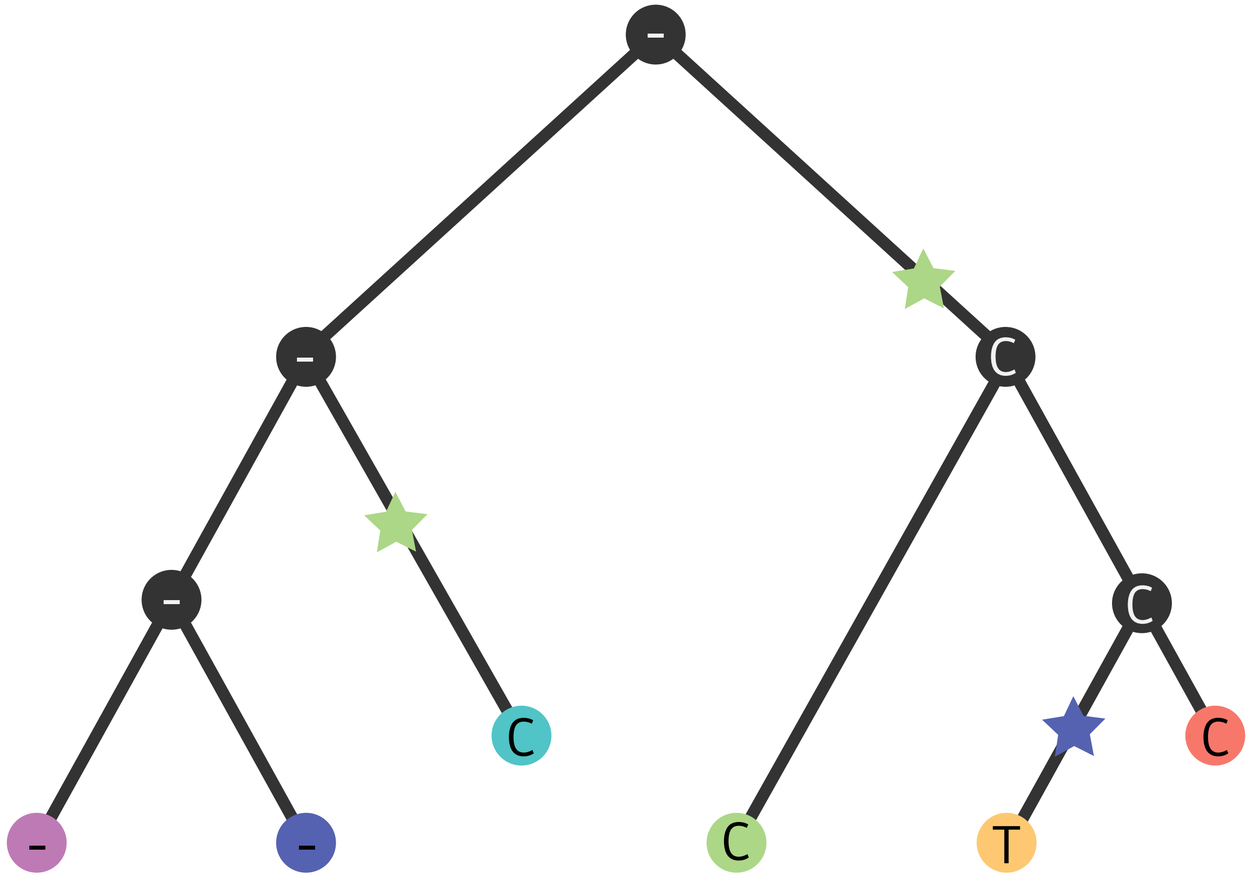
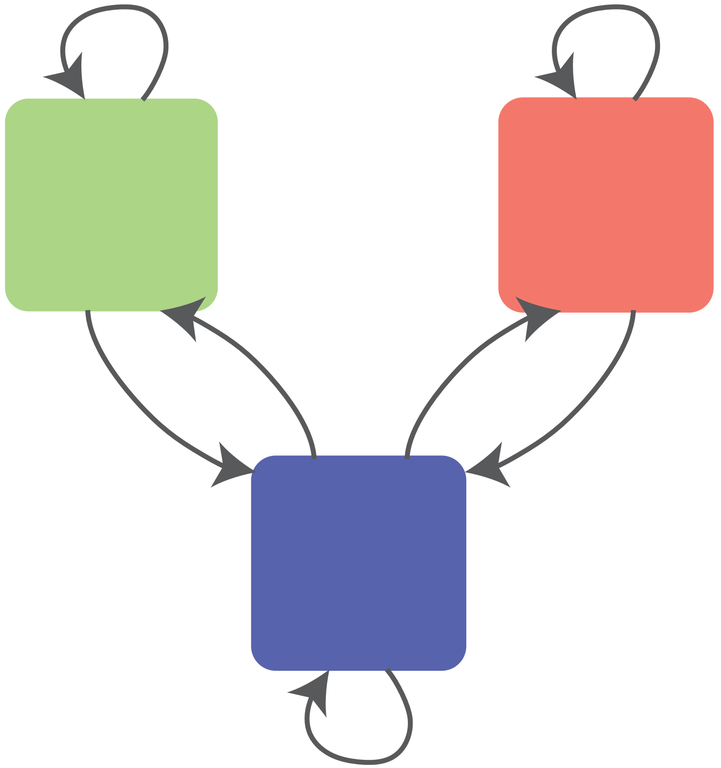
- - C C T C



MODELLING INDELS

USING HMMS

- Process (e.g. TKF91/92) described with an HMM



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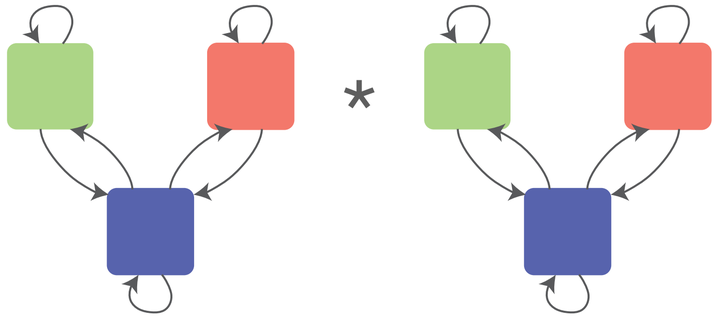
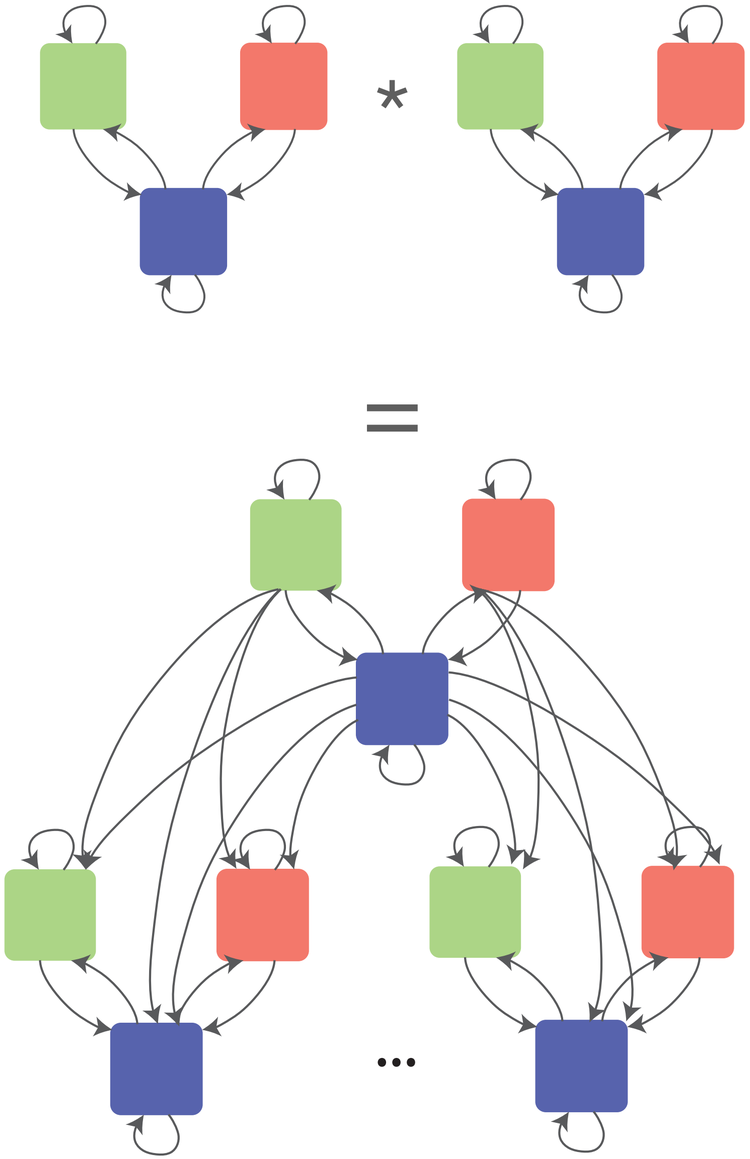


- Process (e.g. TKF91/92) described with an HMM
- Differentiating along a branch explodes the HMM

MODELLING INDELS

USING HMMS

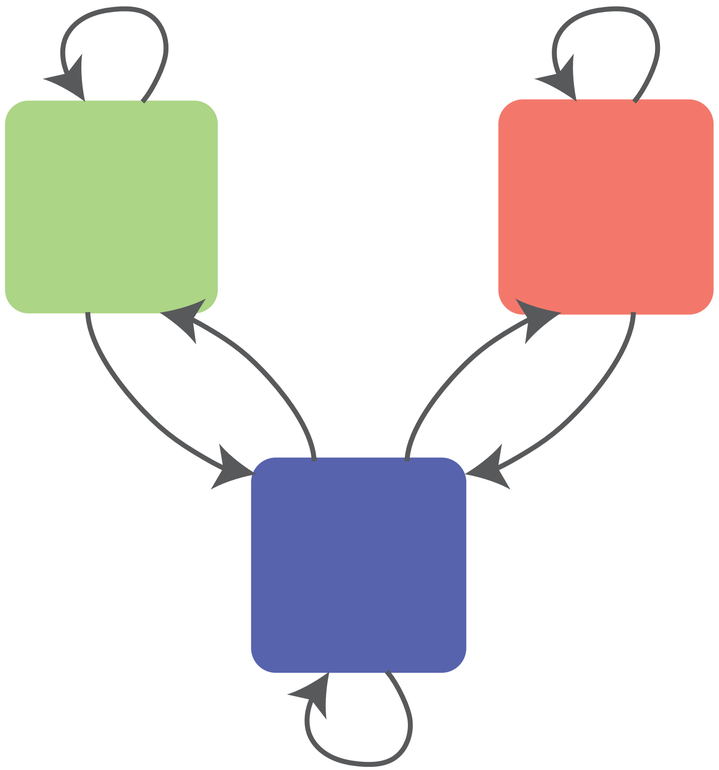


- Process (e.g. TKF91/92) described with an HMM
- Differentiating along a branch explodes the HMM
  - Finite branch length -> infinite states

MODELLING INDELS

USING HMMS

- Process (e.g. TKF91/92) described with an HMM
- Differentiating along a branch explodes the HMM
  - Finite branch length -> infinite states
- Can be simplified!
  - For local likelihood;
  - Global likelihood complexity is still exponential.



MODELLING INDELS...

... is very hard

MODELLING INDELS

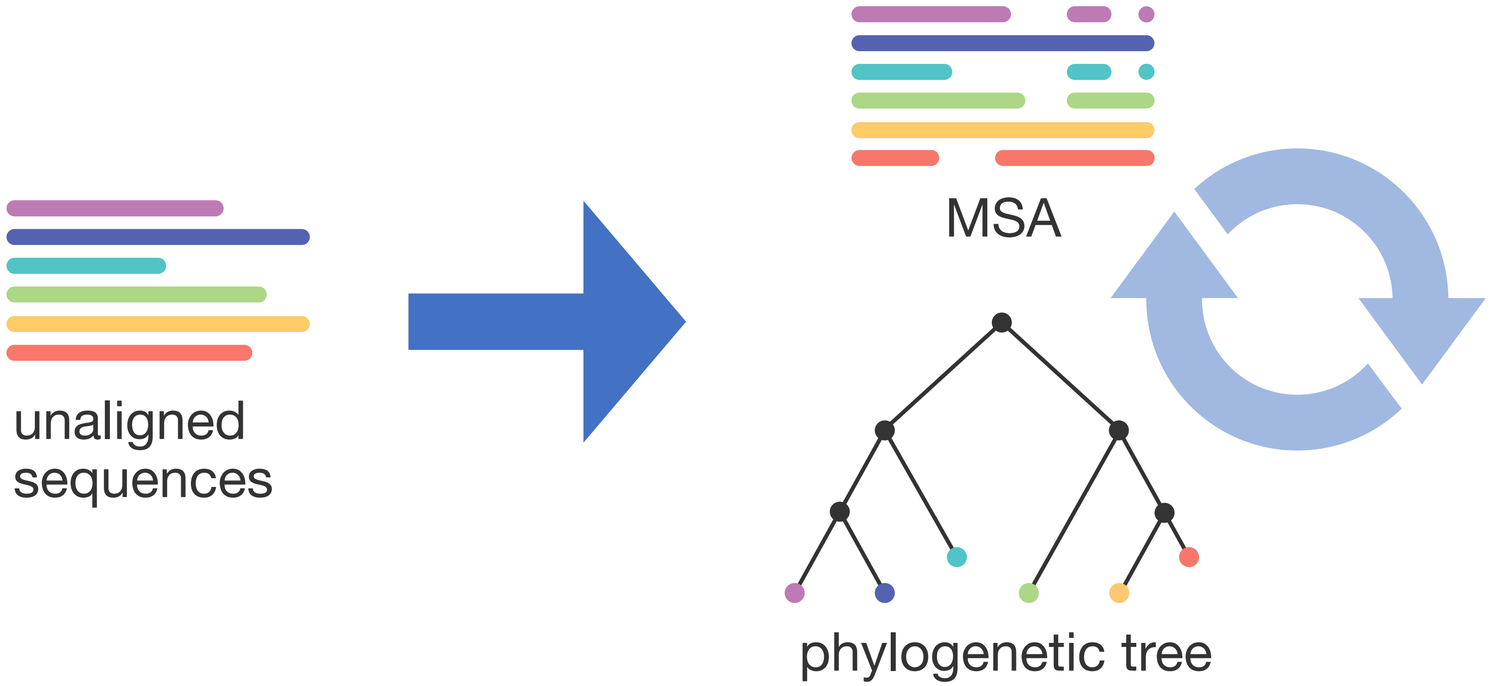
POISSON INDEL PROCESS (PIP)

PIP = Poisson insertion process on a tree
+ Substitution/deletion Markov process

- Properties:
  - Single character insertions/deletions
  - Time-reversible
  - Linear time likelihood

JOINT INFERENCE: THE DREAM

EXPECTATION 2.0



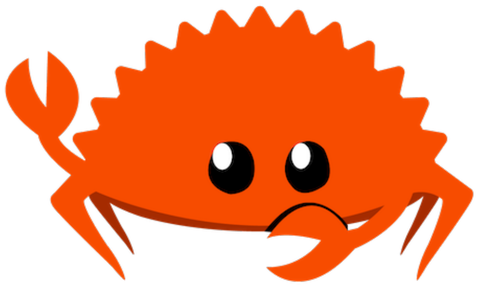
BAli---Phy

JOINT INFERENCE

REALITY

- JATI 1.0 necessary (but not sufficient) conditions:
  - Efficient
    - MSA adjustment in $O(NL^3)$
    - Tree search in $O(N^2L)$
  - Open-source
  - User-friendly

- Implementation:
  - Rust codebase (github.com/acg-team/JATI (private for now))
  - Release information (twitter.com/JulijaPecerska)



TAKEAWAYS

- Indel models are complicated;
- Know your data!!!
- Know your models and priors;
- Know your software and its assumptions.

ACKNOWLEDGEMENTS

- ACGTeam @ ZHAW
- Prof Maria Anisimova 
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