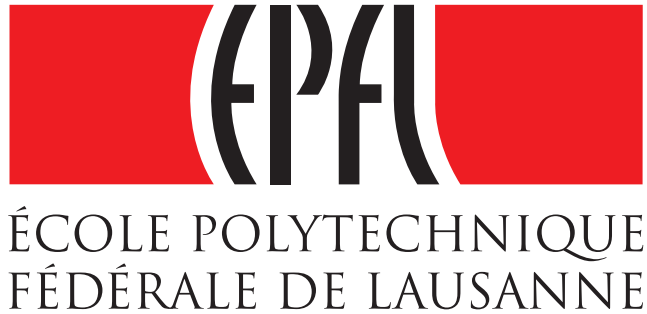


Principled Synteny Analysis

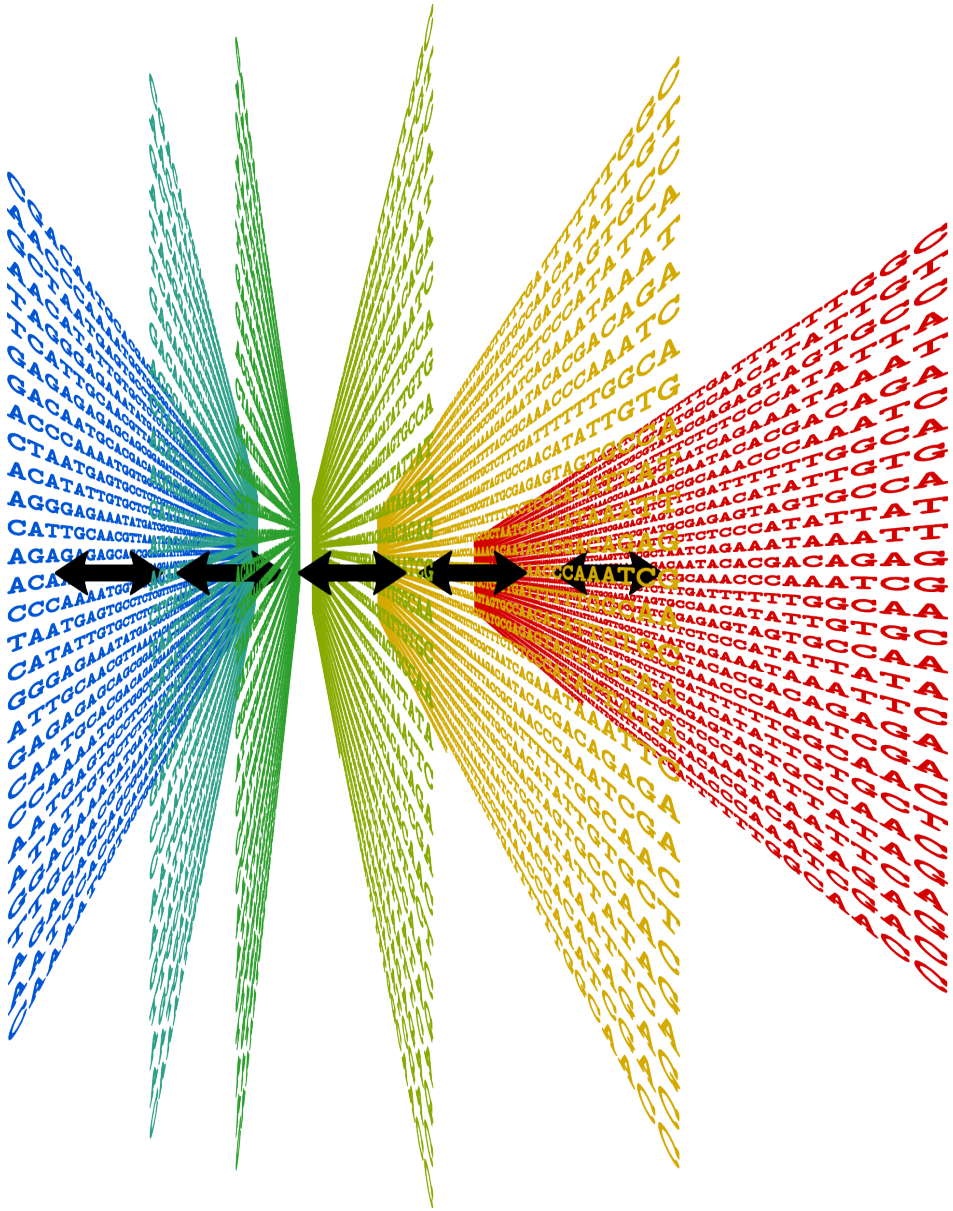
Daniel Doerr, Bernard M.E. Moret

School of Computer and Communication Sciences, EPFL, Lausanne, Switzerland

June 13, 2016

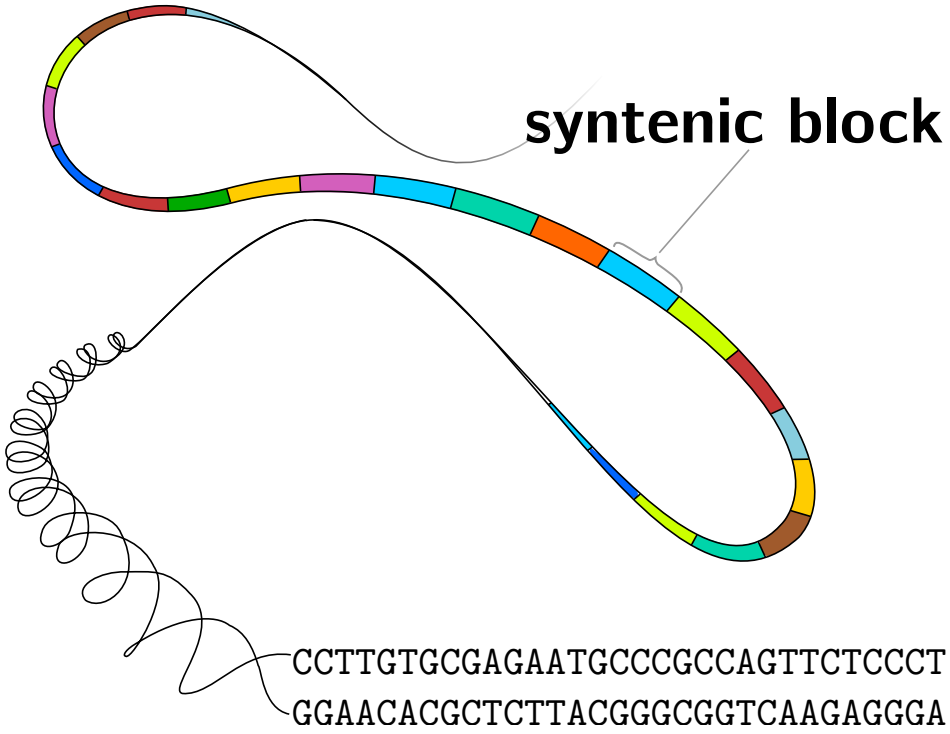
Comparing genomes

- Continued interest in large-scale whole-genome comparisons
- Base-by-base comparison infeasible for big genomes



Abstraction by decomposition

- Genomes decomposed into *syntenic blocks*
- Essential for genome rearrangement studies



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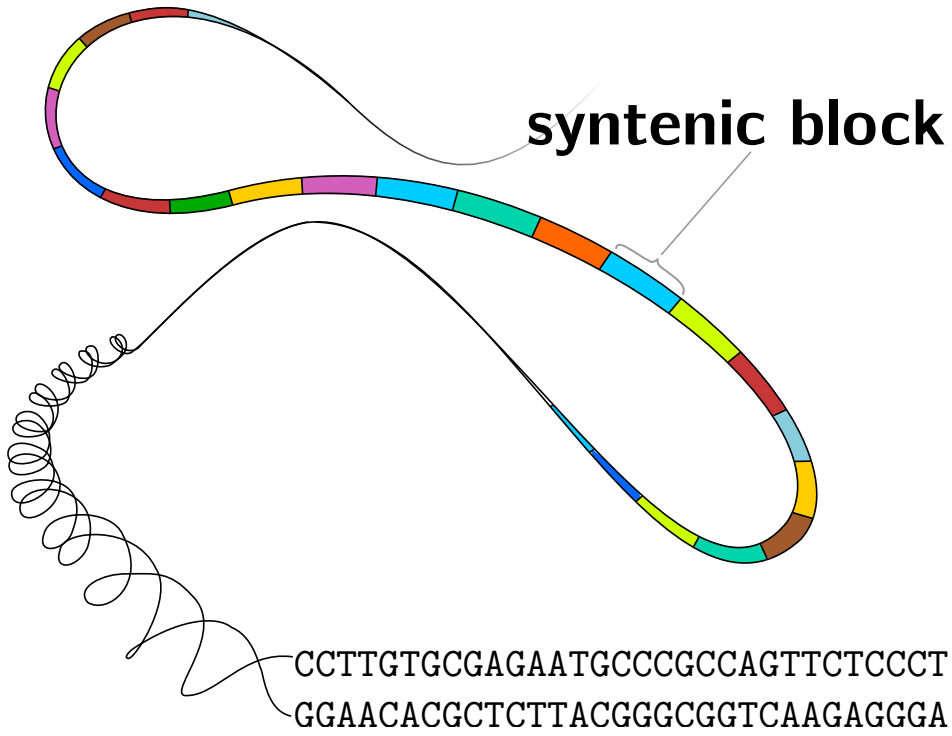

Protein-coding genes form basis for most rearrangement studies

$\Longrightarrow$ Omission of many other conserved genomic regions

What is synteny?

When is a syntenic block conserved? A zoo of definitions:

- *synteny*: Renwick, 1971: "*same ribbon*", co-location on same chromosome
- Collinear
- local rearrangements allowed
- Tool-centric: FISH, GRIMM/DRIMM-Synteny, Cyntenator, i-ADHoRe, Sibelia, CoGe, Satsuma, *etc.*

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Does there exist "one true syntenic block"?

$\Longrightarrow$ Different levels of granularity

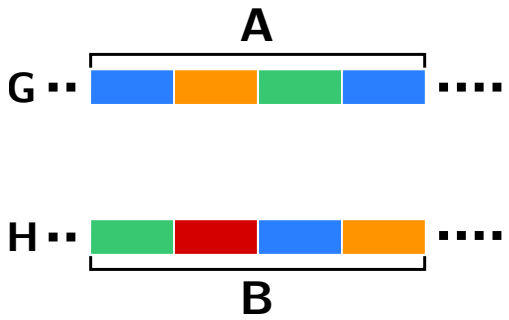
Synteny criterion

syntenic block (SB)

Set of contiguous syntenic blocks

homology assignment between blocks

Set $\mathcal{H}$ of pairwise equivalence relations



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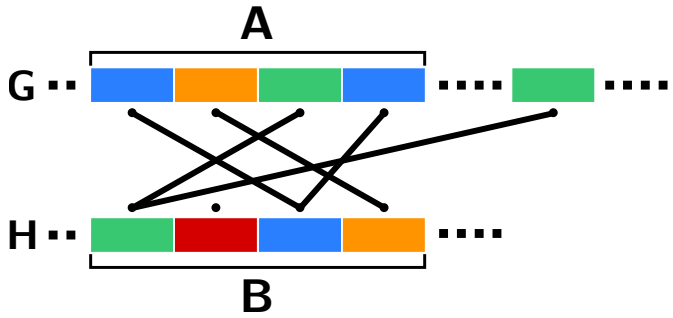
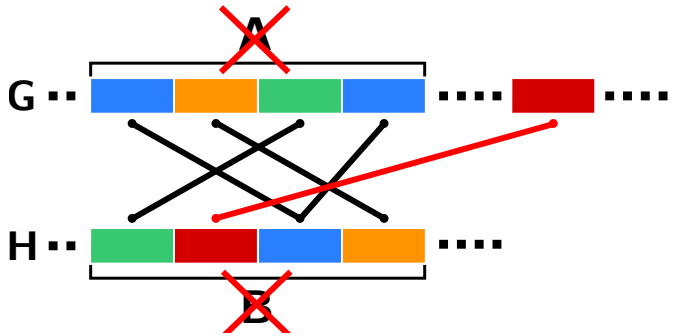


homologous SB pair [Ghiurcuta and Moret, 2014]

Given two genomes G, H and homology assignment $\mathcal{H}$, two SBs $A \subseteq G$ and $B \subseteq H$ are homologous if for each

- $a \in A$:
  $\exists\ (a,h) \in \mathcal{H}, h \in H \implies (a,b') \in \mathcal{H}, b' \in B$
- $b \in B$:
  $\exists\ (b,g) \in \mathcal{H}, g \in G \implies (a',b) \in \mathcal{H}, a' \in A$



Synteny workflow

A workflow for principled synteny analysis

Genome segmentation

Apply synteny criterion to genome segmentation!

Genome segmentation

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Sequence segmentation problem [Visnovská et al., 2013]

Set $\mathcal{S}$ of genomic subsequences is a **segmentation** of genomes $G_1, \ldots, G_k$ if for any $S, S' \in \mathcal{S}$ holds:

- for each site $X \in S$ s.t. $\nexists\, Y \in S'$ and X, Y homologous $\implies \nexists\, S'' \in \mathcal{S} \setminus \{S, S'\}$, s.t. $Z \in S''$ and X, Z homologous; id. for each site $X' \in S'$

```
S   :CG_GATG       AA
S'  :C_AGTTCATGATAAT
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S''':       TT_ATT       TGCAA
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Segmentation invalid!

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- non-overlapping, if S, S' belong to same genome

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```
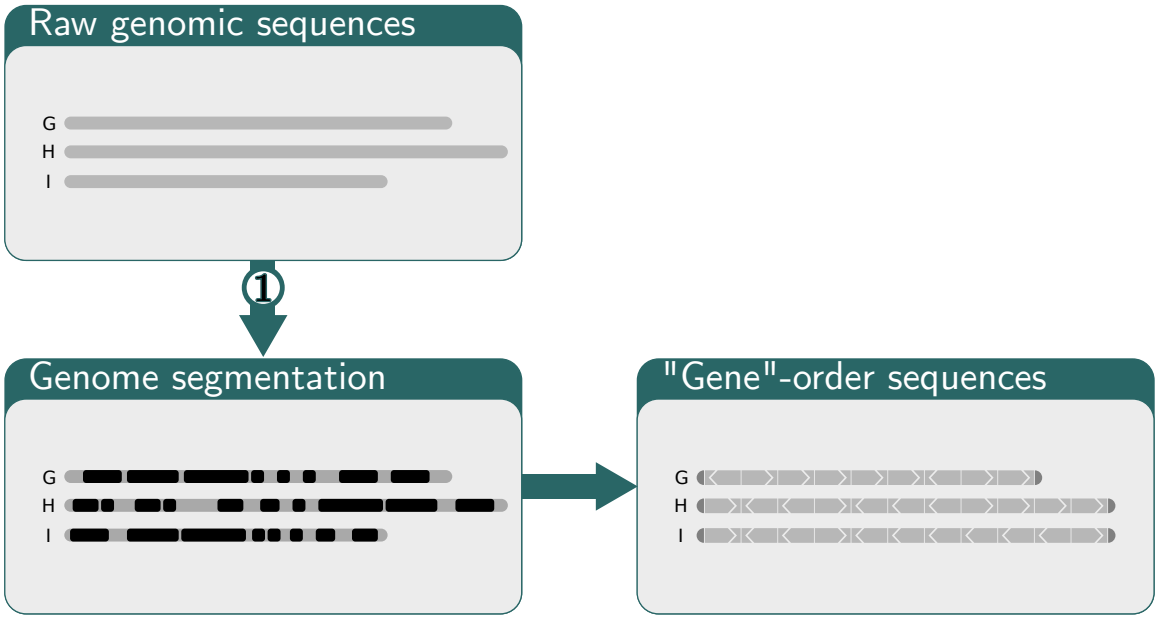
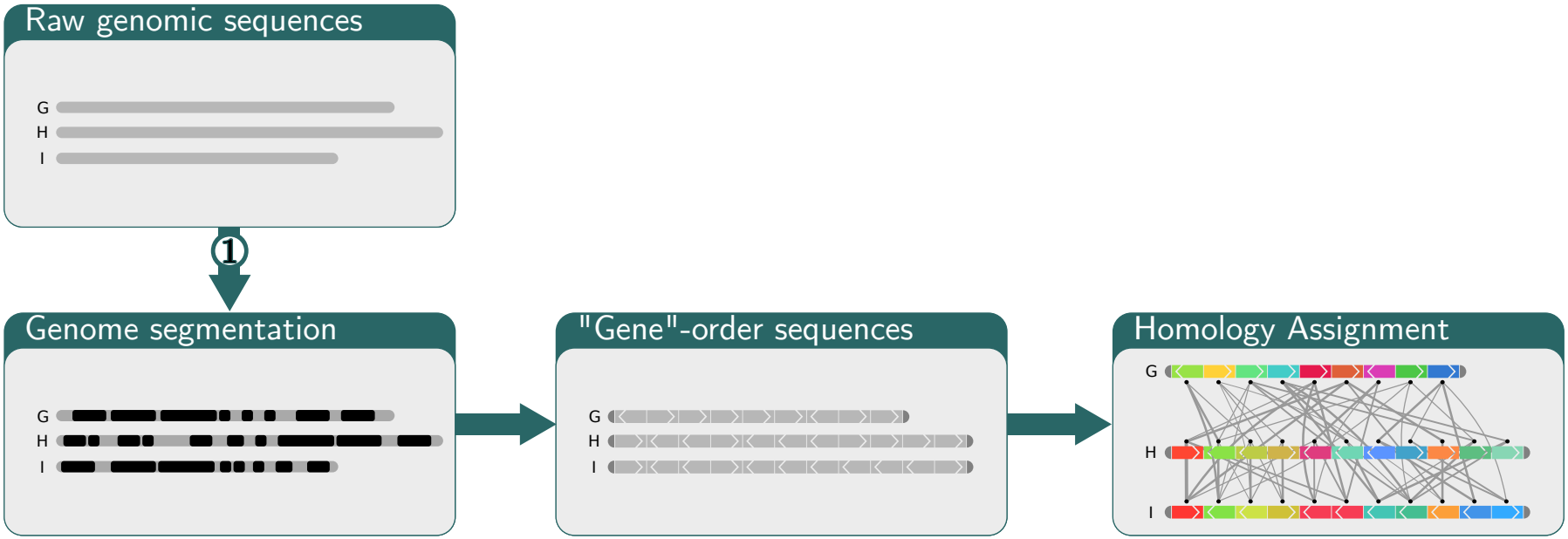

Segmentation invalid!

Synteny workflow



Synteny workflow

LCBB



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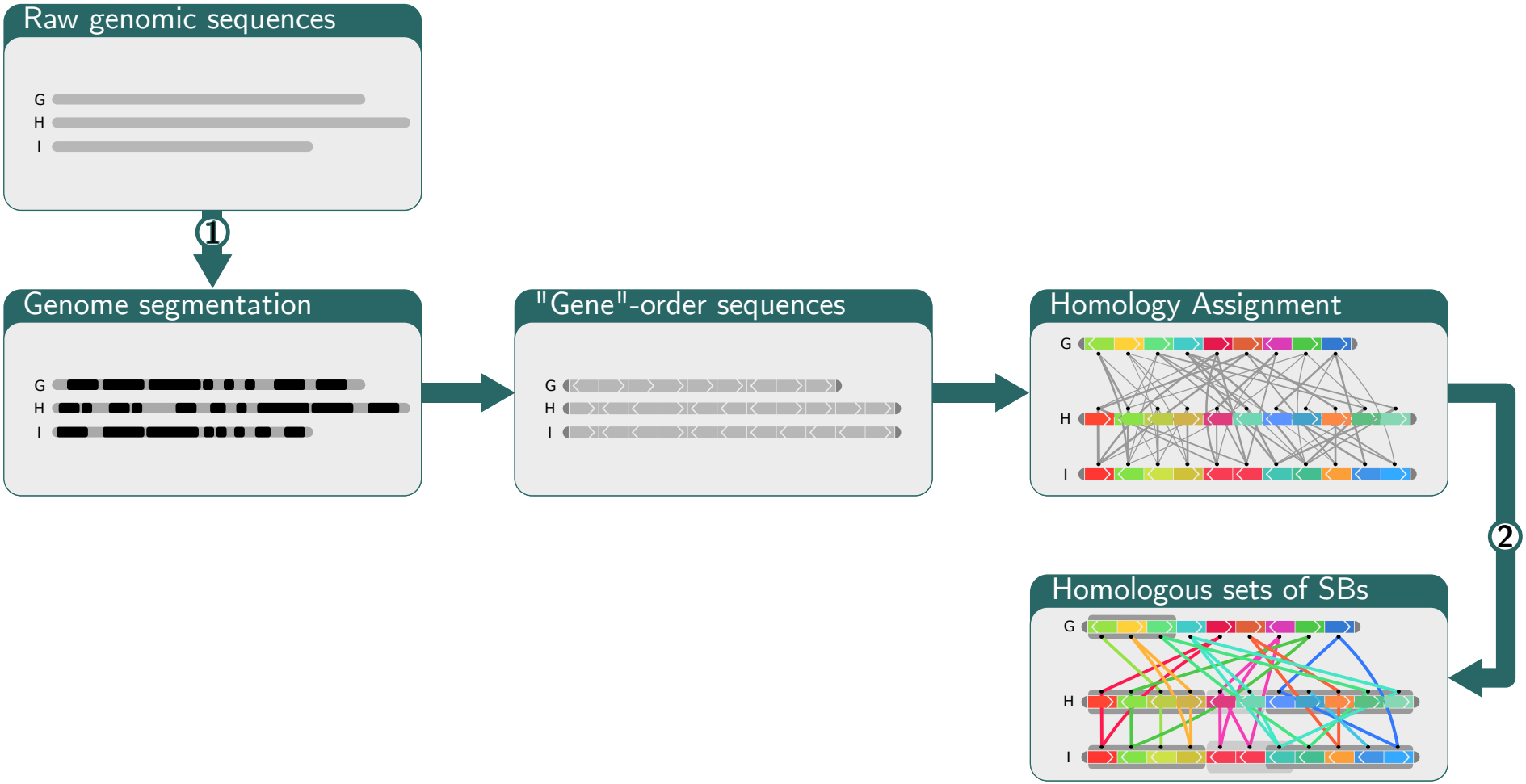
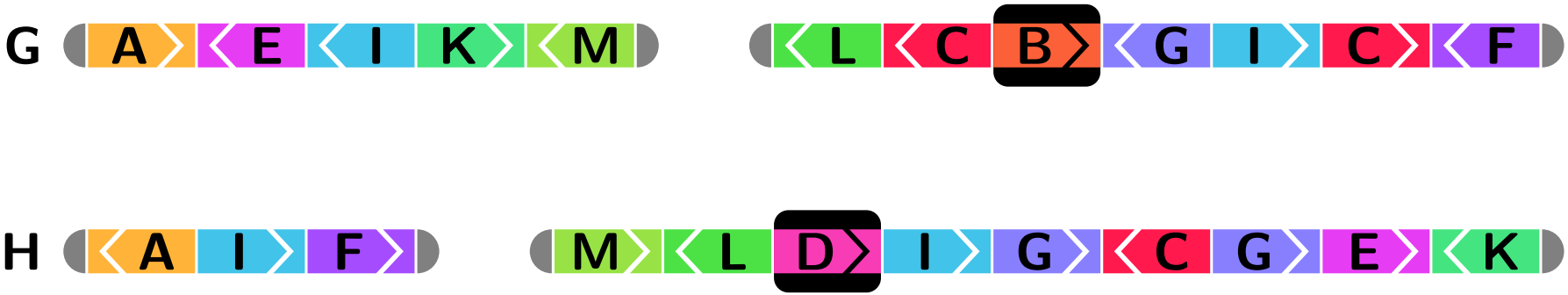


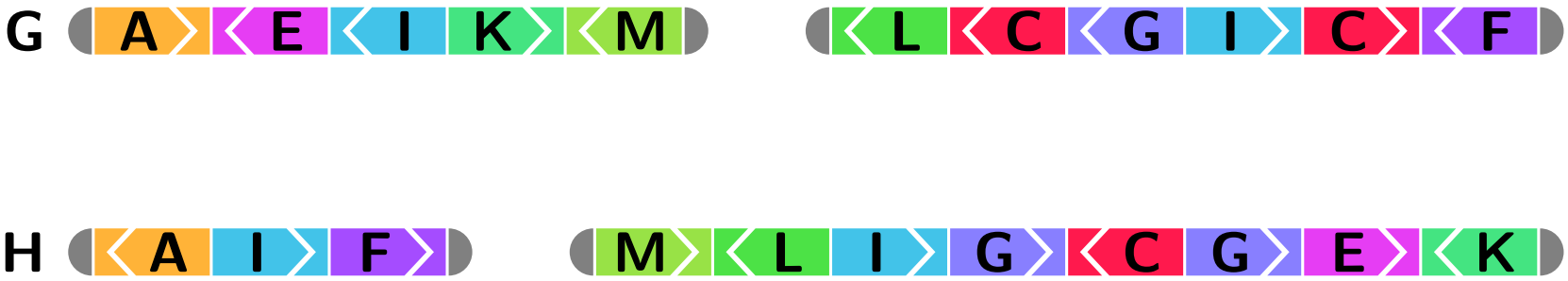
Discovery of homologous SBs



Remove all markers not shared between **G** and **H**

Discovery of homologous SBs

LCBB



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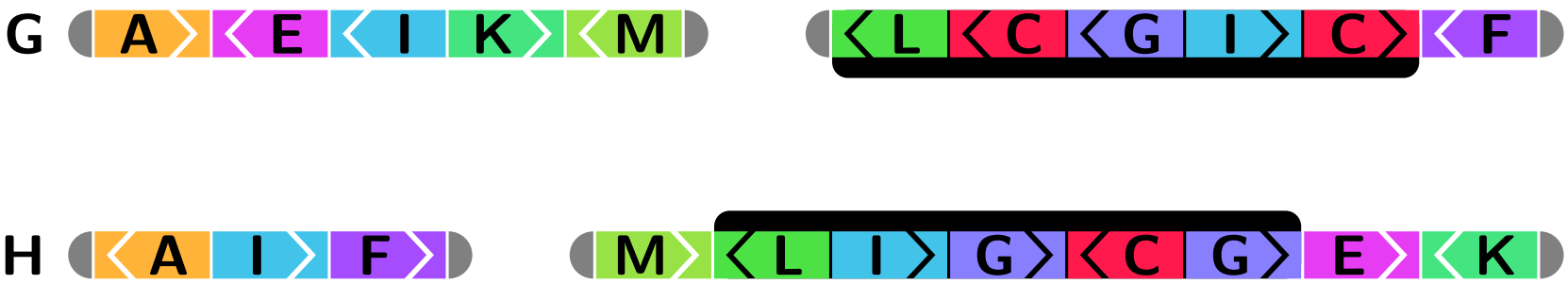
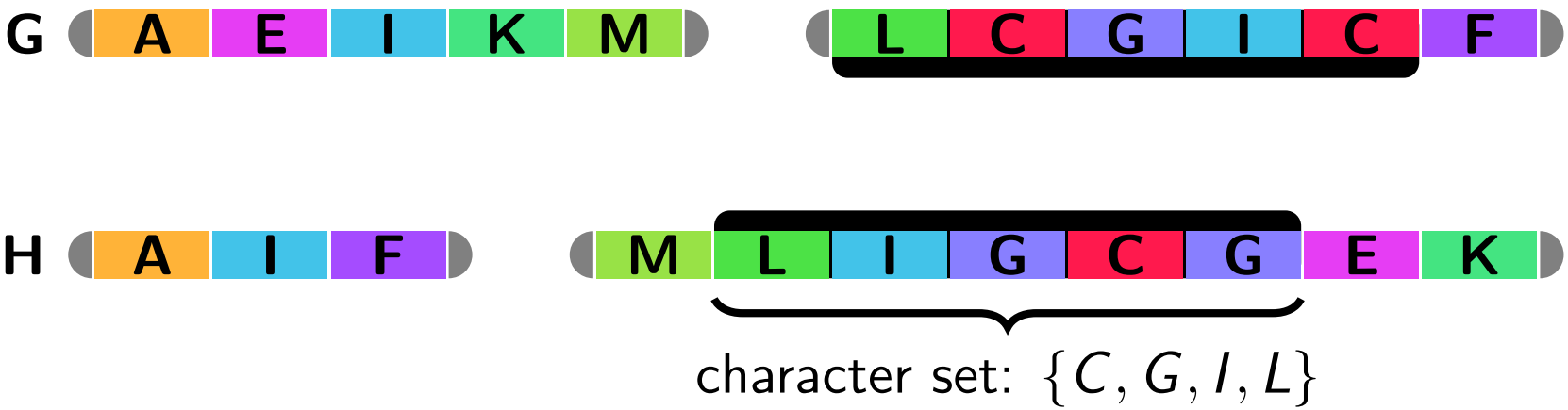


Two blocks are syntenic if each marker in both blocks is homologous to at least one marker of the other block.

Discovery of homologous SBs

LCBB



common intervals: intervals with identical character set

[Uno and Yagiura, 2000, Schmidt and Stoye, 2004]

Non-transitive homology assignments

LCBB

- clustering of genomic markers into homologous groups is error-prone
- Synteny can is a powerful filter for false positive homologies

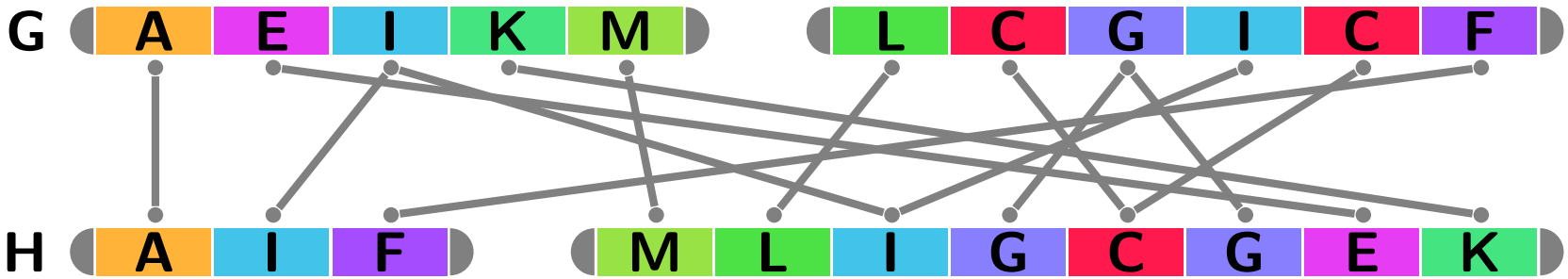
Non-transitive homology assignments

- clustering of genomic markers into homologous groups is error-prone
- Synteny can is a powerful filter for false positive homologies
- Omit clustering by relaxing homology:

non-transitive homology assignment

Let Σ be the universe of markers. A *nontransitive homology assignment* is a *reflexive* and *symmetric* relation, $\tilde{\mathcal{H}} \subseteq \Sigma \times \Sigma$

Discovery of non-transitive homologous SBs

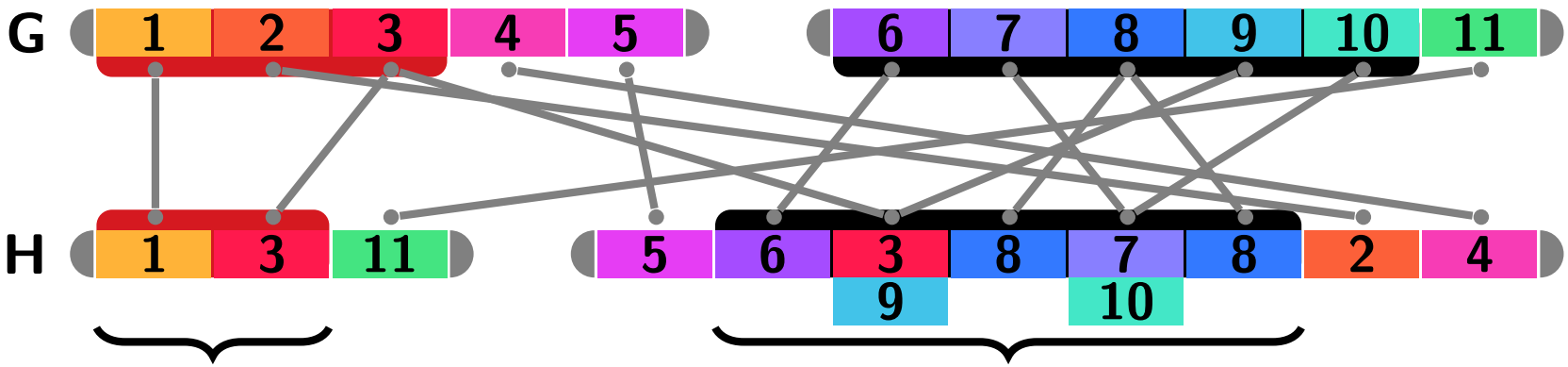


Homology statements: Links between characters

Discovery of non-transitive homologous SBs

LCBB

How many additional homology statements are needed to make an SB pair homologous?



1-approximate, common character set: $\{1, 3\}$

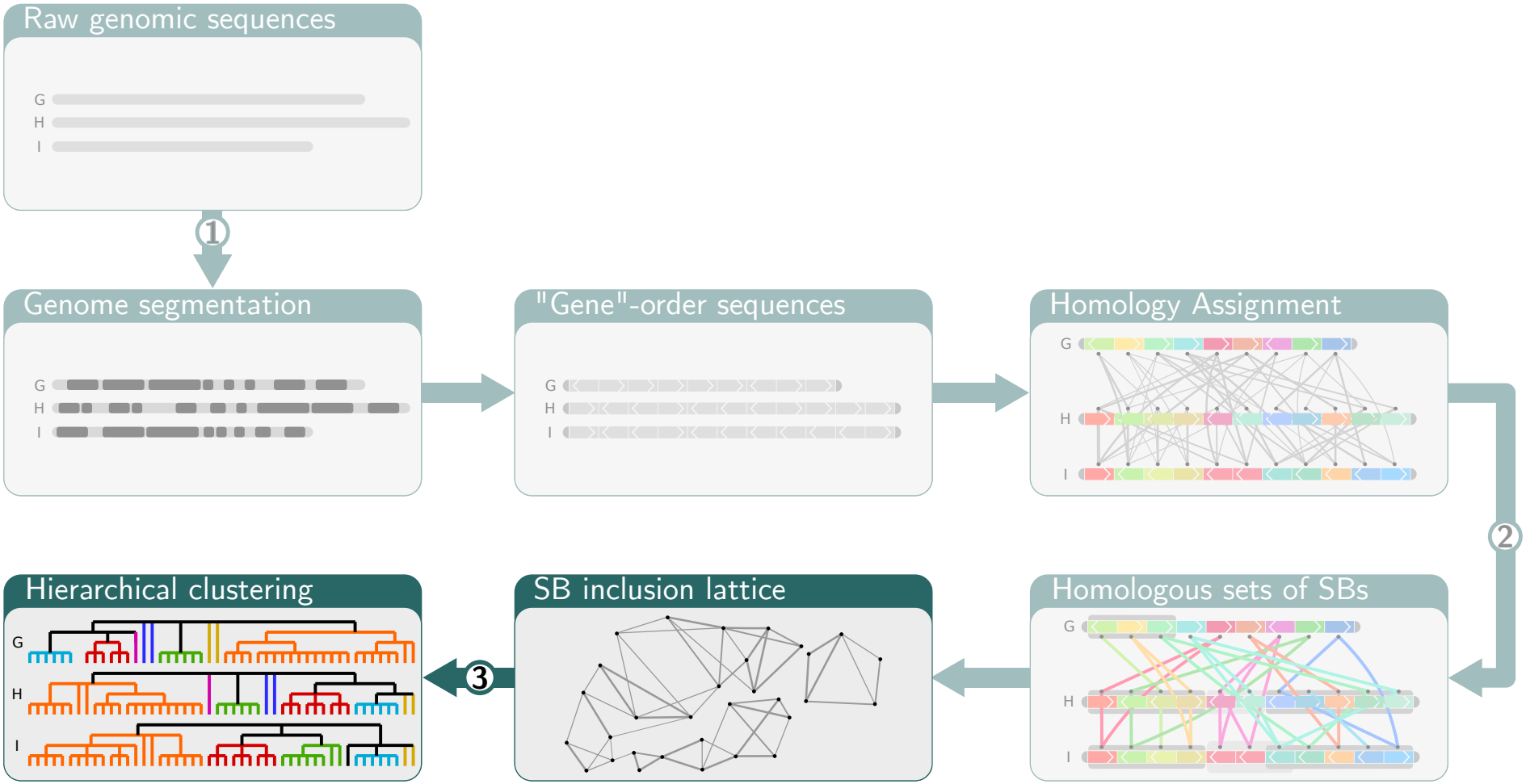
common character set: $\{6, 7, 8, 9, 10\}$

δ-approximate weak common intervals in indeterminate strings

[Doerr et al., 2014]

Synteny hierarchy construction

LCBB



SB inclusion lattice

LCBB

SB inclusion lattice:

- vertex: syntenic block
- directed **black** edge: $v_A \rightarrow v_B$ – syntenic block A subinterval of B
- undirected **colored** edge: v_A—v_B – A is homologous to B

SB hierarchy

LCBB

A set of intervals is **commuting** if for any two of its members A, B holds:

- A subinterval of B, or
- B subinterval of A, or
- A and B are disjoint

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Determine commuting sets of SBs for each genome independently!

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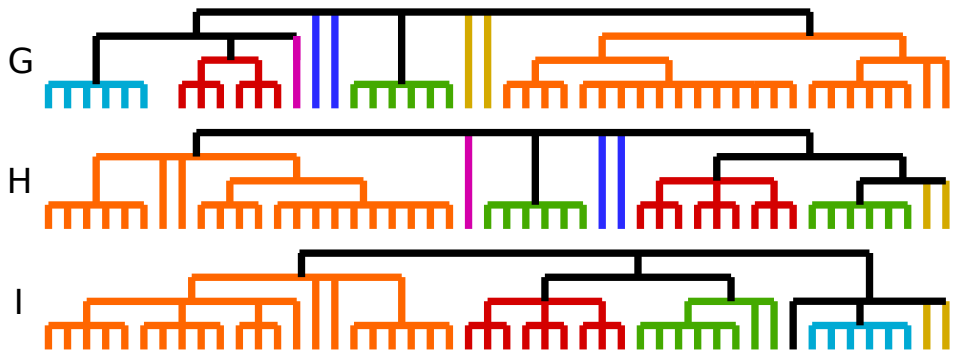

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PriSy

PriSy* – a tool for Principled Synteny Analysis

*working title, release: end of this year

Thank you!

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