

0 0.5 1.0 1.5 20 25 3.0 3.5 4.0 4.5 50 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10.010.

Brush selections

Clustering the locations (sample & ancestral) with a geographic background at various aggregation levels with the help of several methods.



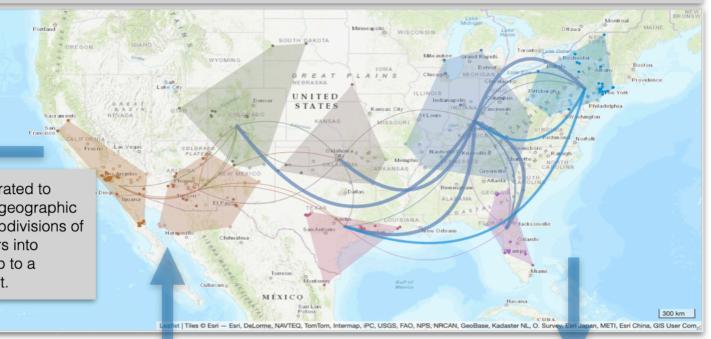
Top-down reading of the phylogenetic tree: each transition of location is represented or the geographic map by a path between locations.



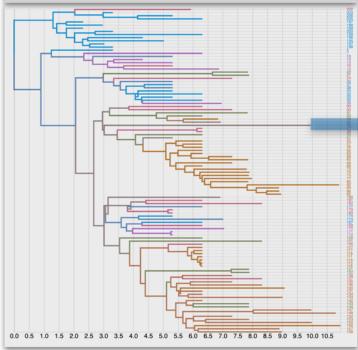
Top-down reading of the phylogenetic tree restricted to the brush selection

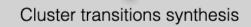


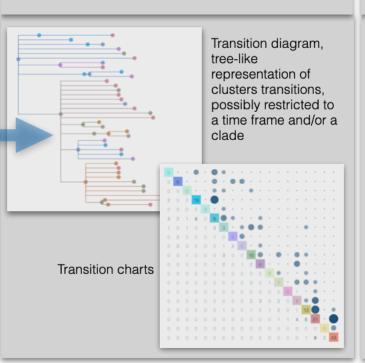
Top-down reading of the transition diagram: paths are based on cluster transitions (centroids)



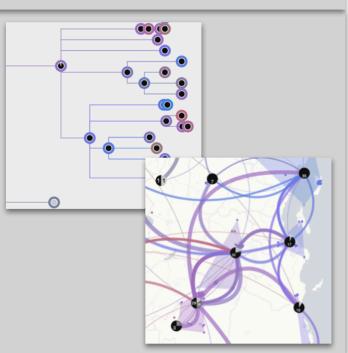
Phylogenetic tree with a 2D color-encoding according to clusters of locations







Compute & superimpose ancestral character traits from a discrete variable



Evolaps Manual

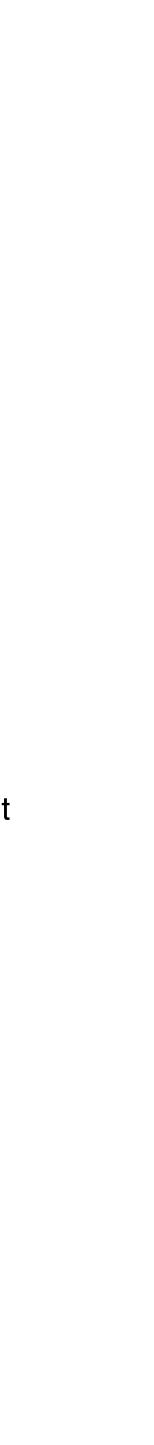
EvoLaps aims at visualizing spatio-temporal spread of epidemics, from phylogenetic trees associated with continuous localities (computed ancestral latitude/longitude pairs associated with computed ancestral sequences from sampled latitude/longitude pairs associated with sampled sequences).

Changes of localities (transitions), in a "Top-Down" reading of the tree (from the root to its leaves), are represented on a cartographic background using paths between them. The bundle of paths is a phylogeographic scenario.

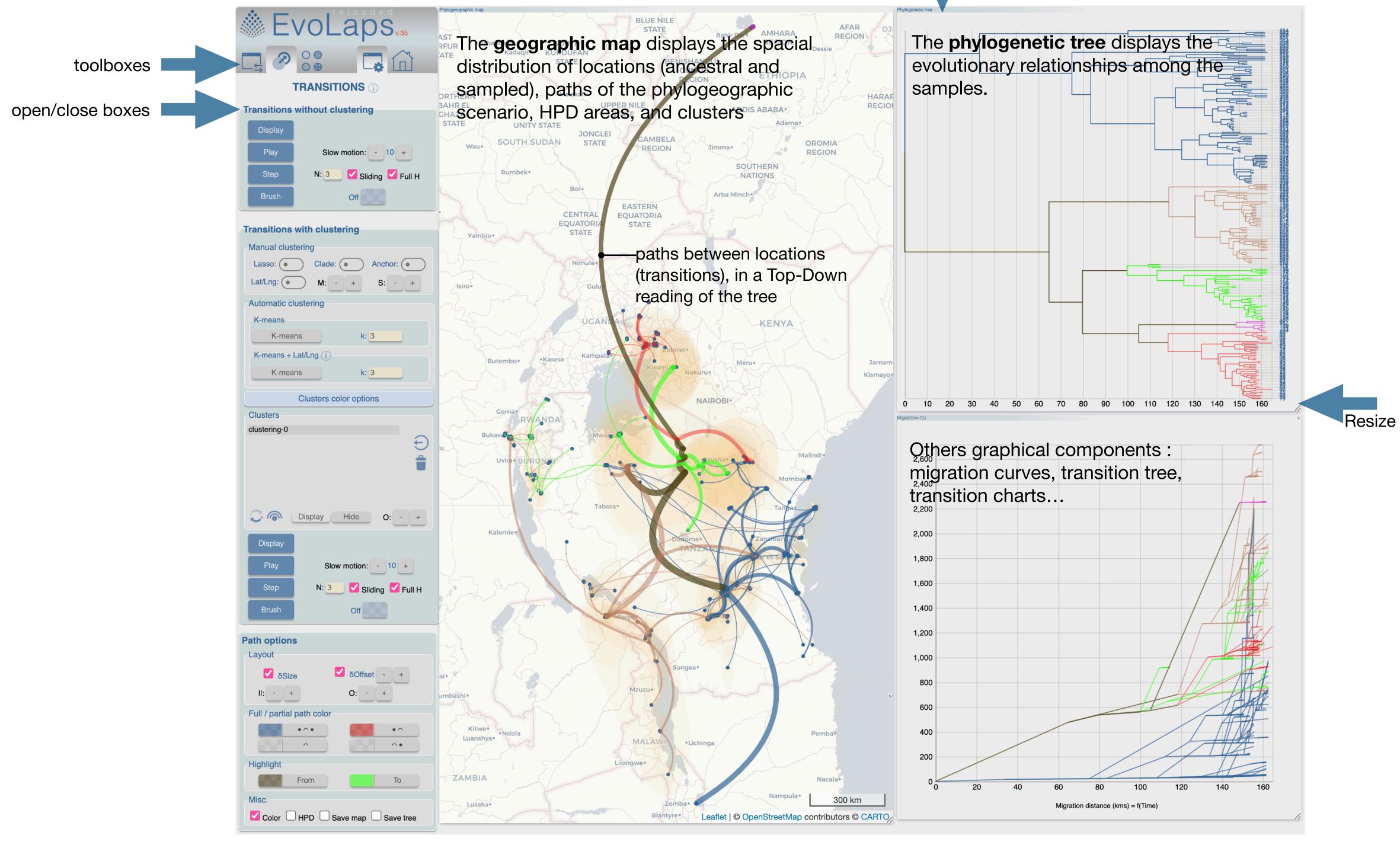
A raw reading of these transitions produces complex scenarios, and EvoLaps helps to analyze them with brush selection, animation, highlight processes, but also with the possibility of discretizing the continuous localities into clusters of regions using different methods/tools of clustering (lasso, anchor, dynamic latitude/longitude grid, K-means).

The dynamic EvoLaps clustering is iterative, allowing more or less detailed phylogeographic scenarios according to specific spatio-temporal phases of it. For instance, an analysis starts with a small number of large clusters, and selected clusters can be subdivided afterwards for having a higher resolution.

EvoLaps also offers tools to corroborate third party variables to the phylogeographic scenario such as the superimposition of heat maps, or the computation of ancestral character states from discrete variables



EvoLaps interface



Drag & drop

EvoLaps interface

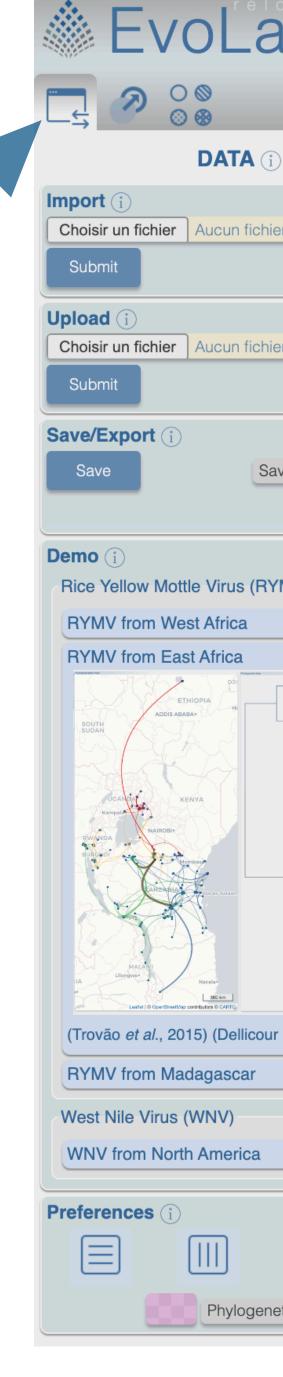
Three toolboxes:

Data: input/output of data.

Submit a maximum clade credibility (MCC) tree obtained by continuous phylogeographic inference. Upload an evolaps analysis file. Library of data sets for demos. Save evolaps analyses or export graphic as SVG files. Preferences of the interface

Transitions: phylogeographic scenario as a bundle of paths between locations (transitions), with or without clustering, in a Top-Down reading of the tree. Path options.

Edition: layouts of the geographic map and the phylogenetic tree, and third party graphical components (transition tree, migration curve, etc.)



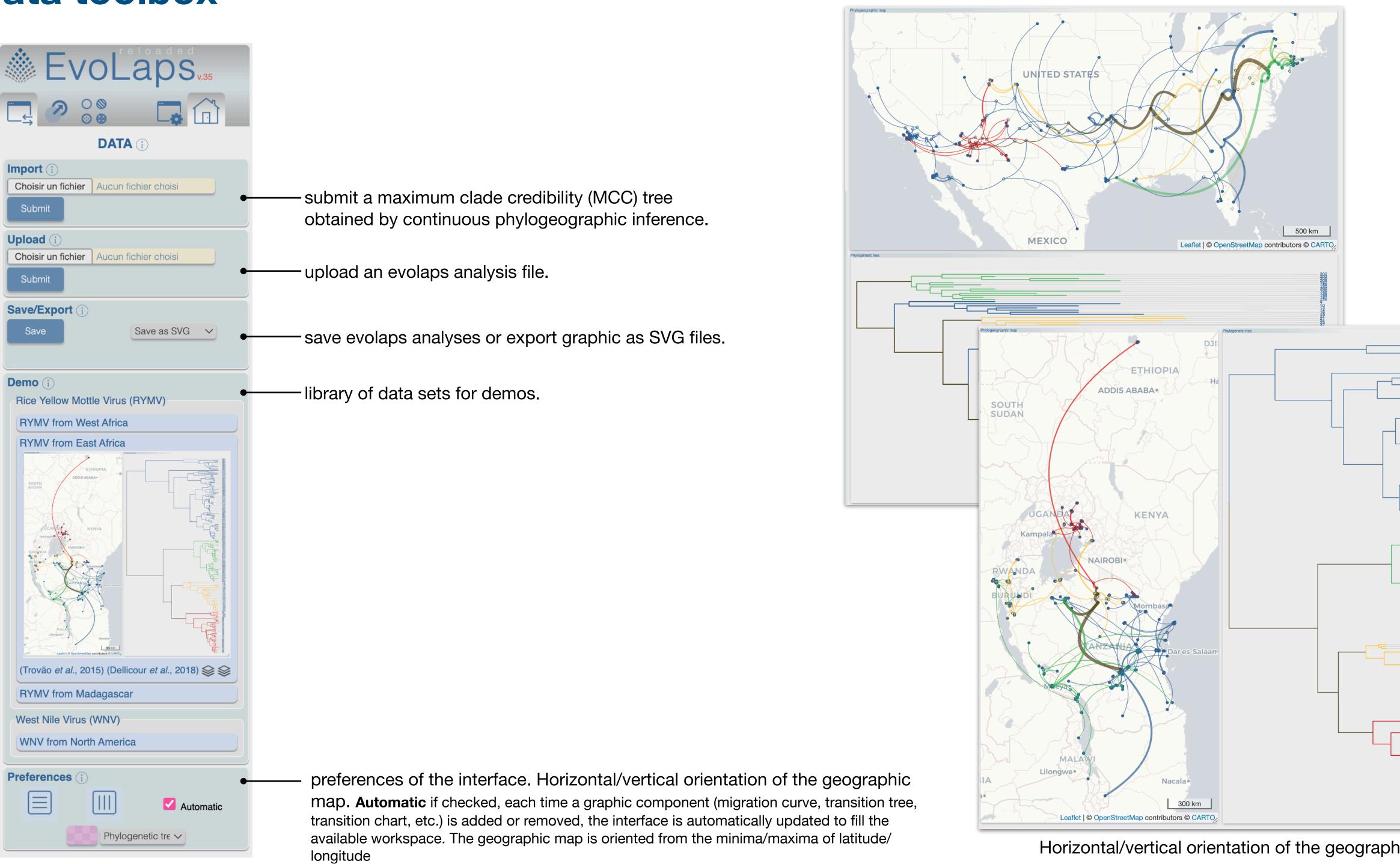
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Highlight	From To
Misc.	HPD Save map Save tree

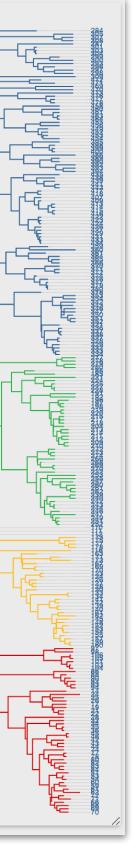
Evolaps.
EDITION (1) =
Geographic map (i)
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Locations
Sampled
Size: - + O: - +
Ancestral
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Heat map (i)
Phylogenetic tree i
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Info
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Info Layout Radial Cartesian Ladderize: \bigcirc up \bigcirc down $\delta \leftrightarrow$: - + δ^{\ddagger} : - +
Info Layout Radial Cartesian Ladderize: up o down $\delta \leftrightarrow$: - + δ^{\ddagger} : - + II: - + Font: - +
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Info Layout Radial Cartesian Ladderize: $up \odot down$ $\delta \leftrightarrow : - + \delta^{\ddagger}: - +$ l: - + Font: - + Scale Scale Most recent sampling $j/mm/aaaa$



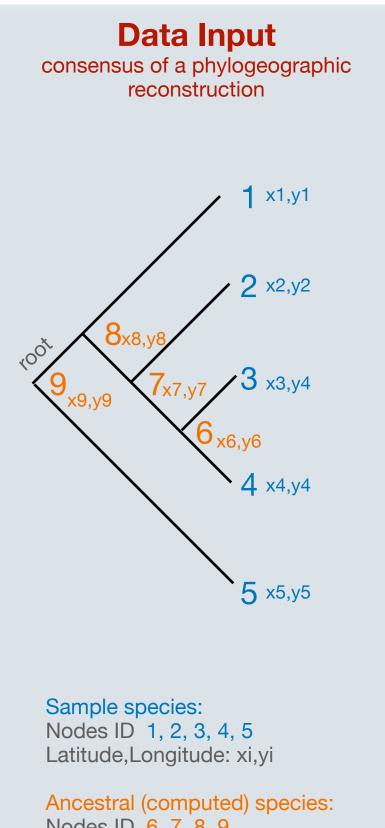
Data toolbox



Horizontal/vertical orientation of the geographic map



Data toolbox, file formats



Nodes ID 6, 7, 8, 9 Latitude,Longitude: xi,yi submit a maximum clade credibility (MCC) tree obtained by continuous phylogeographic inference. Input data (NEXUS format) must contain a rooted tree with sample and ancestral (consensus) lat/Ing coordinates for the tips (samples) and the internal nodes of the tree (ancestral species), respectively.

The variable names saving coordinates must be as following :

Samples:	location1 locatio
	Latitude Longitu
Ancestral(*):	location1_median
	Latitude
HPD:	location1_80%HPD location2_80%HPD

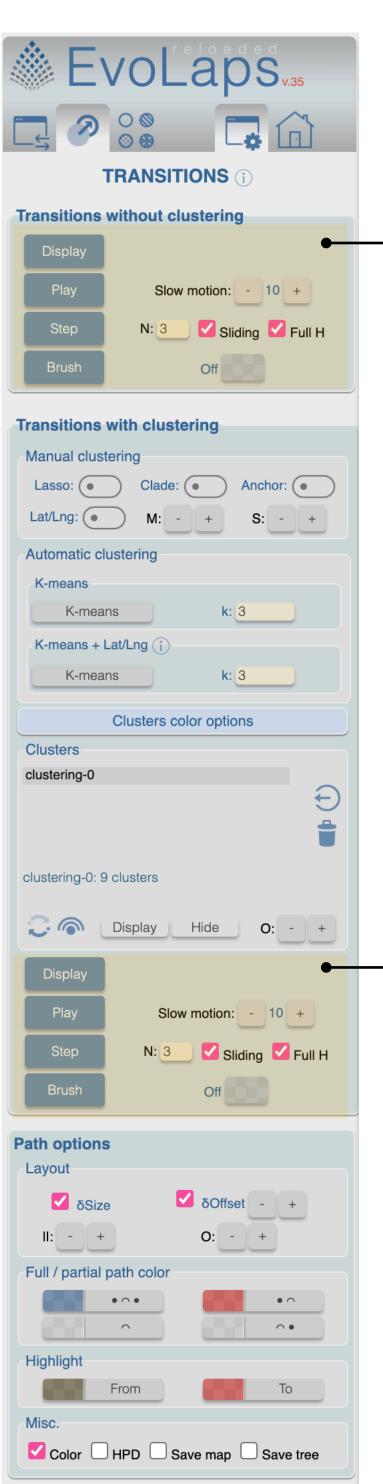
on2

tude

n location2_median	(*) if « location1_median » and « location2_median » variables are not found during the import of the NEXUS file, the parsing process will search for « location1 » and « location2 » variables for ancestral nodes
Longitude	

location1	90%HPD	location1_	95%HPD
location2	90%HPD	location2	95%HPD

Transition toolbox, with and without clustering



The phylogeographic scenario can be animated gradually over time, or in time interval steps, over the whole phylogenetic tree or over a particular clade.

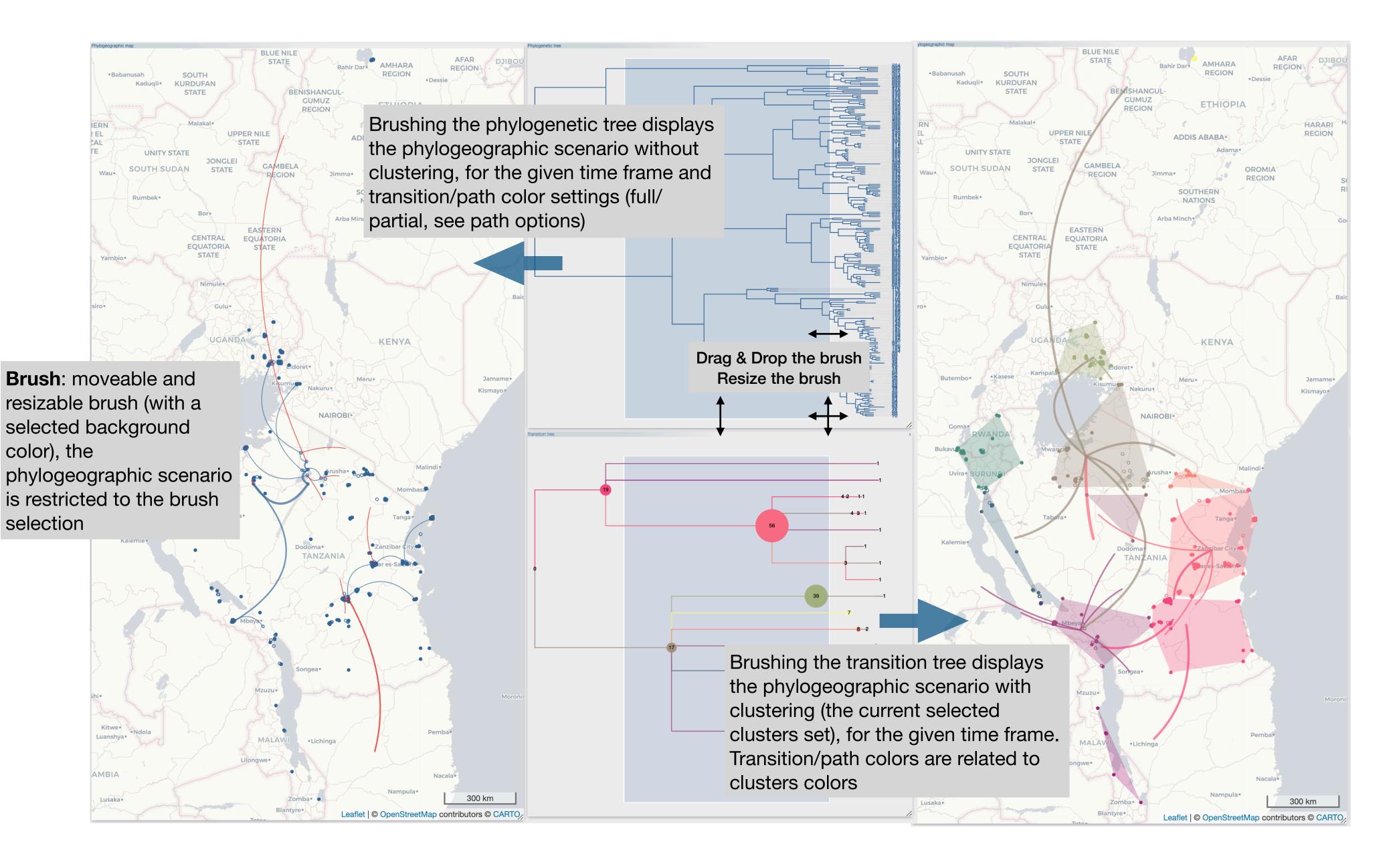
- Display: the phylogeographic scenario is displayed.
- brush is resizable and moveable.
 - Slow motion speed of the animation
- Step:
 - N: set a number of steps
 - Sliding ON: a brush width is computed and the brush is moved from the tree root to its leaves, the phylogeographic scenario is displayed step by step
 - up to the leaves
 - Full H ON: the brush height covers the tree height
- Brush: see below

• Play: the phylogeographic scenario is animated smoothly at a given speed, thanks to a brush covering the tree. This

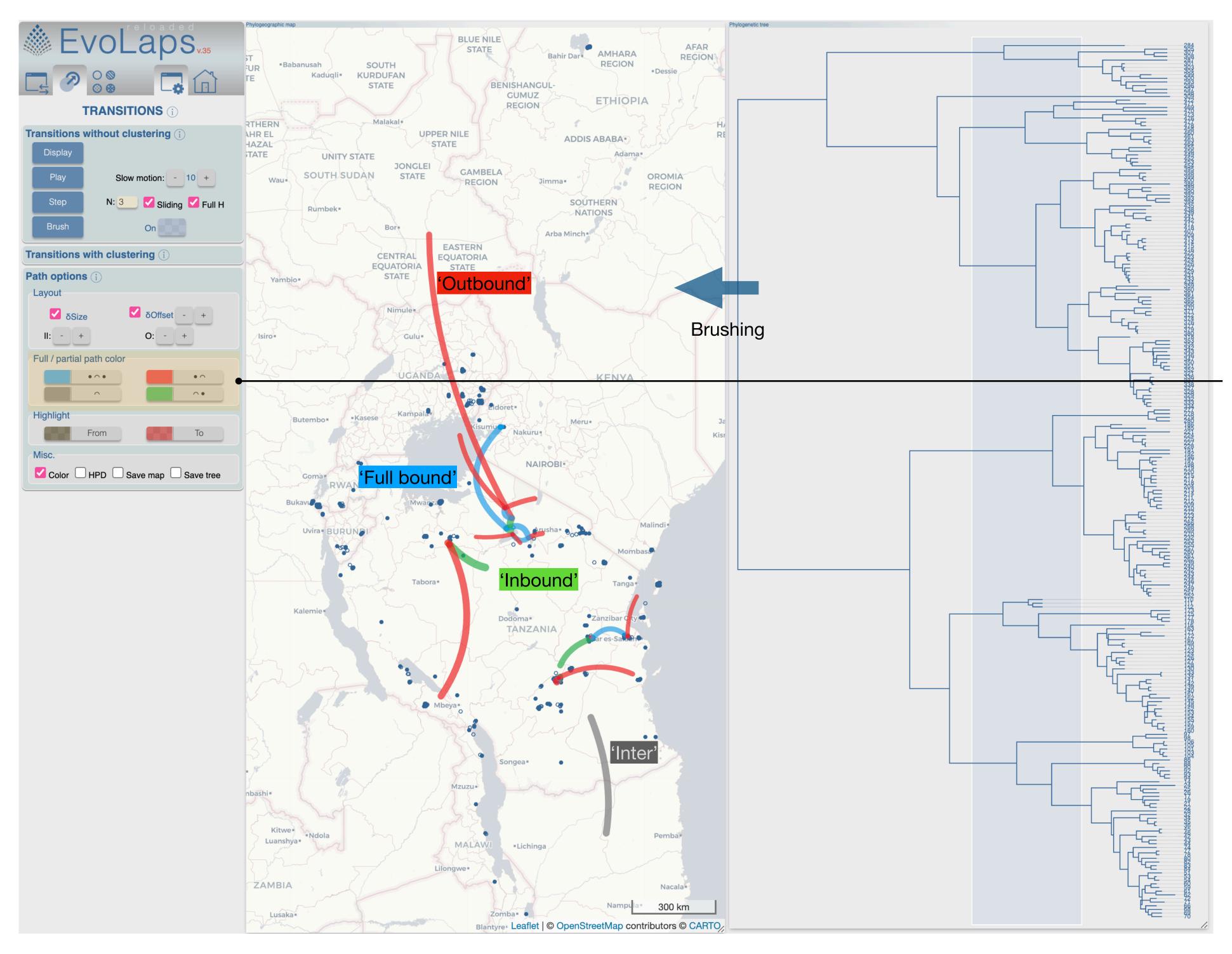
• Sliding OFF: an initial brush width is computed, then for each step the brush width is increased of this initial width

Transition toolbox, brushing the phylogenetic and/or the transition trees





Transition toolbox, paths options, full/partial paths



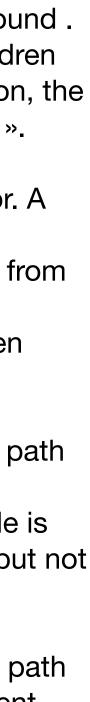
path color

'Full bound': Color of full bound . If a node and one of its children are inside the brush selection, the corresponding path is « full ».

'Outbound': Outbound color. A path is « Outbound » if the corresponding parent node from the tree is inside the brush selection but not the children node

'Inbound': Inbound color. A path is « Inbound » if the corresponding children node is inside the brush selection, but not the parent node

'Inter': Inter bound color. A path is « Inter » if neither the parent node nor the children are inside the brush selection

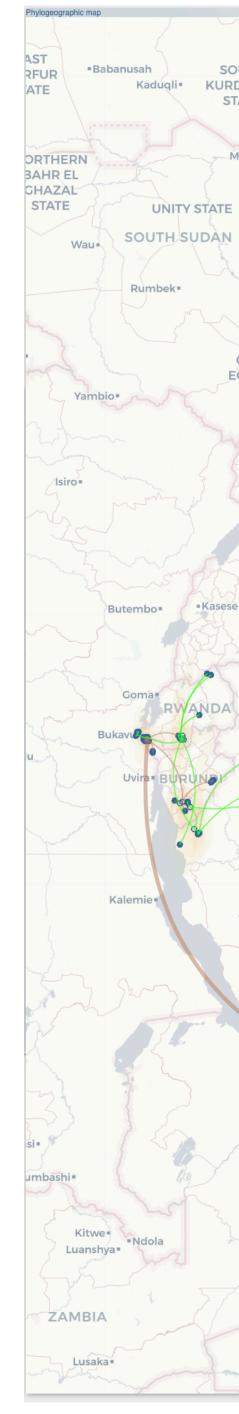


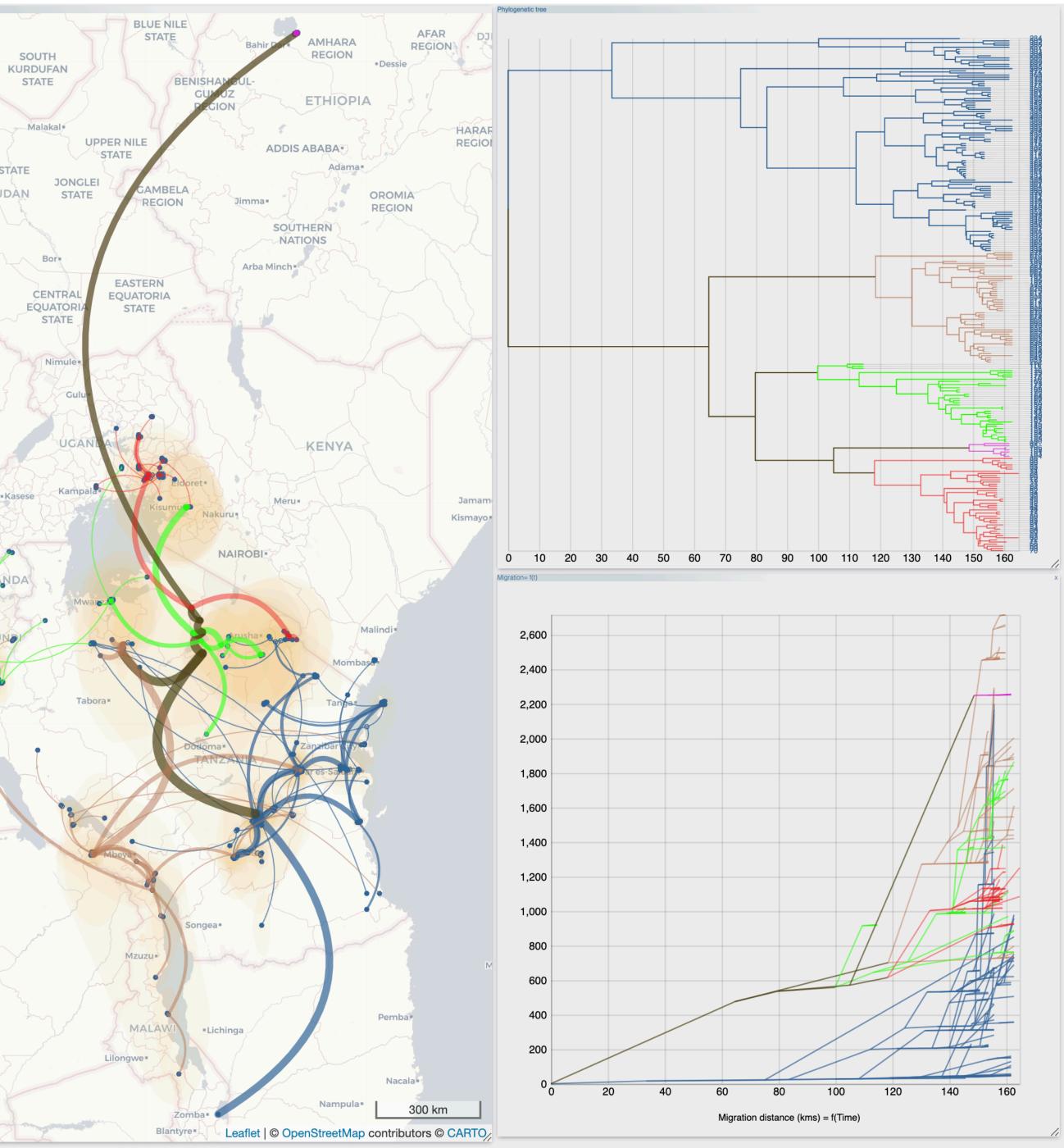
Transition toolbox, paths options, highlight paths

Evolaps _{v.35}
TRANSITIONS (i)
Transitions without clustering (i)
Transitions with clustering (i)
Path options (i) Layout
Size δOffset - +
II: - + O: - +
Full / partial path color
Highlight From To
Misc. Color HPD Save map Save tree
Color

Highlight From & To,

highlight color selection (from: backward/to: forward). The coloring of the transitions is done on the fly and in an interconnected way between the graphic components (here the geographical map by pointing paths, the phylogenetic tree by pointing branches and the migration distance curves, by pointing segments).





Transition toolbox, paths options, layout

Evolap	e d S _{v.35}
TRANSITIONS (i)	
Transitions without clustering (i)
Transitions with clustering (i)	
Path options (i) Layout	
δSize δOffset II: - + O: -	- + +
Full / partial path color	• ^ •
Highlight From	То
Misc. Color HPD Save map	Save tree

Paths options (either with or without clustering)

- **∂Size** width path width linked to the depth of the transition in the scenario
- **Offset** paths curvature linked to the depth of the transition in the scenario,
- Offset -/+: curvature intensity
- || width of paths. Relative values
- O opacity of paths. Relative values

Transition toolbox, clustering

Evolaps.	
TRANSITIONS (1)	
Transitions without clustering (i)	Clustering methods
Transitions with clustering Manual clustering Lasso: Clade: Anchor: Lat/Lng: M: + S: - Automatic clustering K-means K-means K-means K-means K-means K-means K: 3 Clusters color options Select	 Lasso clustering from the geographical map, click automatically with the cluster centroid if 'Color scale' Clade clustering select a node from the phylogen current color picker otherwise Anchor clustering click the geographic map to de cluster centroid if 'Color scale' is checked, from the Lat/Lng clustering grid of parallel/meridian bound produce a more accurate space division K-means algorithm for clustering. Set the desired satisfying output. K-means + Lat/Lng K-means output set minimum
color	Clusters colors
Automatic	Color picker
Set: Steiger V	2D color matrices
	 Colors from clusters. Clic a cluster color and the cluster
•	
Colors from clusters	
Clusters	Olyestere list
clustering-0	Clusters list
clustering-2	 submit ans save the current clusters
	 cluster selection : display
C O: - +	
Display	 reset clustering, display locations without cluster, or
Play Slow motion: - 10 +	
Step N: 3 Sliding Full H	
Brush Off	
Path options (i)	

k and drag the mouse around a set of locations to define a new cluster. Color is set ale' is checked, from the color picker otherwise letic tree. Color is set automatically with the cluster centroid if 'Color scale' is checked, from the

eposit an anchor, anchor can be moved, or deleted (ctrl-click). Color is set automatically with the le the color picker otherwise. Moving an anchor do not change its color ds. M: mesh density of Lat/Lng grid, S: bounds size. Bounds can be dragged and dropped to

number of clusters (3 by default) and click the « K-means » button. Click it again until a

n and maximum of latitude/longitude bounds.

urrent color (color picker) will be updated with this cluster color. 'Command-clic' a cluster color

display/hide clusters, 'o': clusters opacity

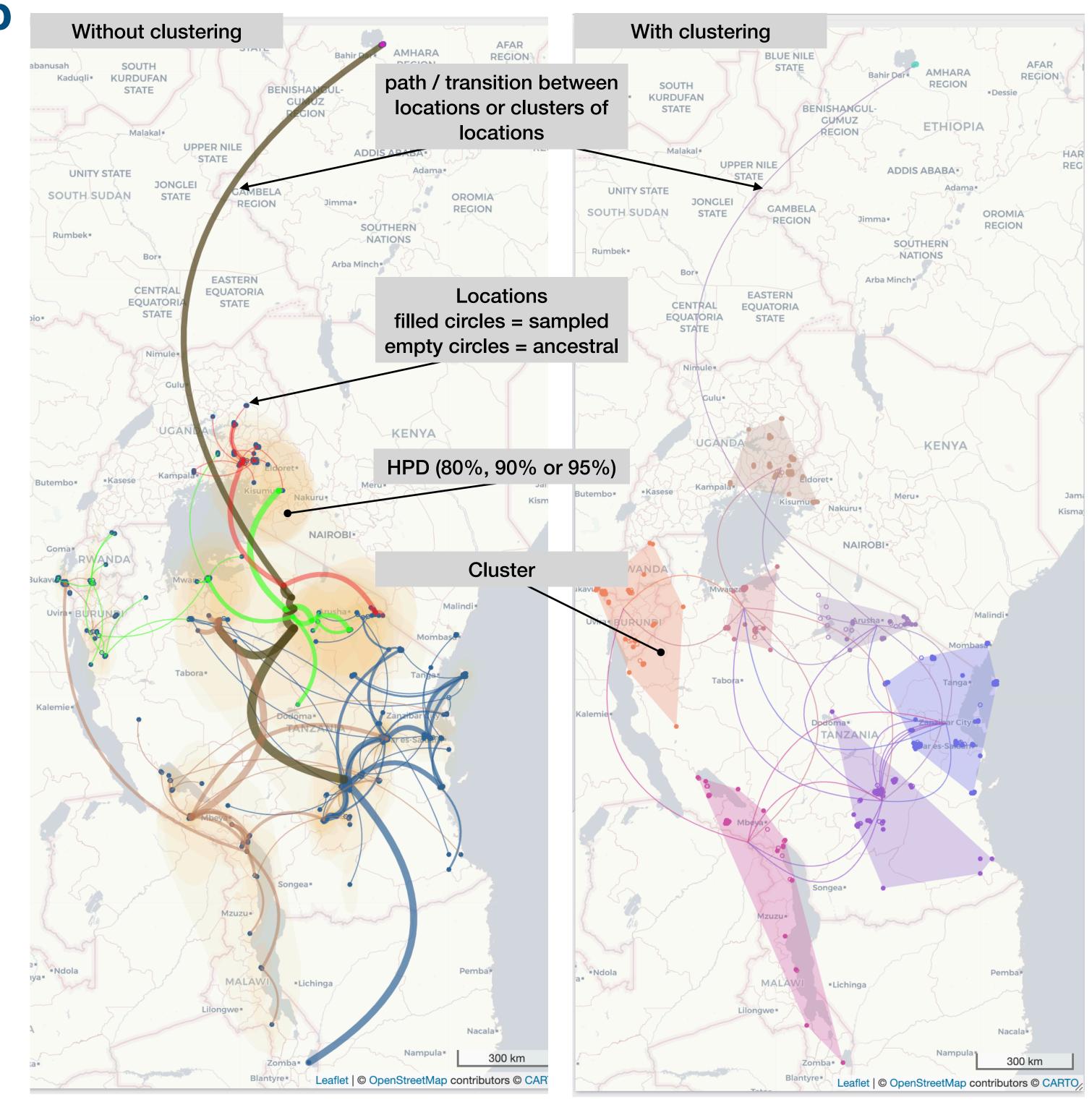




Edition toolbox, geographic map

Evolaps _{v.35}
Geographic map (i)
Positron Labels ~
Locations
Sampled
Size: - + O: - +
Ancestral
Size: - + O: - + HPD Threshold: 80% ~
Lat: 10.43701530. Lng: 27.376924910
Heat map (i)
Choisir un fichier Aucun fichier choisi
Submit
Gradient
0.2 0.5 1
Layout
Opa.: (i) - + Blur: (i) - +
Rad.: (i) - + Max.: (i) - +
Zoo.: i - +
Reset Delete
Phylogenetic tree (i)
Transition tree (i)
Migration distance = f(t) i
Inter-cluster exchange charts (i)
Ancestral character states (i)

- Layout: map tiles selection
- Locations: Size & Opacity of sampled (filled circles) and ancestral (empty circles) locations
- HPD: display on/off the Highest Posterior Density, with a selected x% interval (shortest interval in parameter space that contains x% of the posterior probability). Color & Opacity.
- Lat/Lng: location of the mouse pointer on the map
- HeatMap: see below



Edition toolbox, geographic map, heat map

Evolaps _{v.35}
EDITION (i) =
Geographic map (i)
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Locations
Sampled
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Ancestral
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Lat: 10.43701530. Lng: 27.376924910
Heat map (i)
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Submit
Gradient
0.2 0.5 1
Layout
Opa.: (i) - + Blur: (i) - +
Rad.: i - + Max.: i - +
Zoo.: i - +
Reset Delete
Phylogenetic tree i
Transition tree (i)
Migration distance = f(t) (i)
Inter-cluster exchange charts (i)
Ancestral character states (i)

CSV file format of the heat map data, the first row must be labelled as following: intensity, lat, lng

🛑 😑 📄 HeatMapData...

intensity, lat, lng 2325,45.361233,11.790552 53,45.31259,9.59238 51,43.14271,11.81649 309,45.90461,9.33011 1063,42.88085,11.67425 270,40.12402,8.823119 53,42.22549,14.01037 2,41.098854,9.524106 636,45.40004,8.9175 320,44.14204,10.66073 4,40.50801,15.81357 197,40.3349,18.29753 12,37.02547,14.49382 37,41.15882,15.33145 2,44.47495,6.99029 100,40.49239,16.15812 12,43.550728,10.507817

- Heat map gradient: threshold and color selection
- Layout:
 - **Opa**: minimum opacity the heat will start at
 - Blur: amount of blur
 - Rad: radius of each 'point' of the heatmap
 - Max: maximum point intensity
 - **Zoo**: zoom level where the points reach maximum intensity (intensity scales with zoom)
- Reset: reset the gradient and the layout of the heat map
- **Delete**: delete the heat map

Edition toolbox, phylogenetic tree

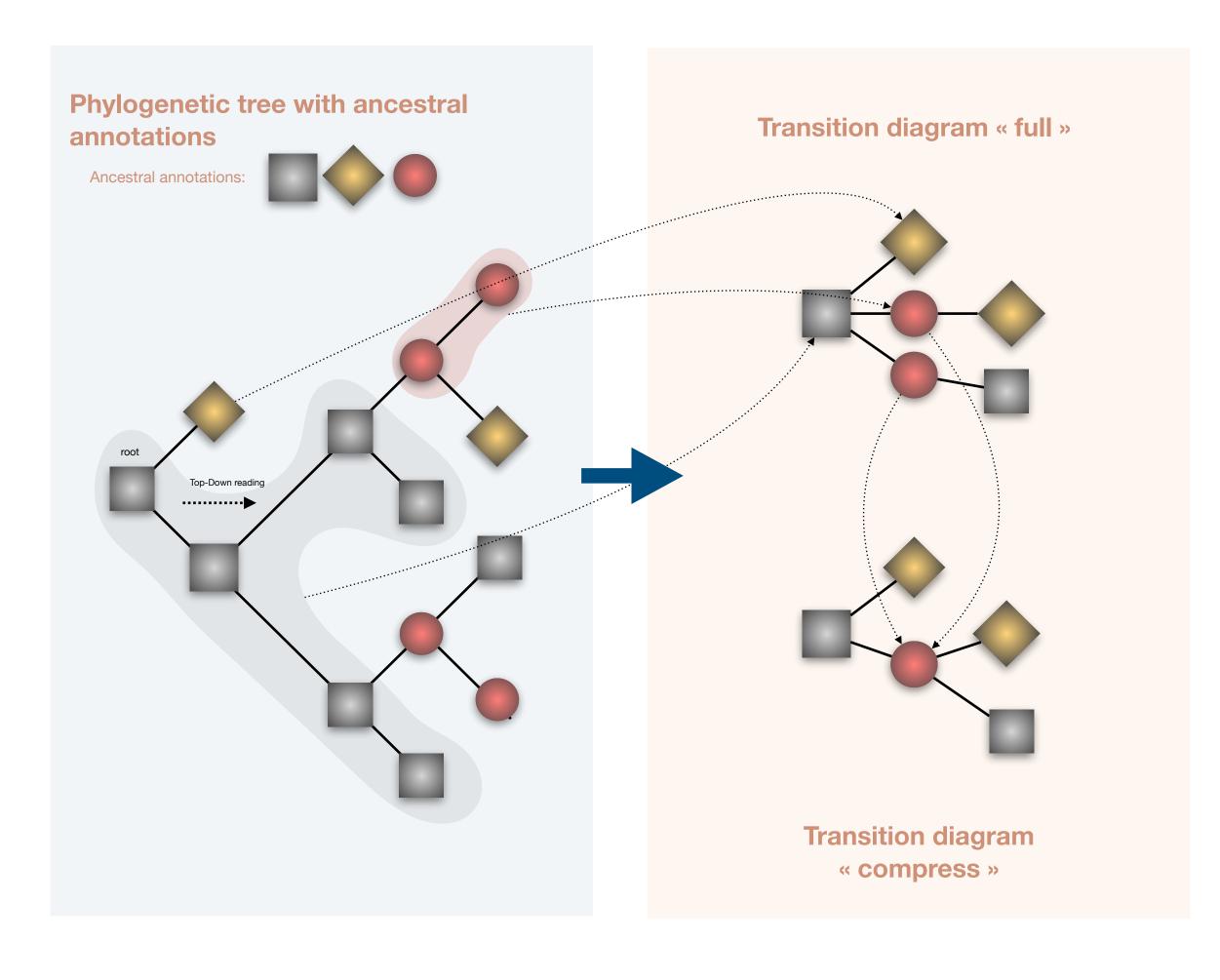
Evolaps _{v.35}
EDITION (i) =
Geographic map (i)
Phylogenetic tree i Info 240 leaves, 479 nodes, 478 transitions. Max depth: 18 (160)
Layout
Radial Cartesian
Ladderize: 🔵 up 🦲 down
δ↔: - + δ [‡] : - +
II: - + Font: - +
Scale
Time scale
Most recent sampling
Transition tree (i)
Migration distance = f(t) (i)
Inter-cluster exchange charts (i)
Ancestral character states i

- Mode Radial/Cartesian
- Ladderization up/down
- Horizontal expansion
- Vertical expansion
- Edges width
- Leaf label font (size)
- Scale

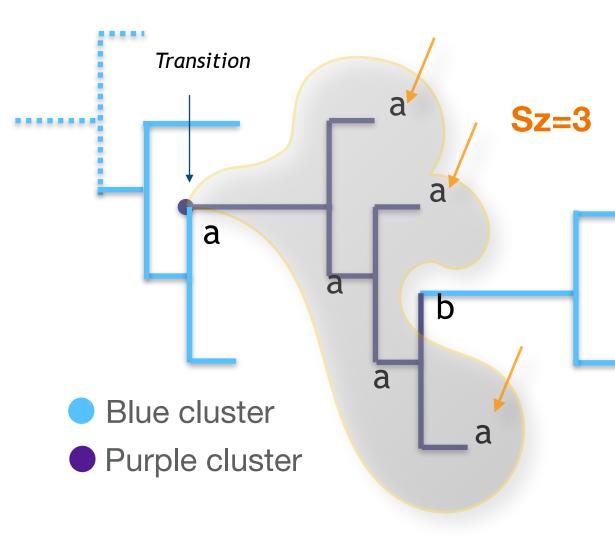
Edition toolbox, transition tree

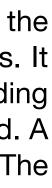
Evolaps _{v.35}				
EDITION (i) =				
Geographic map (j)				
Phylogenetic tree (i)				
Transition tree (i) Layout				
Full Compressed				
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$\delta \leftrightarrow : \begin{array}{ccccccccccccccccccccccccccccccccccc$				
Node				
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Migration distance = f(t) (i)				
Inter-cluster exchange charts (i)				
Ancestral character states (i)				

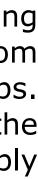
A transition is defined as an inferred change of geographical cluster between subsequent nodes of the tree in a top-down reading (from the tree root to its tips in a recursive process). The transition tree is a multi-furcating tree-like representation, summarizing all transition suites. It gives a synthetic view of a phylogeographic pattern without the geographical constraints. A default diagram starts with a node corresponding to the ancestral root state *i*. A node is inserted in the transition diagram when a cluster transition *i* -> *j* is observed until the tips are reached. A compressed version of the diagram is available by collapsing identical transitions having the same ancestor in the default version. The diagram is then read from its root to its tips: each transition is projected on the geographic map as a path between region clusters



Sz is the number of descendants being in the same cluster along the path from a node of phylogenetic tree to its tips. In case of a compressed version of the transition diagram, Sz values are simply added.



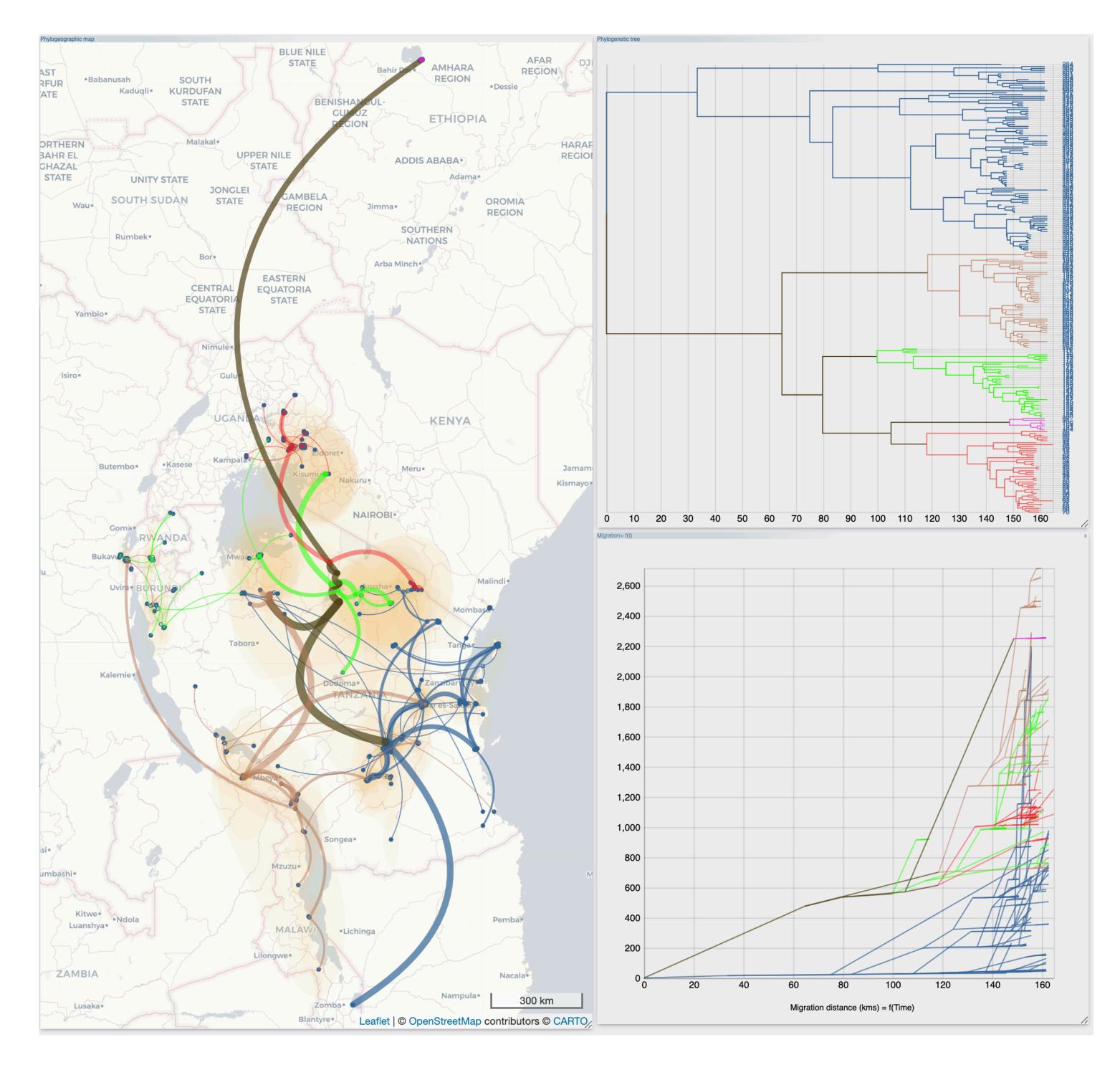




b

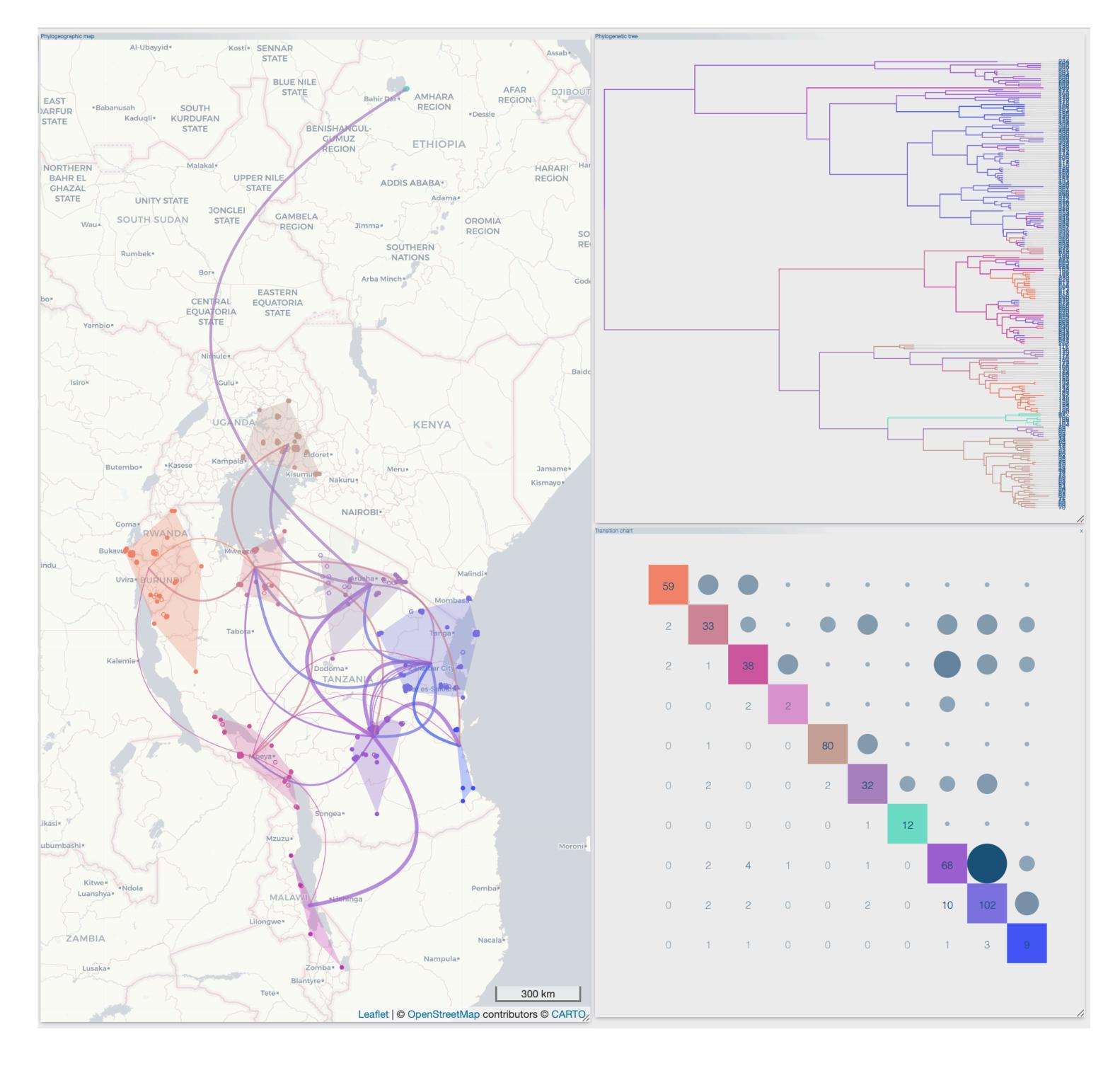
Edition toolbox, migration distance = f(t)

Evolaps _{v.35}
EDITION (i) $\equiv_{\dot{\pi}}$
Geographic map (i)
Phylogenetic tree (i)
Transition tree i
Migration distance = f(t) (i) Display
Inter-cluster exchange charts (i)
Ancestral character states (i)



Edition toolbox, inter-clusters exchange charts

🗼 Εν	/OLAPS _{v.35}				
EDITION (i) =					
Geographic m	nap (j)				
Phylogenetic t	tree (i)				
Transition tree	e (i)				
Migration distance = f(t) (i)					
Inter-cluster e a<=>b	exchange charts (i)				
a->b	i a->b (Lat/Lng) i				
Ancestral character states (i)					

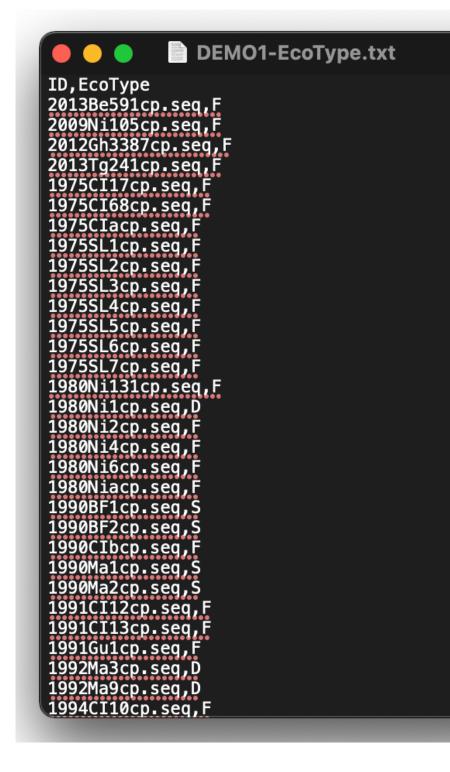


Edition toolbox, ancestral character states

Compute ancestral character states from a discrete variable (ecology, epidemiology,...) and superimpose the output to an existing phylogeographic scenario

Ceographic map () Phylogenetic tree () Transition tree () Migration distance = f(t) () Inter-cluster exchange charts () Choisir un fichier Aucun fichier choisi Model: F81 Joint Priors: Equiprob. Tree freq. Submit Output Display size Geographic map + Phylogenetic tree - + Transition tree - + Transition tree - + Transition tree	Event	oĽa	aded DS_{v.35}			
Geographic map () Phylogenetic tree () Transition tree () Migration distance = f(t) () Inter-cluster exchange charts () Ancestral character states () Choisir un fichier Aucun fichier choisi Model: ● F81 Joint Priors: ● Equiprob. ● Tree freq. Submit Output Display size ● Geographic map - + Phylogenetic tree - + Yransition tree - + Threshold: M Yery single hue		8				
Phylogenetic tree () Transition tree () Migration distance = f(t) () Inter-cluster exchange charts () Ancestral character states () Choisir un fichier Aucun fichier choisi Model: ● F81 Joint Priors: ● Equiprob. ● Tree freq. Submit Output Display Size ● Geographic map - + Phylogenetic tree - + Transition tree - + Threshold: M Color scale:	EDITION (i) =					
Transition tree () Migration distance = f(t) () Inter-cluster exchange charts () Ancestral character states () Choisir un fichier Aucun fichier choisi Model: ● F81 Joint Priors: ● Equiprob. ● Tree freq. Submit Output Display Size ● Geographic map - + Phylogenetic tree - + Transition tree - + Threshold: M Color scale: grey single hue	Geographic ma	p (i)				
Migration distance = f(t) () Inter-cluster exchange charts () Ancestral character states () Choisir un fichier Aucun fichier choisi Model: ● F81 Joint Priors: ● Equiprob. ● Tree freq. Submit Output Display Size ● Geographic map ● Phylogenetic tree ● Transition tree • + Threshold: M Color scale:	Phylogenetic tre	e i				
Inter-cluster exchange charts () Ancestral character states () Choisir un fichier Aucun fichier choisi Model: ● F81 Joint Priors: ● Equiprob. ● Tree freq. Submit Output Display Size ● Geographic map - + Phylogenetic tree - + Transition tree - + Threshold: M Color scale:	Transition tree (ì				
Ancestral character states () Choisir un fichier Aucun fichier choisi Model: ● F81 Joint Priors: ● Equiprob. ● Tree freq. Submit Output Display Size ● Geographic map ● + ● Phylogenetic tree ● + ● Transition tree ● + Color scale:	Migration distar	nce = f(t) (i)			
Choisir un fichier Aucun fichier choisi Model: ● F81 Priors: ● Equiprob. ● Tree freq. Submit Output Display size □ Geographic map - + Phylogenetic tree - + ✓ Transition tree - + Threshold: M Color scale:	Inter-cluster exc	change cha	rts 🕕			
Priors: Equiprob. Submit Output Display Size Geographic map Phylogenetic tree Phylogenetic tree Transition tree Threshold: M Geographic map						
Submit Output Display Geographic map Phylogenetic tree Phylogenetic tree Transition tree Threshold: M Grey single hue	Model: OF81		◯ Joint			
Output Display Geographic map Phylogenetic tree Phylogenetic tree Transition tree Transition tree M Color scale:	Priors: O Equ	iprob.	Tree freq.			
Display size Geographic map - + Phylogenetic tree - + Phylogenetic tree - + Transition tree - + Threshold: M ✓ Geographic map - +	Submit					
Size Geographic map Phylogenetic tree Transition tree Threshold: M Color scale: grey single hue ✓	Output					
Size Geographic map Phylogenetic tree Transition tree Threshold: M Color scale: grey single hue ✓						
Size Geographic map Phylogenetic tree Transition tree Threshold: M Color scale: grey single hue ✓						
Geographic map - + Phylogenetic tree - + Transition tree - + Threshold: M M ✓ Color scale: grey single hue ✓	Display					
 Phylogenetic tree - + → Transition tree - + Threshold: M ✓ Color scale: grey single hue ✓ 						
Transition tree - + Threshold: M Color scale: grey single hue			- +			
Threshold: M Color scale: grey single hue						
Color scale: grey single hue V	Transition tree	•	- +			
	Threshold:	М	~			
Oracity		grey single h	nue 🗸			
Opacity: - +	Opacity:	- +				

- 1. Select a csv file putting in regards sequence labels from the phylogenetic tree with a discrete variable. In this example the EcoType variable has 3 modalities : F, D and S
- 2. Select a method to compute ancestral character states, either « F81 » or « Joint »,
- 3. Select priors « Equiprob. » or « Tree freq. »
- 4. Submit, according to the number of sequences and the number of modalities of the discrete variable, computing ancestral character states may take a little while
- 5. Select an ancestral character set from the listbox, check on/off target(s) to display ancestral states on the geographic map, the phylogenetic tree and the transition diagram
- Treshold used to display ancestral character states (M= majority)
- Colors scale of piecharts displaying ancestral character states
- Opacity of piecharts displaying ancestral character states
- Check on/off to display piecharts of ancestral character states
- Size of piecharts displaying ancestral character states
- Ancestral character states are NOT dependent of the clustering used to establish the phylogeographic scenario.
- probability >= of a threshold, for each of the nodes underlying to the cluster
- majority minus a percentage of its value.



• Geographic map A piechart associated to a cluster displays the number of times each modality of the discrete variable under study has a

• Phylogenetic tree For each node of the phylogenetic tree, the associated piecharts display the modalities of the discrete variable under study having a probability >= of a threshold. The threshold is the probability of the majority for the given node or the probability of the

• Transition diagram A Piechart associated to a node of the transition diagram displays the number of times each modality of the discrete variable under study has a probability >= of a threshold, for each of the tree nodes and the sequences underlying the node of the transition diagram. The threshold is the probability of the majority or the probability of the majority minus a percentage of its value.



Computing the marginal posterior probabilities of every state for each of the tree nodes (F-81-like) and the joint ancestral scenario with the maximal posterior probability

Appendix



Computing the marginal posteriors probabilities (F81-like)

Probability of changes along a branch of length 1 is expressed as:

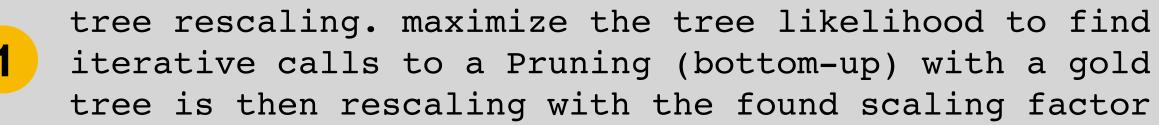
$$PC(i \rightarrow j/l) = (1 - e^{-\mu l}) \pi_{j \text{ if } j \neq i}$$

= $e^{-\mu l} + (1 - e^{-\mu l}) \pi_{i \text{ otherwise}}$

With πi equilibrium frequency (priors) at the tree tips or equal probability

with $\mu=1/(1-\sum_{i}\pi_{i}^{2})$ (normalization factor)

Computing the marginal posteriors probabilities is done in four steps:





2 bottom-up computation of 'down' conditional likelihoods (post-order recursion using the pruning algorithm)



3 top-down computation of 'up' conditional likelihoods (pre-order recursion)



computation of the states marginal posterior probabilities knowing the 'down' and 'up' conditional likelihoods

user supplied, roughly estimated from the state frequencies observed

tree rescaling. maximize the tree likelihood to find the scaling factor with 1 iterative calls to a Pruning (bottom-up) with a gold number or Brent search. The

Computing the marginal posteriors probabilities (F81-like)

tree rescaling. maximize the tree likelihood to find the scaling factor with iterative calls to a Pruning (bottom-up) with a gold number or Brent search. The tree is then rescaling with the found scaling factor. G, D = Left and Right descendant respectively

$$L(T) = \sum_{i} \pi_{i} Ldown(T/i)$$

$$Ldown(T/i) = \left[\sum_{j} PC(i \rightarrow j/l_{g}) Ldown(G/j) \right] * \left[\sum_{j} PC(i \rightarrow j/l_{d}) Ldown(D/j) \right]$$

$$Ldown(F/i) = 1 \text{ if the tip F is annotated with i, 0 otherwise}$$

bottom-up computation of 'down' conditional likelihoods (post-order recursion using the pruning algorithm)

3 top-down computation of 'up' conditional likelihoods (pre-order recursion) The 'up' likelihood of G is calculated from the 'down' likelihood of D and the 'up' likelihood of their common father, and vice versa.

$$Lup(G/i) = \left[\sum_{j} PC(i \rightarrow j/l_g) Lup(T/j) \left[\sum_{k} PC(j \rightarrow k/l_d) Ldown(D/k) \right] \right]$$
$$Lup(D/i) = \left[\sum_{j} PC(i \rightarrow j/l_d) Lup(T/j) \left[\sum_{k} PC(j \rightarrow k/l_g) Ldown(G/k) \right] \right]$$
$$Lup(T/j) = 1 \text{ si } T \text{ is the whole tree}$$

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computation of the states marginal posterior probabilities knowing the 'down' and 'up' conditional likelihoods

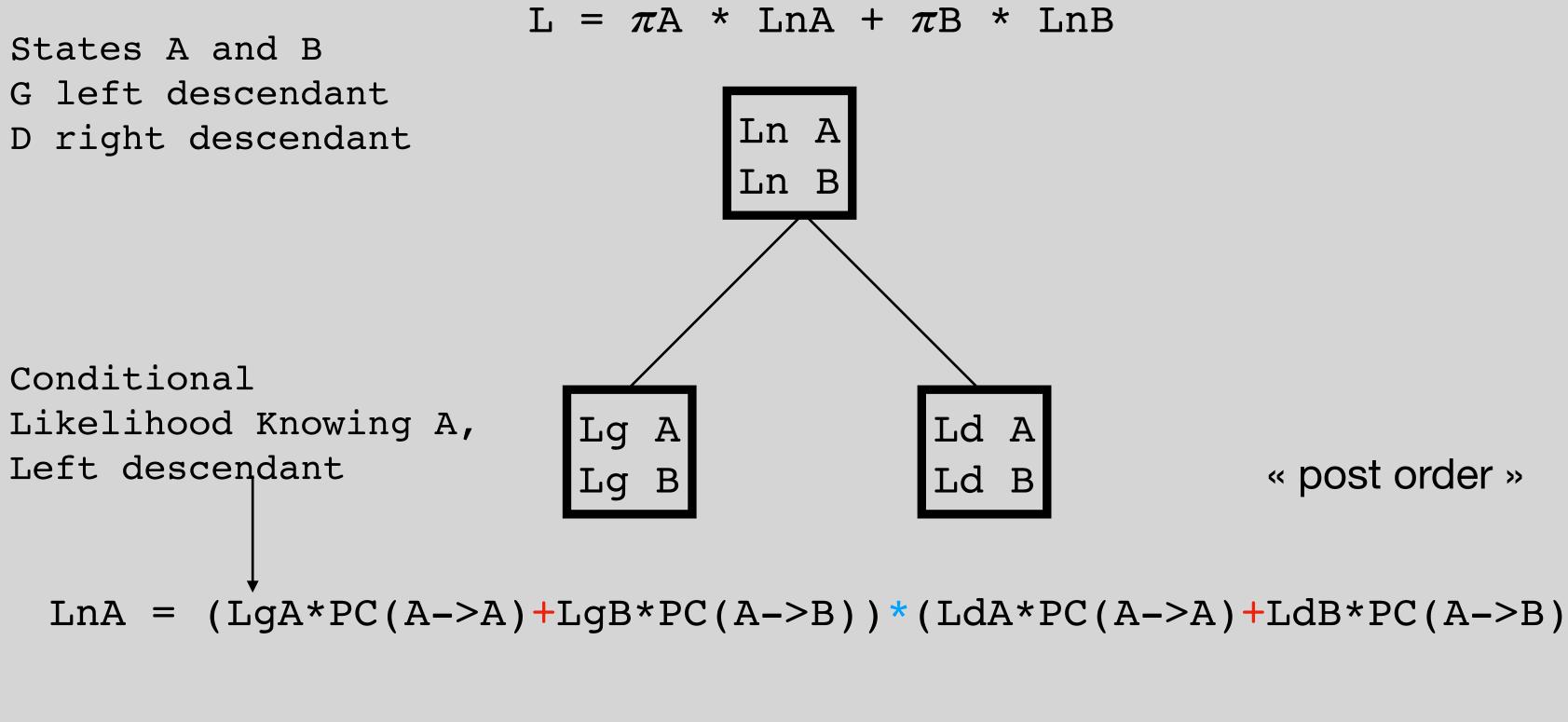
Post(N,i)=
$$\pi_i$$
 Ldown(N/i) Lup(N/i) / L
L(T)= $\sum_i \pi_i$ Ldown(N/i) Lup(N/i)

(T)

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The pruning algorithm (Felsenstein 1981)

 $L(T) = \sum_{i} \pi_{i} Ldown(T/i)$

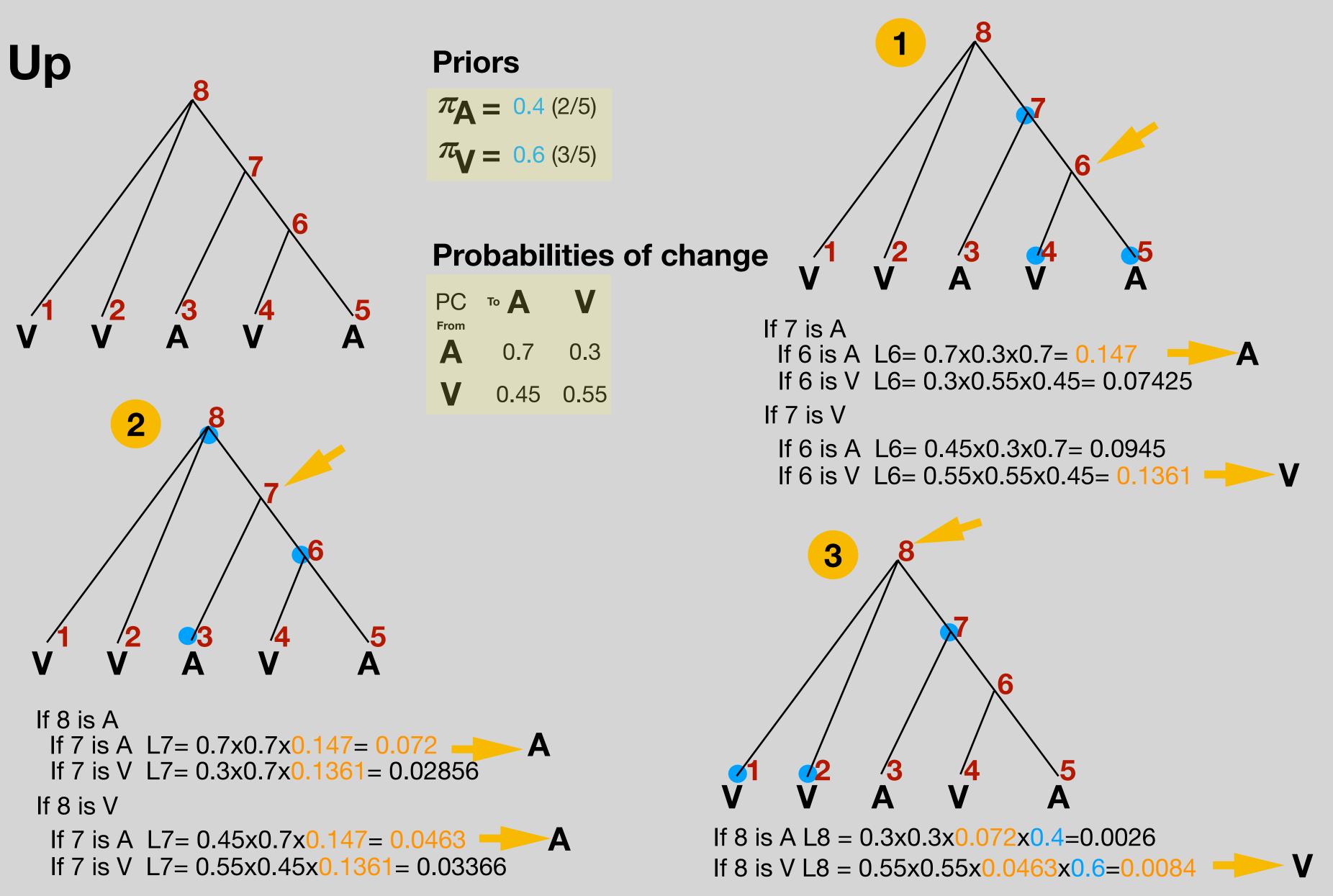


LnB = (LgA*PC(B->A)+LgB*PC(B->B))*(LdA*PC(B->A)+LdB*PC(B->B))

 $Ldown(T/i) = \left[\sum_{i} PC(i \rightarrow j/l_g) Ldown(G/j)\right] * \left[\sum_{i} PC(i \rightarrow j/l_d) Ldown(D/j)\right]$ Ldown(F/i) = 1 if the tip F is annotated with i, 0 otherwise

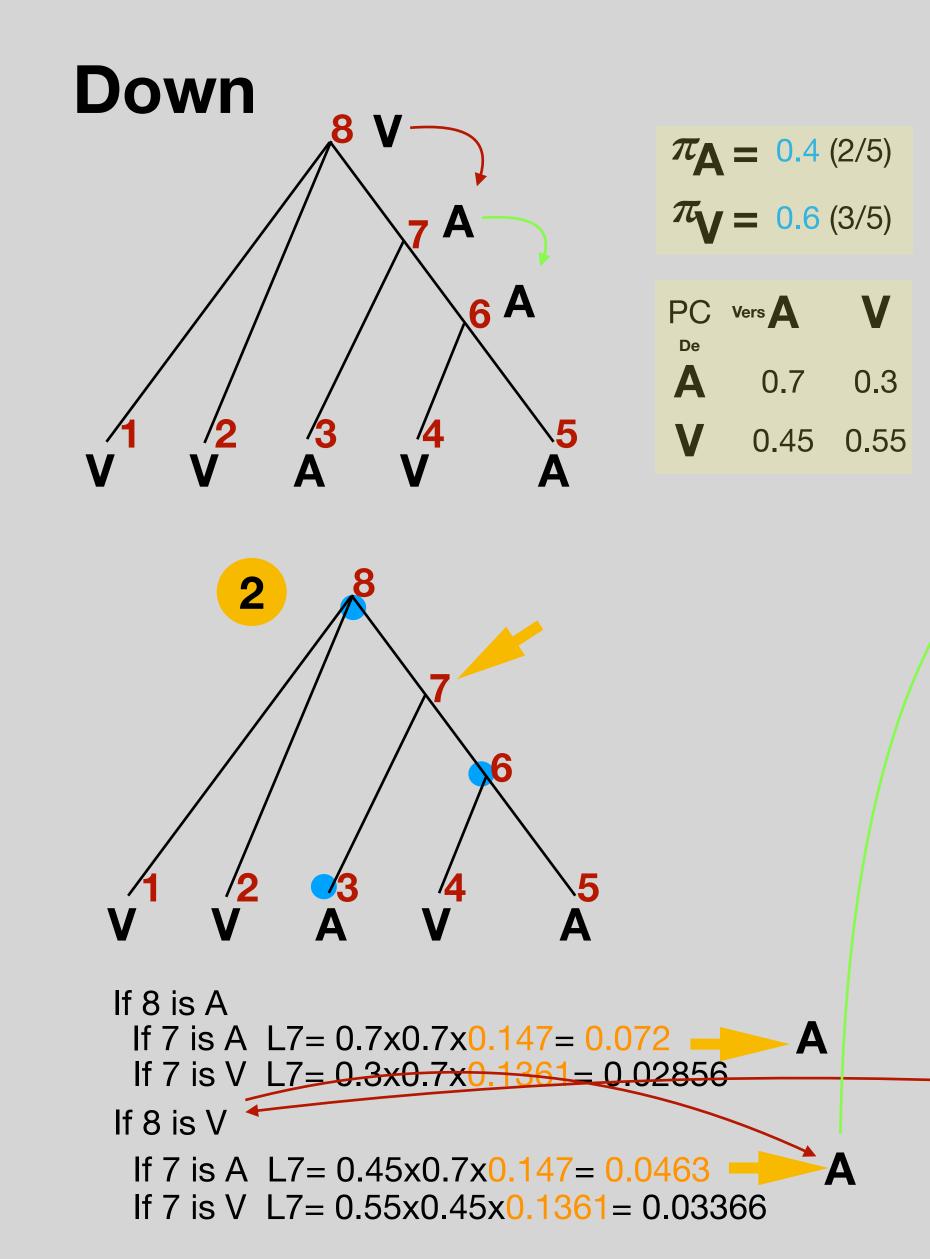
Computing the joint scenario, example





(Yang, 1995) (Pupko, 2000)

Computing the joint scenario, example



Tree scaling, then : Up + Down

(Yang, 1995) (Pupko, 2000)

