
Kingman's Unlabeled n -Coalescent

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Outline – Talk Outline

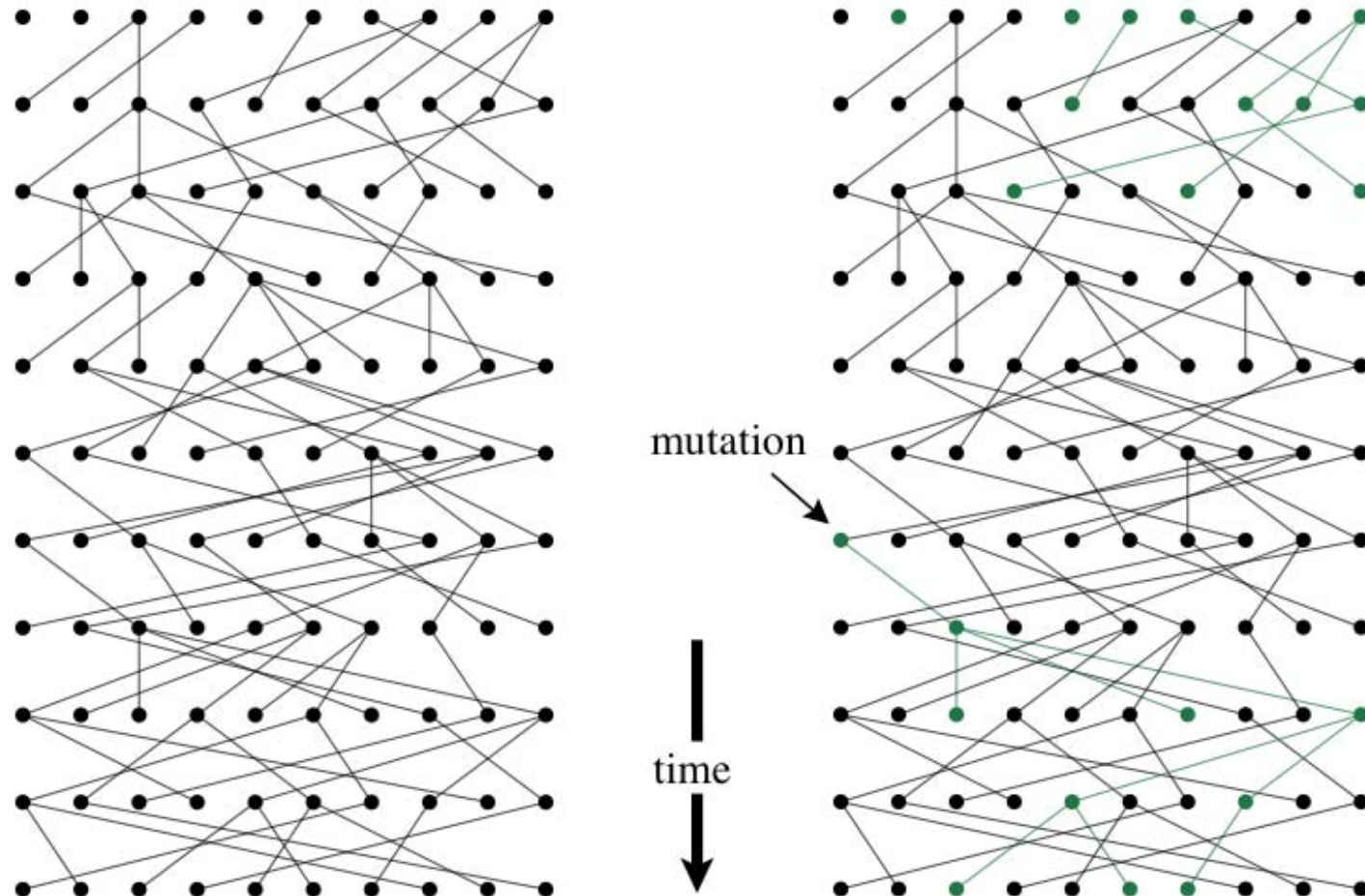
- The Coalescent Models
- Computationally Intensive Likelihoods
- A Paritllay-ordered Coalescent Experiments Graph
- Unlabeled n -Coalescent
- Results
- Summary
- Acknowledgments

Data and Model 1: $\phi \equiv \theta \in \Phi$, $\theta = 4N_e\mu$ (scaled mutation rate)

The Wright-Fisher Model – Random Mating, Constant Size, No Recombination/Selection

A **Population** of $N = 10$ homologous DNA seqs. of length m and the **Population History** of site i

	:	1	2	3	4	5	6	7	8	9	10
1	:	A	A	A	A	A	A	A	A	A	C
2	:	G	G	G	G	G	G	G	G	G	G
...	:										
i	:	T	T	A	A	A	A	A	A	A	A
...	:										
k	:	...									

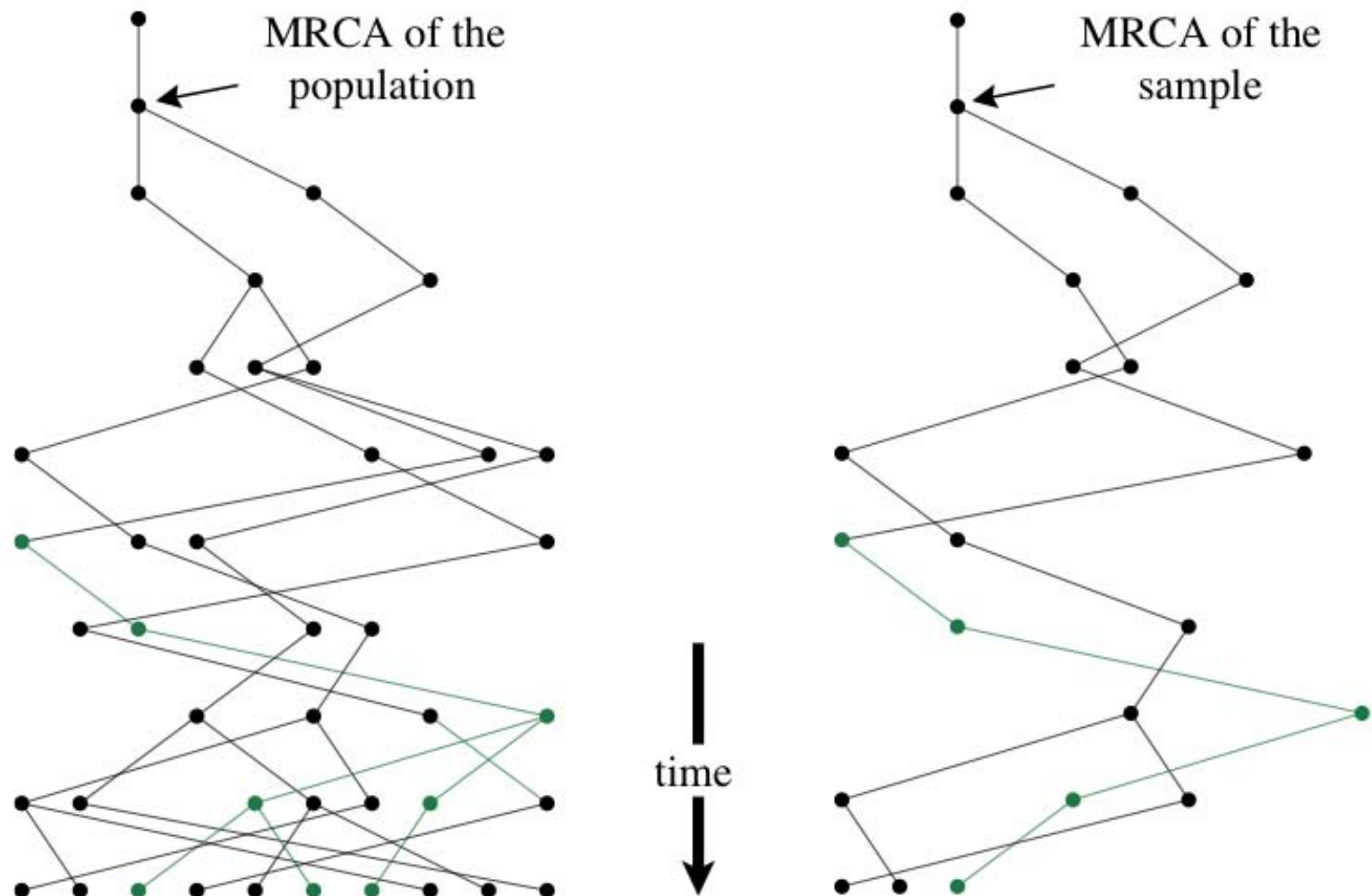


Data and Model 1: $\phi \equiv \theta \in \Phi$, $\theta = 4N_e\mu$ (scaled mutation rate)

The Wright-Fisher Model – Random Mating, Constant Size, No Recombination/Selection

Ex: **Data** of 3 homologous DNA sequences at site i , its **Population History** and the **Sample History** of sampled individuals 1,2, and 3.

 : 1 2 3
i : T T A



Model 1: $\phi \equiv \theta \in \Phi, \theta = 4N_e\mu$ (scaled mutation rate)

The Coalescent Approximation of the Wright-Fisher (W-F) Model (Kingman, 1982)

A **Sample Coalescent Sequence or c -sequence** ($\{\{1\}, \{2\}, \{3\}\}, \{\{1, 2\}, \{3\}\}, \{\{1, 2, 3\}\}$) and **coalescent times or epoch times** $t_i, i \in \{3, 2\}$.

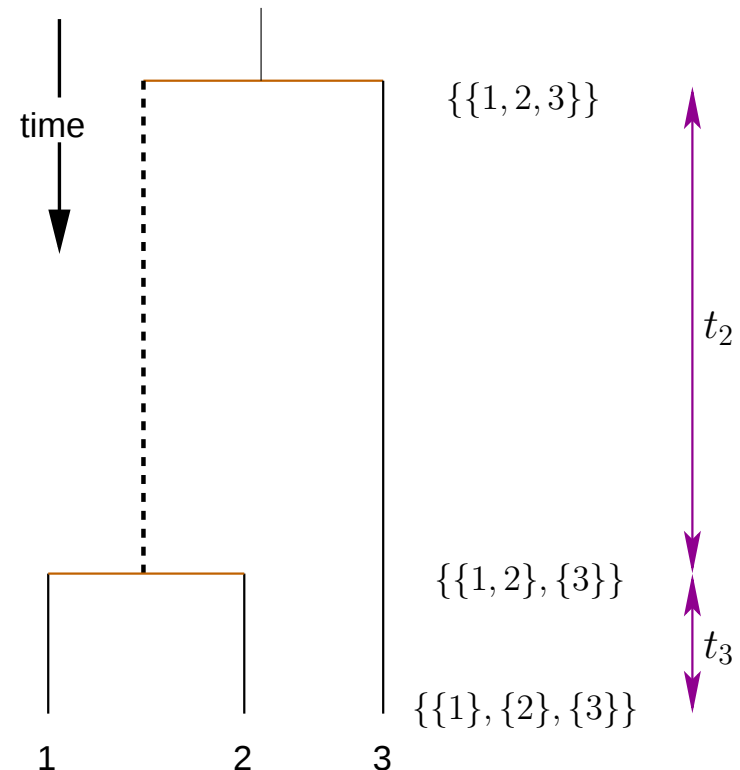
- Offspring “choose” parents uniformly and independently in W-F model
- $\Pr(2 \text{ lineages coalesce in } 1 \text{ generation}) = 1/N$
- $\Pr(2 \text{ lines. are distinct } > g \text{ gens.}) = (1 - 1/N)^g$
- Rescaled time t is g in units of N gens. Then, $\Pr(2 \text{ lines. remain distinct } > t)$ is

$$(1 - 1/N)^{\lfloor Nt \rfloor} \xrightarrow{N \rightarrow \infty} e^{-t}$$

- **Lineage Death Process:** In general, the R.V. T_i that any pair of i lineages coalesce is approximately exponentially distributed for large N .

$$T_i \sim \text{Exponential} \left(\binom{i}{2} \right)$$

- **Uniform Binary Fusion** of two extant lineages.



Model 1: $\phi \equiv \theta \in \Phi, \theta = 4N_e\mu$ (scaled mutation rate)

The Coalescent Approximation of the Wright-Fisher (W-F) Model (Kingman, 1982)

- The n -Coalescent is a continuous time Markov Chain on $\mathbb{C}_n \equiv \bigcup_{i=1}^n \mathbb{C}_n^i$, the set partitions of $\{1, \dots, n\}$, with rates $q(c_h | c_g), c_g, c_h \in \mathbb{C}_n$:

$$q(c_h | c_g) = \begin{cases} -i(i-1)/2 & : \text{if } c_g = c_h \in \mathbb{C}_n^i \\ 1 & : \text{if } c_h \succ_c c_g \\ 0 & : \text{o.w.} \end{cases}$$

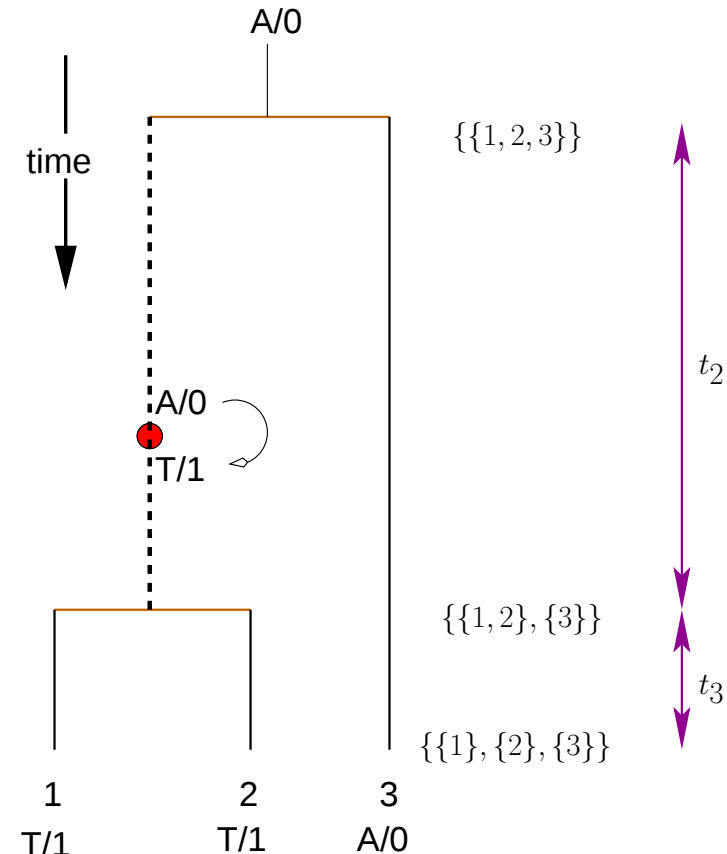
$$c_h \prec_c c_g \Leftrightarrow c_h = c_g \setminus c_{g,j} \setminus c_{g,k} \cup (c_{g,j} \cup c_{g,k})$$

a realization $c = (c_n, c_{n-1}, \dots, c_1) \in \mathcal{C}_n$

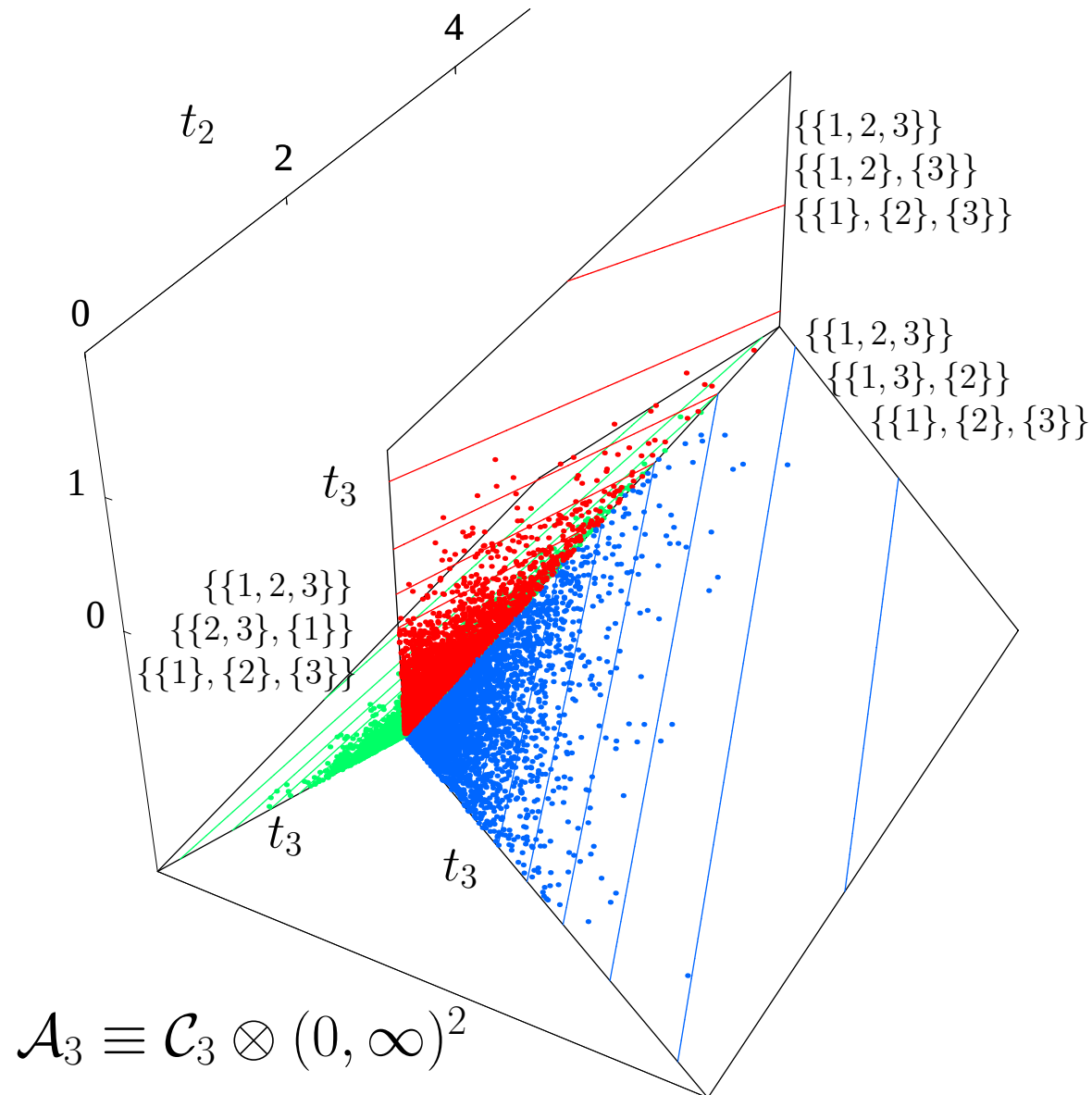
- Superimpose indep. mutations

$$\sim \text{Poisson}(\theta/2 \equiv 2N\mu)$$

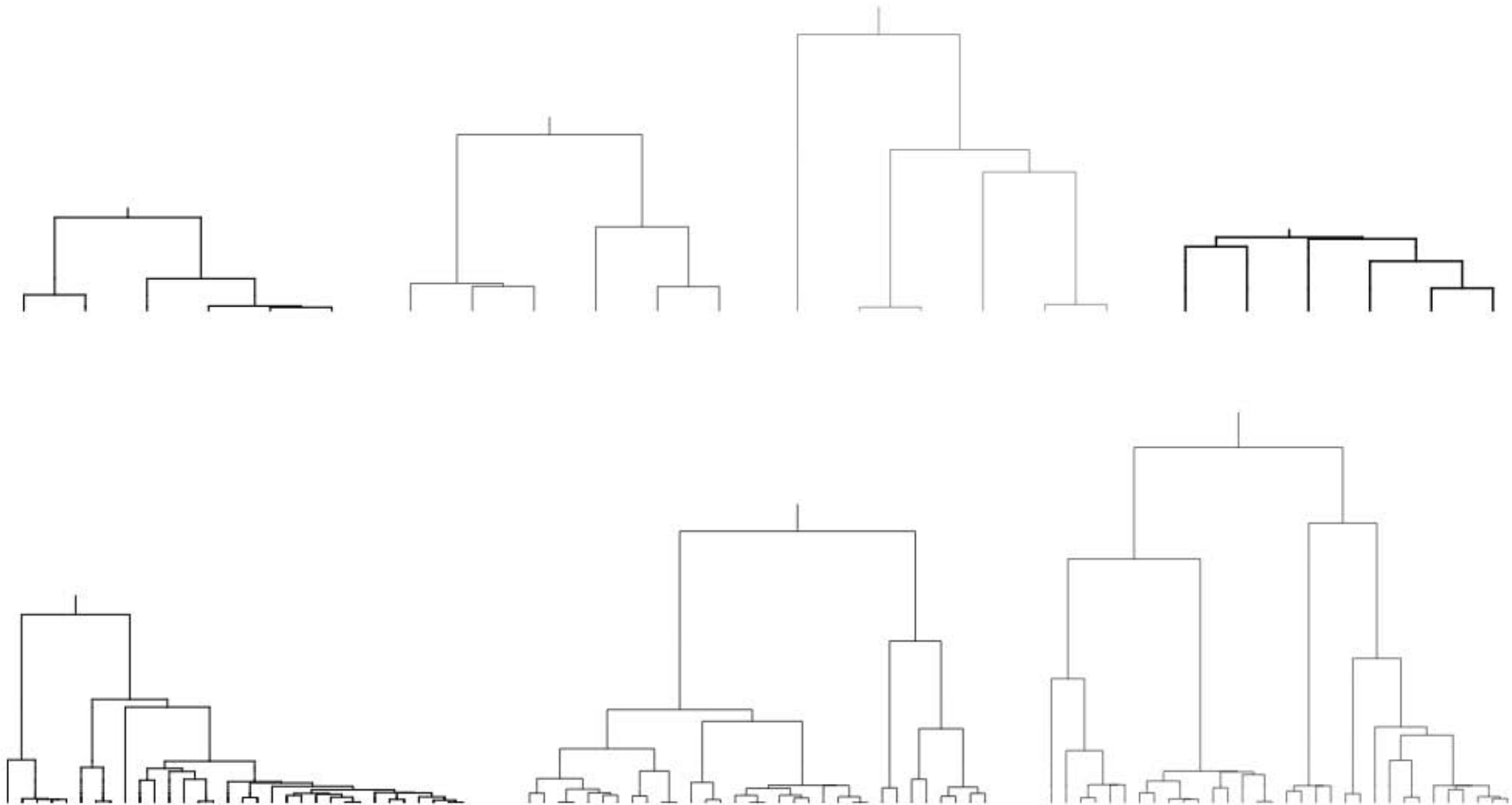
∞ -many-sites mutation model



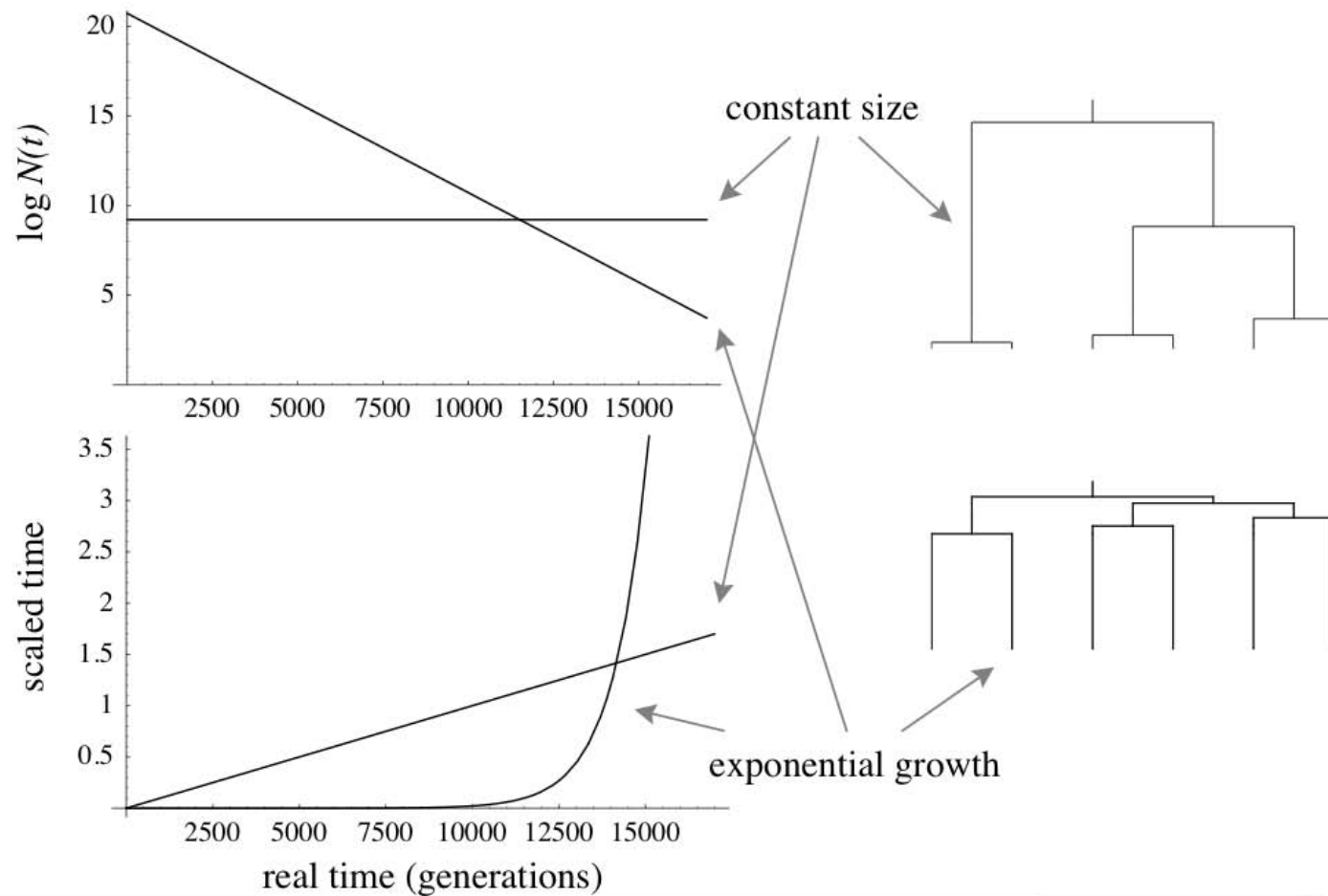
Coalescent Space $\mathcal{A}_n \equiv \mathcal{C}_n \otimes (0, \infty)^{n-1}$ when $n = 3$ (Model 1)



Realizations from $\mathcal{A}_n \equiv \mathcal{C}_n \otimes (0, \infty)^{n-1}$ under Model 1, $n = 6, 32$

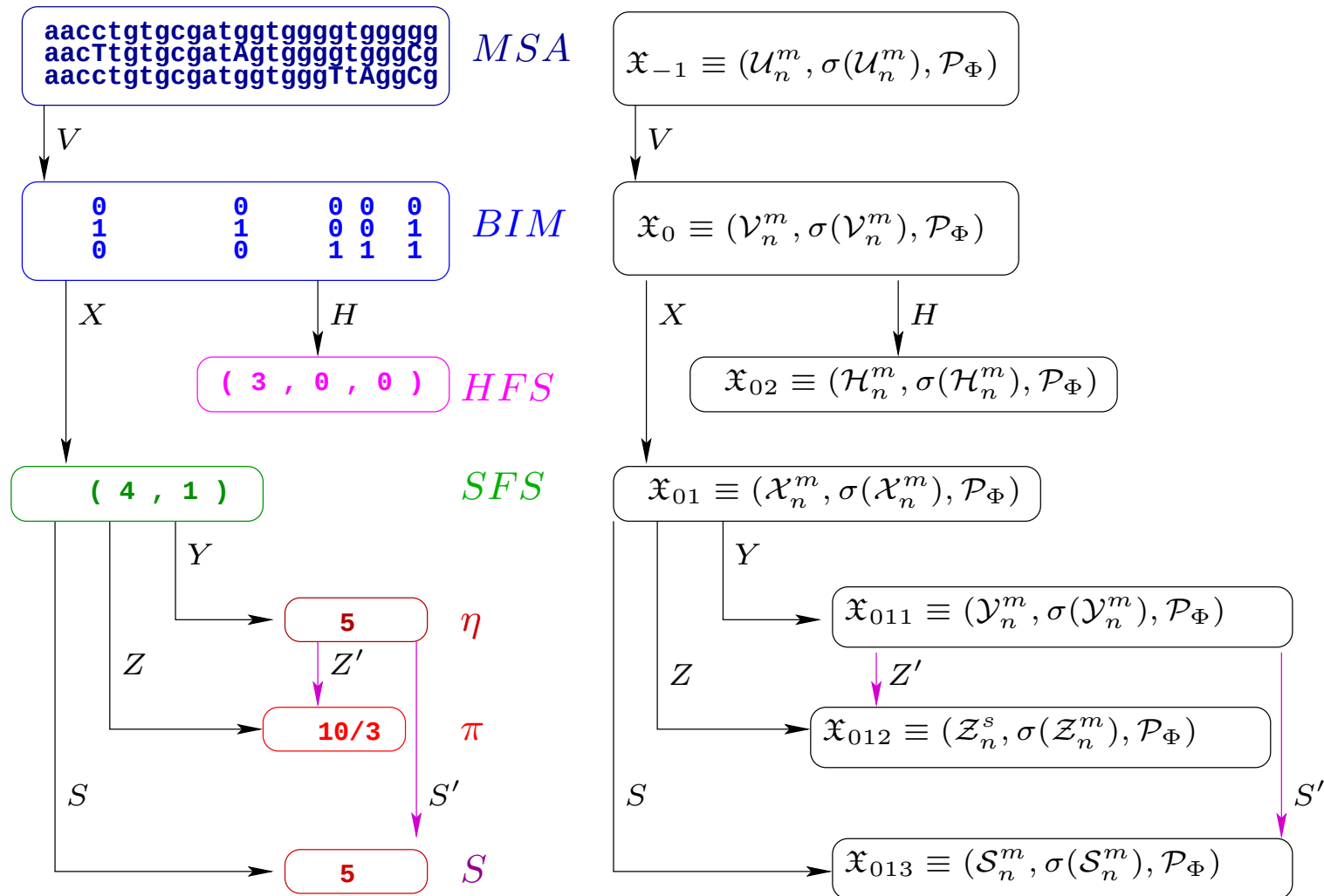


Model 2 : $\phi \equiv (\theta, \nu) \in \Phi$, $\theta = 4N_e\mu$ (scaled mutn. rate) , ν (exp. growth rate)



Figures 1-6 of M. Nordburg, Coalescent Theory, 2000

Coalescent Sample Spaces – Partially Ordered Experiments Graph



- (1) Every directed acyclic subgraph of the POEG indexes a Martingale
- (2) Each node of the POEG is a tri-sequential asymptotic family of Experiments

Likelihood

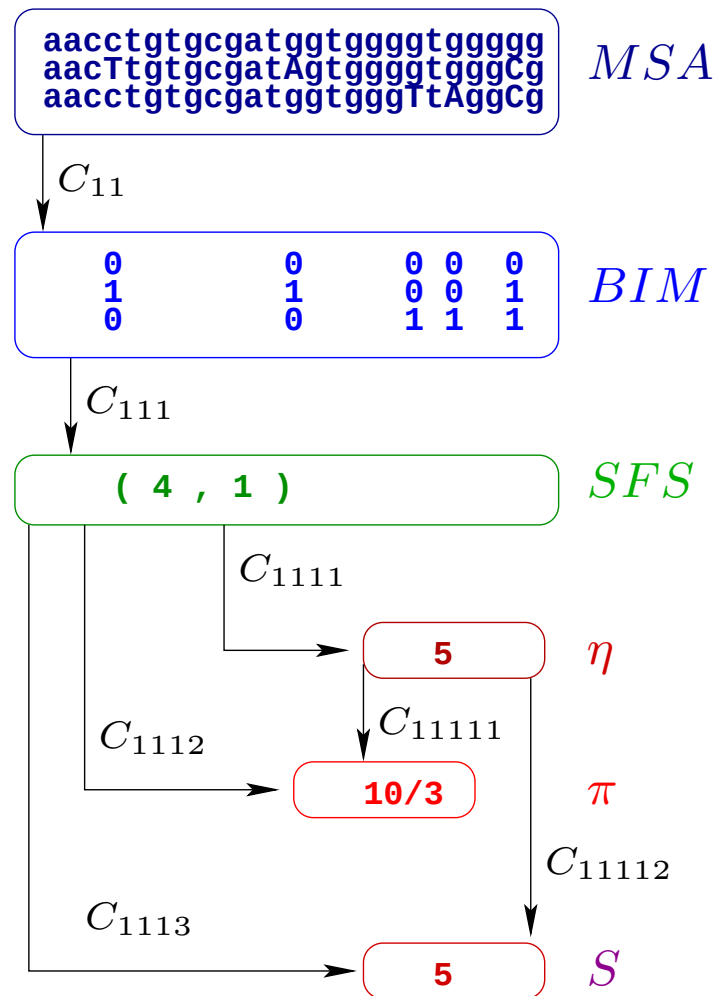
Likelihood, $P(D|\phi)$, is computed by **Integrating Missing-Data**:

$$\sum_{c \in \mathbb{C}_n} \int_{t \in (0, \infty)^{n-1}} P(D|c, t, \phi) P(c, t|\phi) dt \, dc$$

Cardinalities of the state spaces of the standard n -coalescent on $\mathbb{C}_n$ and the unlabeled n -coalescent on $\mathbb{F}_n$ (to be seen in the sequel).

n	4	10	30	60	90
$ \mathbb{C}_n $	15	1.2×10^5	8.5×10^{23}	9.8×10^{59}	1.4×10^{101}
$ \mathbb{F}_n $	5	42	5.6×10^3	9.7×10^5	5.7×10^7
$ \mathbb{F}_n / \mathbb{C}_n $	0.33	3.6×10^{-4}	6.6×10^{-21}	9.9×10^{-55}	4.0×10^{-94}

Likelihood is computationally prohibitive at MSA/BIM Resolns.



Exact Methods :

MSA 10,000 Auto-validating i.i.d. Posterior Samples in MRS SY2006 – **novel** (3/4 leaved phylogenetic tree spaces)

≈ 200 CPU sec for $n \leq 3$,

:- ($\rightarrow$ impractical for $n > 4$

BIM Complete Recursion in PTREE G1980 (1 Locus, $\theta = 10$, C-Model 1)

:- ($\rightarrow$ out of stack for $n > 4$

Approximate Methods :

MSA MCMC in COALESCE KYF1998 : $n < 200$ & heuristic

BIM SIS in GENETREE GT1994 : $L(\theta|v) \cong 4$ CPU hrs / θ

The **Bottom Line**: Exact Genome Scanning at fine DNA resolution is currently impractical for $n > 4$

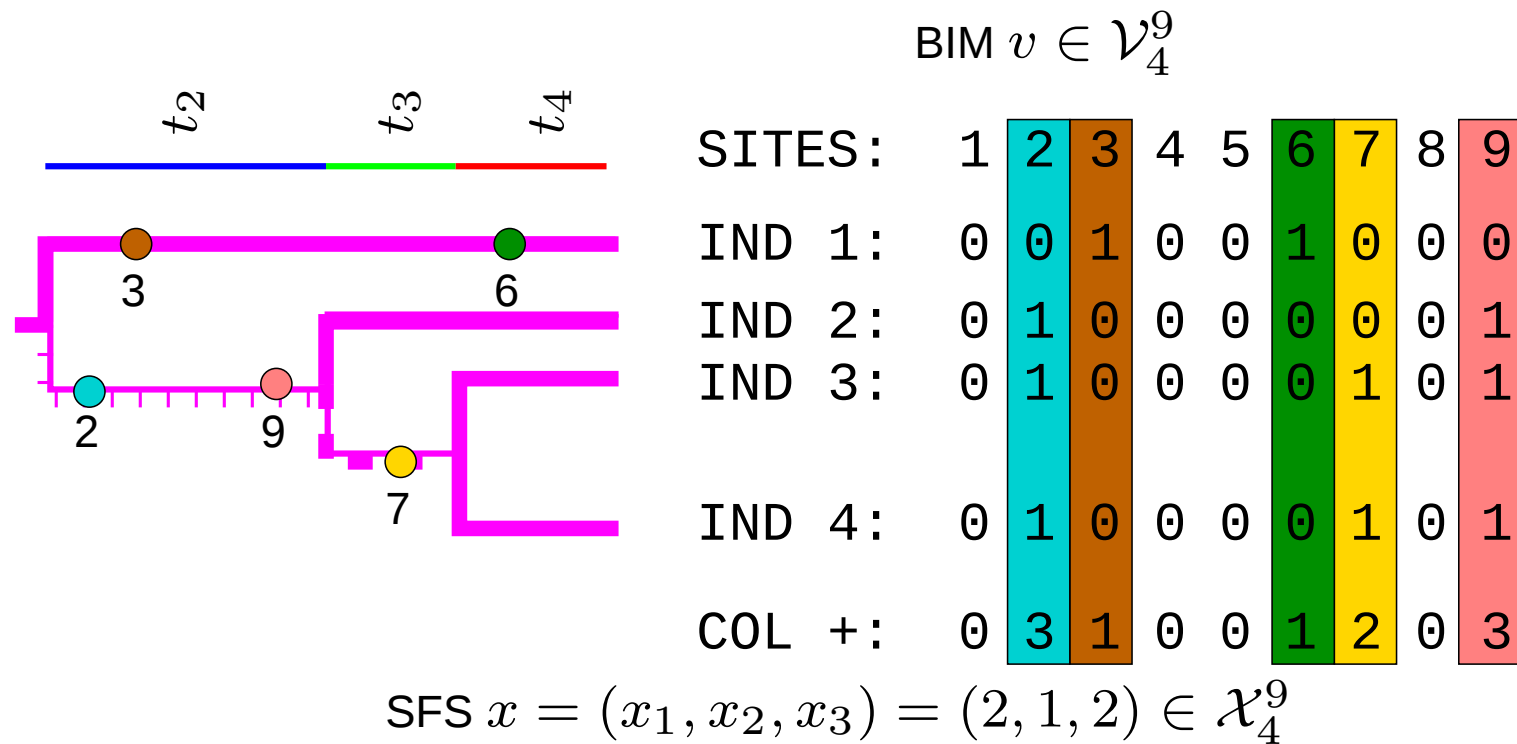
A **Solution**: Inference at coarser empirical resolutions, eg. **SFS** and its sub-experiments – **novel**

∞ -many-sites M-Model: BIM $v \in \mathcal{V}_n^m \rightarrow$ SFS $x \in \mathcal{X}_n^m$

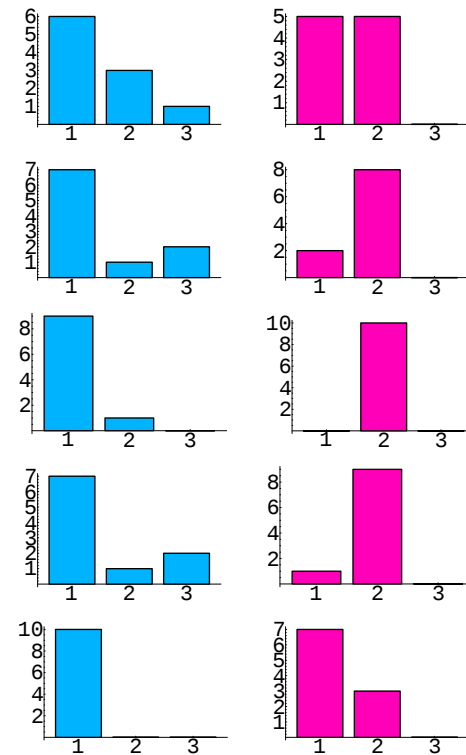
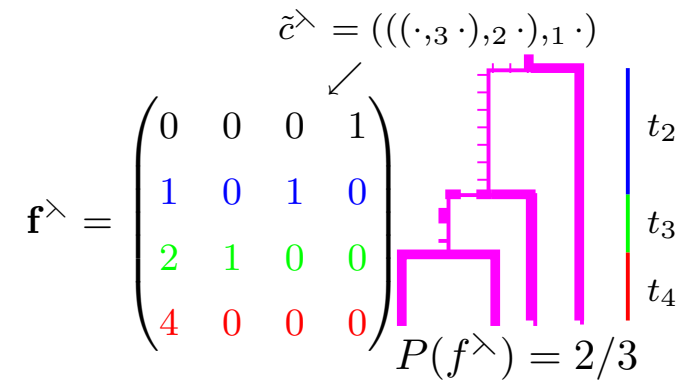
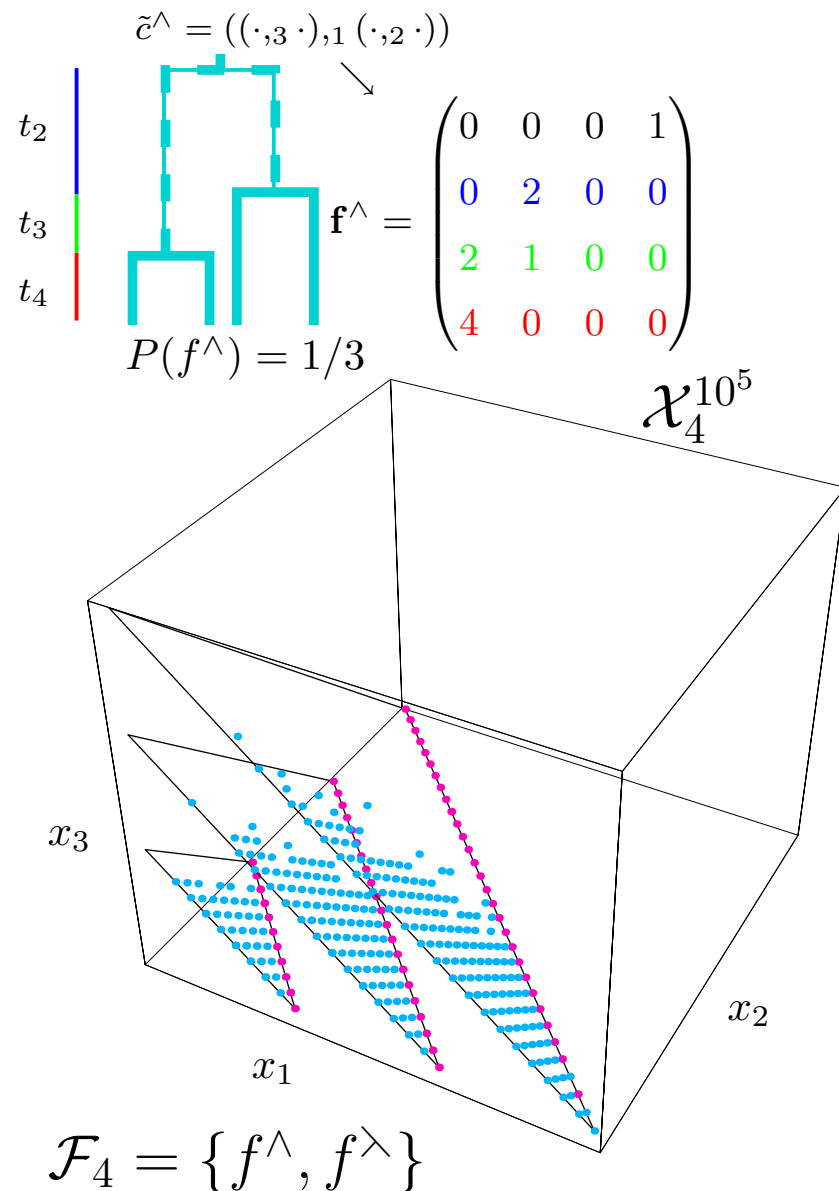
Let $v \in \mathcal{V}_n^m \equiv \{0, 1\}^{n \times m}$ be a BIM, then the SFS

$$x \equiv (x_1, \dots, x_{n-1}) \in \mathcal{X}_n^m \equiv \{x \in \mathbb{Z}_+^{n-1} : \sum_{i=1}^{n-1} x_i \leq m\}$$

$$x_i = N_i(v^T \cdot (1, 1, \dots, 1)), \quad N_i(y_1, y_2, \dots, y_s) = \sum_{j=1}^s \mathbf{1}_{\{i\}}(y_j), \quad i = 1, \dots, n-1.$$

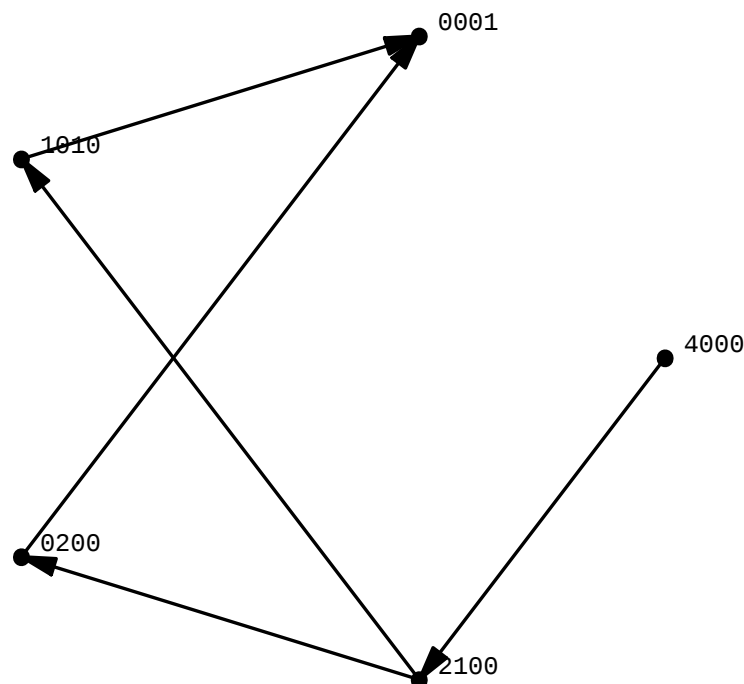


Coalescent Tree Shape, f -Sequence and Site Frequency Spectrum

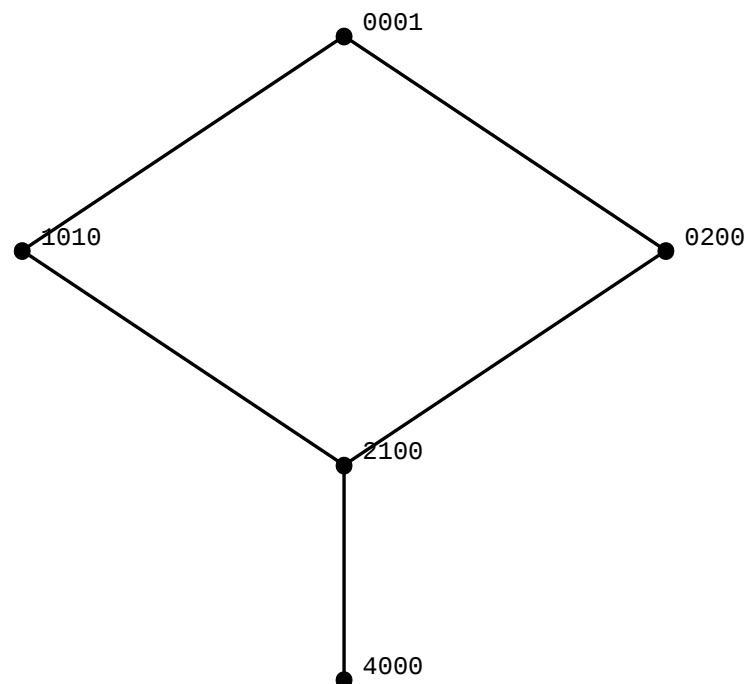


Examples of c -sequence $\rightarrow f$ -sequence, when $n = 4$

Transition-Diagram



Hasse-Diagram



Ex 1:

$[\{1\}, \{2\}, \{3\}, \{4\}], [\{1, 2\}, \{3\}, \{4\}], [\{1, 2, 3\}, \{4\}], [\{1, 2, 3, 4\}] \rightarrow$
 $[(4, 0, 0, 0), (2, 1, 0, 0), (1, 0, 1, 0), (0, 0, 0, 1)]$

Ex 2:

$[\{1\}, \{2\}, \{3\}, \{4\}], [\{1, 2\}, \{3\}, \{4\}], [\{1, 2\}, \{3, 4\}], [\{1, 2, 3, 4\}] \rightarrow$
 $[(4, 0, 0, 0), (2, 1, 0, 0), (0, 2, 0, 0), (0, 0, 0, 1)]$

Kingman's Unlabeled n -Coalescent

Consider, the integer partitions of n with i blocks:

$$\mathbb{F}_n^i \equiv \{f_i \equiv (f_{i,1}, f_{i,2}, \dots, f_{i,n}) \in \mathbb{Z}_+^n : \sum_{j=1}^n j f_{i,j} = n, \sum_{j=1}^n f_{i,j} = i\}.$$

where $f_{i,j}$ denotes the number of lineages subtending j leaves at the i -th epoch.

Proposition (Kingman's Unlabeled n -coalescent). *It is the continuous time Markov chain on $\mathbb{F}_n \equiv \bigcup_{i=1}^n \mathbb{F}_n^i$, the set of integer partitions of n , whose infinitesimal generator $\mathbf{q}(f_h | f_g)$ for any two states $f_g, f_h \in \mathbb{F}_n$ is:*

$$\mathbf{q}(f_h | f_g) = \begin{cases} -i(i-1)/2 & : \text{if } f_g = f_h, f_g \in \mathbb{F}_n^i \\ f_{g,j} f_{g,k} & : \text{if } f_h = f_g - e_j - e_k + e_{j+k}, j \neq k, f_g \in \mathbb{F}_n^i, f_h \in \mathbb{F}_n^{i-1} \\ (f_{g,j})(f_{g,j}-1)/2 & : \text{if } f_h = f_g - e_j - e_k + e_{j+k}, j = k, f_g \in \mathbb{F}_n^i, f_h \in \mathbb{F}_n^{i-1} \\ 0 & : \text{otherwise} \end{cases}$$

Initial state: $f_n = (n, 0, 0, \dots, 0)$ and absorbing state: $f_1 = (0, 0, \dots, 1)$.

Any realization of the chain is an f -sequence: $f = (f_n, f_{n-1}, \dots, f_1) \in \mathcal{F}_n$.

Kingman's Unlabeled n -Coalescent

Proposition (Probability of an f_i). *The probability of an $f_i \in \mathbb{F}_n^i$ is:*

$$P(f_i) = \frac{i!}{\prod_{j=1}^i f_{i,j}!} \binom{n-1}{i-1}^{-1}$$

Kingman's Unlabeled n -Coalescent

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Proposition (Probability of an f -sequence).

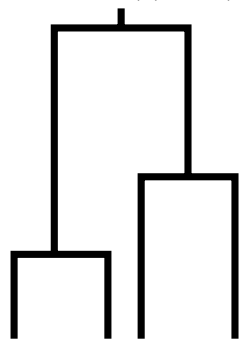
$$P(f) = \prod_{i=2}^n P(f_i | f_{i-1}) = \frac{2^{\mathfrak{T}(f)}}{(n-1)!} \prod_{i=2}^n \ddot{f}_i$$

where,

- $\mathfrak{T}(f)$ is the number of distinctly-sized lineage splits
- $\ddot{f}_i$ is the number of lineages at the beginning of the i -th epoch that subtend the same number of leaves as the lineage that was split then.

c-sequence, $c \in \mathcal{C}_n \rightarrow$ **c-shape**, $\tilde{c} \in \tilde{\mathcal{C}}_n \rightarrow$ **f-sequence**, $f \in \mathcal{F}_n$

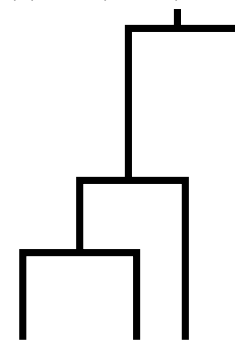
$$\tilde{c}^\wedge = ((\cdot, 3 \cdot),_1 (\cdot, 2 \cdot))$$



$$\mathbf{f}^\wedge = \begin{pmatrix} 0 & 0 & 0 & 1 \\ 0 & 2 & 0 & 0 \\ 2 & 1 & 0 & 0 \\ 4 & 0 & 0 & 0 \end{pmatrix}$$

$$n = 4$$

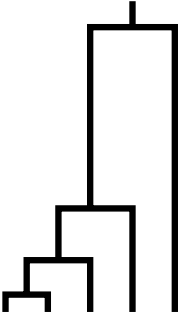
$$\tilde{c}^\lambda = (((\cdot, 3 \cdot),_2 \cdot),_1 \cdot)$$



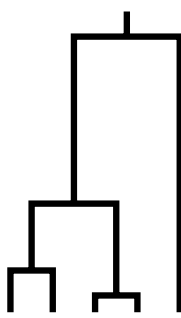
$$\mathbf{f}^\lambda = \begin{pmatrix} 0 & 0 & 0 & 1 \\ 1 & 0 & 1 & 0 \\ 2 & 1 & 0 & 0 \\ 4 & 0 & 0 & 0 \end{pmatrix}$$

c-sequence, $c \in \mathcal{C}_n \rightarrow$ **c-shape**, $\tilde{c} \in \tilde{\mathcal{C}}_n \rightarrow$ **f-sequence**, $f \in \mathcal{F}_n$

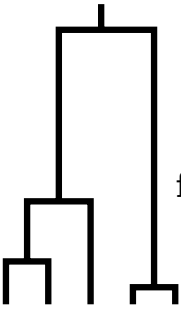
$$n = 5$$

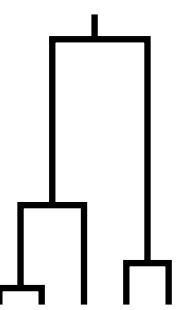
$$\tilde{c}^{(a)} = (((\cdot, 4 \cdot), 3 \cdot), 2 \cdot), 1 \cdot)$$


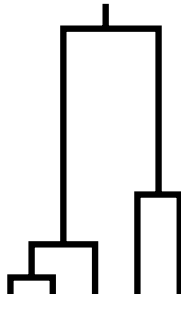
$$f^a = \begin{pmatrix} 0 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 1 & 0 \\ 2 & 0 & 1 & 0 & 0 \\ 3 & 1 & 0 & 0 & 0 \\ 5 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$\tilde{c}^{(b)} = (((\cdot, 4 \cdot), 2 (\cdot, 3 \cdot)), 1 \cdot)$$


$$f^b = \begin{pmatrix} 0 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 1 & 0 \\ 1 & 2 & 0 & 0 & 0 \\ 3 & 1 & 0 & 0 & 0 \\ 5 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$\tilde{c}^{(c)} = ((\cdot, 4 \cdot), 1 ((\cdot, 3 \cdot), 2 \cdot)) \quad \tilde{c}^{(d)} = (((\cdot, 4 \cdot), 2 \cdot), 1 (\cdot, 3 \cdot))$$


$$f^{c/d} = \begin{pmatrix} 0 & 0 & 0 & 0 & 1 \\ 0 & 1 & 1 & 0 & 0 \\ 1 & 2 & 0 & 0 & 0 \\ 3 & 1 & 0 & 0 & 0 \\ 5 & 0 & 0 & 0 & 0 \end{pmatrix}$$


$$\tilde{c}^{(e)} = (((\cdot, 4 \cdot), 3 \cdot), 1 (\cdot, 2 \cdot))$$


$$f^e = \begin{pmatrix} 0 & 0 & 0 & 0 & 1 \\ 0 & 1 & 1 & 0 & 0 \\ 2 & 0 & 1 & 0 & 0 \\ 3 & 1 & 0 & 0 & 0 \\ 5 & 0 & 0 & 0 & 0 \end{pmatrix}$$

c -sequence, $c \in \mathcal{C}_n \rightarrow$ **c -shape**, $\tilde{c} \in \tilde{\mathcal{C}}_n \rightarrow$ **f -sequence**, $f \in \mathcal{F}_n$

The number of c -sequences corresponding to the given f is

$$|F^{-1}(f)| = 2^{1-n} n! (n-1)! P(f) = n! 2^{\mathfrak{T}(f)+1-n} \prod_{i=2}^n \ddot{f}_i$$

Let $\mathfrak{J}(\tilde{c})$ be the number of cherries of a c -shape $\tilde{c} \in \tilde{\mathcal{C}}$.

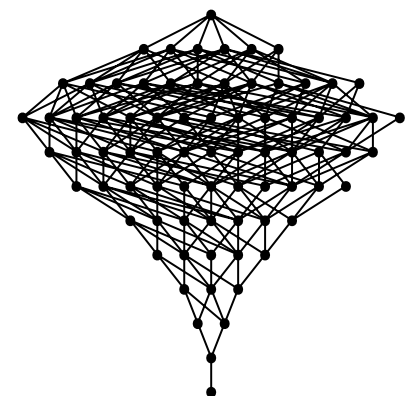
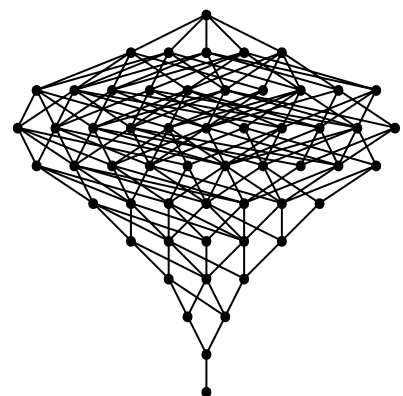
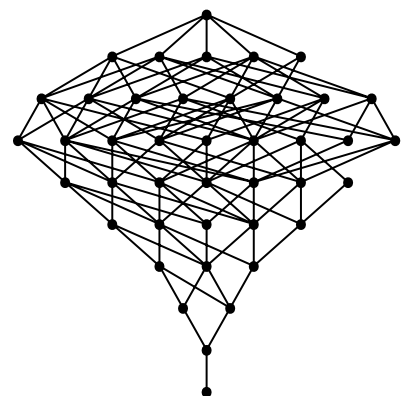
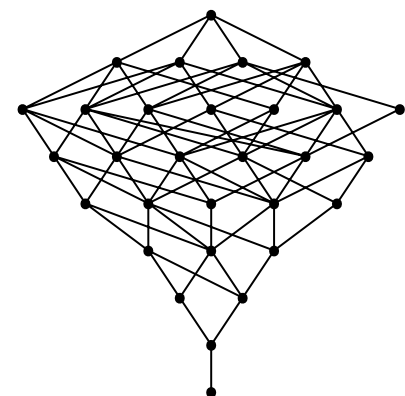
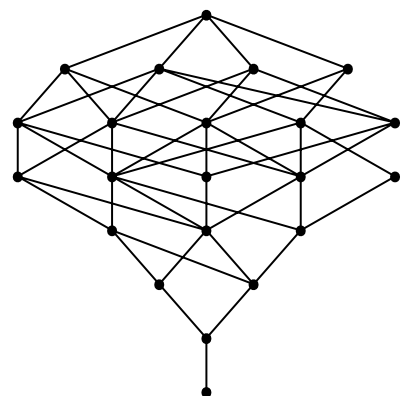
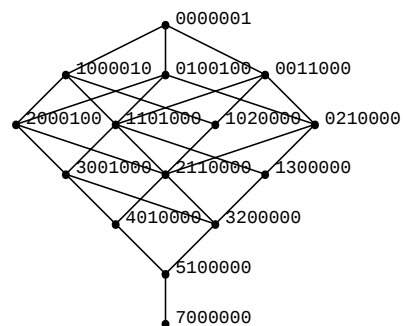
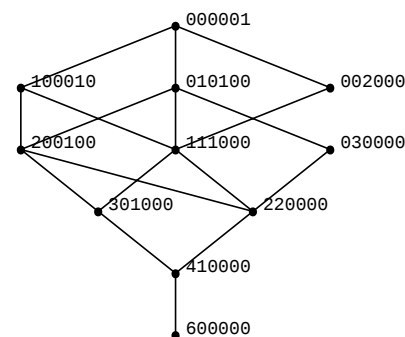
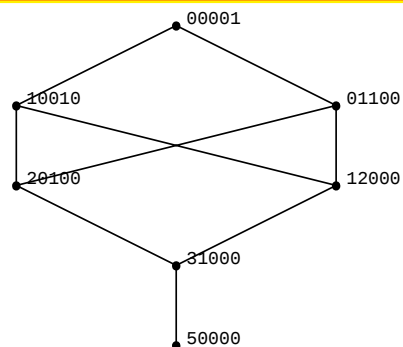
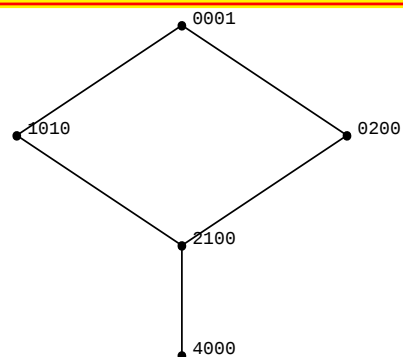
$$|\tilde{C}^{-1}(\tilde{c})| = 2^{1-n} n! (n-1)! P(\tilde{c}) = n! 2^{-\mathfrak{J}(\tilde{c})} \quad (Tajima, 1983)$$

The number of c -shapes corresponding to the given f is

$$|\tilde{C}(F^{-1}(f))| = 2^{-\mathfrak{J}(f)} \prod_{i=2}^n \ddot{f}_i,$$

$\mathfrak{B}(f) \equiv n - 1 - \mathfrak{T}(f) - \mathfrak{J}(f)$, the number of balanced splits that are not cherries.

Hasse Diagram of the Poset making $\mathcal{F}_n$ ($n = 4, \dots, 12$)



Simulating f -sequences: for SFS, Shape Stats, ...

1: **input:**

1. scaled mutation rate θ

2. sample size n

2: **output:** a SFS sample x from the n -coalescent

3: generate an f -sequence under the unlabeled n -coalescent

4: draw $t \sim T = (T_2, T_3, \dots, T_n)$, where T_i 's are independently distributed as Exponential $\left(\binom{i}{2}\right)$

5: $l \leftarrow t^T \cdot \mathbf{f}$ and $l_{\bullet} = \sum_{i=1}^{n-1}$

6: draw x from Poisson-Multinomial distribution

$$e^{-\theta l_{\bullet}} (\theta l_{\bullet})^{\sum_{i=1}^{n-1} x_i} \prod_{i=1}^{n-1} \bar{l}_i^{x_i} / \prod_{i=1}^{n-1} x_i!$$

7: **return:** x

Various tree shape statistics are further summaries of the f -sequence

$\tilde{s}$ -sequence or **Aldous shape statistic** (Aldous, 2001)

$$\tilde{S}(f_n, f_{n-1}, \dots, f_1) = \tilde{s} \equiv (\tilde{s}_n, \tilde{s}_{n-1}, \dots, \tilde{s}_2) : \mathcal{F}_n \rightarrow \tilde{\mathcal{S}}_n:$$

$$\begin{aligned} \tilde{s}_i &\equiv (\tilde{s}_{i,1}, \tilde{s}_{i,2}) \equiv \left(\max(\|f\|_i), \min(\|f\|_i) 2^{-\mathbf{1}_{\{0\}}(\max(\|f\|_i) - \min(\|f\|_i))} \right), \\ \|f\|_i &\equiv \{j | f_{i,j} - f_{i-1,j} \in \mathbb{N} : j \in \{1, 2, \dots, n\}\}. \end{aligned}$$

$$\mathfrak{Q}_n \equiv \{Q_I(\tilde{s}) = q_I \equiv \sum_{i=n}^2 \tilde{s}_{i,1} \mathbf{1}_I(\tilde{s}_{i,1}) : \tilde{\mathcal{S}}_n \rightarrow \mathcal{Q}_{I,n}, I \in \mathbf{2}^{\{2,3,\dots,n\}} \setminus \emptyset\}$$

$Q_{\{2,3,\dots,n\}}(\tilde{s}) = q_{\{2,3,\dots,n\}} = \sum_{i=n}^2 \tilde{s}_{i,1}$ is the **Sackin's index**

$Q_{\{2\}}/2 = q_{\{2\}}/2$ is the **number of cherries**

$(n^2 - 3n + 2)^{-1} \sum_{i=n}^2 (\tilde{s}_{i,1} - 2\tilde{s}_{i,d})$ is the **Colless' index**

Note: There are $2^{n-1} - 3$ others in the family $\mathfrak{Q}_n$

Likelihood of a Site Frequency Spectrum

Proposition (Likelihood of SFS). *Let $a \in \mathcal{A}_n$ be a given coalescent tree, c be its c -sequence, $f = F(c)$ be its f -sequence, $t \equiv (t_2, t_3, t_n) \in (0, \infty)^{n-1}$ be its epoch times and let*

$$l \equiv (l_1, \dots, l_{n-1}) = t^T f = \left(\sum_{i=2}^n t_i f_{i,1}, \dots, \sum_{i=2}^n t_i f_{i,n-1} \right), \quad l_{\bullet} \equiv \sum_{i=2}^n l_i, \quad \bar{l}_i \equiv \frac{l_i}{l_{\bullet}}$$

be its lineage lengths subtending $1, 2, \dots, n - 1$ leaves, the total tree-size, and relative lineage lengths respectively.

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Proposition (Likelihood of SFS). Let $a \in \mathcal{A}_n$ be a given coalescent tree, c be its c -sequence, $f = F(c)$ be its f -sequence, $t \equiv (t_2, t_3, t_n) \in (0, \infty)^{n-1}$ be its epoch times and let

$$l \equiv (l_1, \dots, l_{n-1}) = t^T f = \left(\sum_{i=2}^n t_i f_{i,1}, \dots, \sum_{i=2}^n t_i f_{i,n-1} \right), \quad l_{\bullet} \equiv \sum_{i=2}^n l_i, \quad \bar{l}_i \equiv \frac{l_i}{l_{\bullet}}$$

be its lineage lengths subtending $1, 2, \dots, n-1$ leaves, the total tree-size, and relative lineage lengths respectively.

$$P(x|\phi, a) = P(x|\phi, l = t^T f) = e^{-\theta l_{\bullet}} (\theta l_{\bullet})^S \prod_{i=1}^{n-1} \bar{l}_i^{x_i} / \prod_{i=1}^{n-1} x_i!$$

Likelihood of a Site Frequency Spectrum

Proposition (Likelihood of SFS). Let $a \in \mathcal{A}_n$ be a given coalescent tree, c be its c -sequence, $f = F(c)$ be its f -sequence, $t \equiv (t_2, t_3, t_n) \in (0, \infty)^{n-1}$ be its epoch times and let

$$l \equiv (l_1, \dots, l_{n-1}) = t^T f = \left(\sum_{i=2}^n t_i f_{i,1}, \dots, \sum_{i=2}^n t_i f_{i,n-1} \right), \quad l_{\bullet} \equiv \sum_{i=2}^n l_i, \quad \bar{l}_i \equiv \frac{l_i}{l_{\bullet}}$$

be its lineage lengths subtending 1, 2, ..., $n - 1$ leaves, the total tree-size, and relative lineage lengths respectively.

$$P(x|\phi, a) = P(x|\phi, l = t^T f) = e^{-\theta l_{\bullet}} (\theta l_{\bullet})^S \prod_{i=1}^{n-1} \bar{l}_i^{x_i} / \prod_{i=1}^{n-1} x_i!$$

$$P(x|\phi) = \frac{1}{\prod_{i=1}^{n-1} x_i!} \sum_{f \in F_n^c(x^{\otimes})} P(f) \left(\int_{t \in (0, \infty)^{n-1}} \left(e^{-\theta l_{\bullet}} (\theta l_{\bullet})^S \prod_{i=1}^{n-1} \bar{l}_i^{x_i} \right) P(t|\phi) \right)$$

$$\text{where, } F_n(x^{\otimes}) \equiv \bigcup_{\{h: x_h^{\otimes}=1\}} \{f \in \mathcal{F}_n : \sum_{i=1}^n f_{i,h} = 0\}$$

$$X^{\otimes}(x) = x^{\otimes} \equiv (x_1^{\otimes}, \dots, x_{n-1}^{\otimes}) \equiv (\mathbf{1}_{\mathbb{N}}(x_1), \dots, \mathbf{1}_{\mathbb{N}}(x_{n-1})) \in \{0, 1\}^{n-1}$$

An Importance Sampler over $F_n^c(x^{\otimes})$

Proposition (A Proposal over $F_n^c(x^{\otimes})$). For a given $x \in \mathcal{X}_n^m$, consider the following discrete time Markov chain on the augmented state space $\mathbb{F}_n \times \{0, 1\}^{n-1} \ni (f_h, z_h)$:

$$P^*((f_h, z_h)|(f_g, z_g)) = \begin{cases} P(f_h|f_g)/\Sigma(f_g, z_g) & : \text{if } (f_h, z_h) \prec_{f,z} (f_g, z_g), \\ 0 & : \text{otherwise} \end{cases}$$

where,

$$\Sigma(f_g, z_g) = \sum_{(j,k) \in H(f_g, z_g)} P(f_g - e_{j+k} + e_j + e_k | f_g),$$

$$H(f_g, z_g) = \{(j, k) : f_{g,j+k} > 0, 1 \leq j \leq \max\{\min\{\hat{g}, j+k-1\}, \lceil \frac{j+k}{2} \rceil\} \leq k \leq j+k-1\},$$

$$\hat{g} = \max\{i : z_{g,i} = 1\},$$

$$(f_h, z_h) \prec_{f,z} (f_g, z_g) \Leftrightarrow f_h = f_g + e_j + e_k - e_{j+k}, z_h = z_g - \mathbf{1}_{\{1\}}(z_{g,j}) e_j - \mathbf{1}_{\{1\}}(z_{g,k}) e_k$$

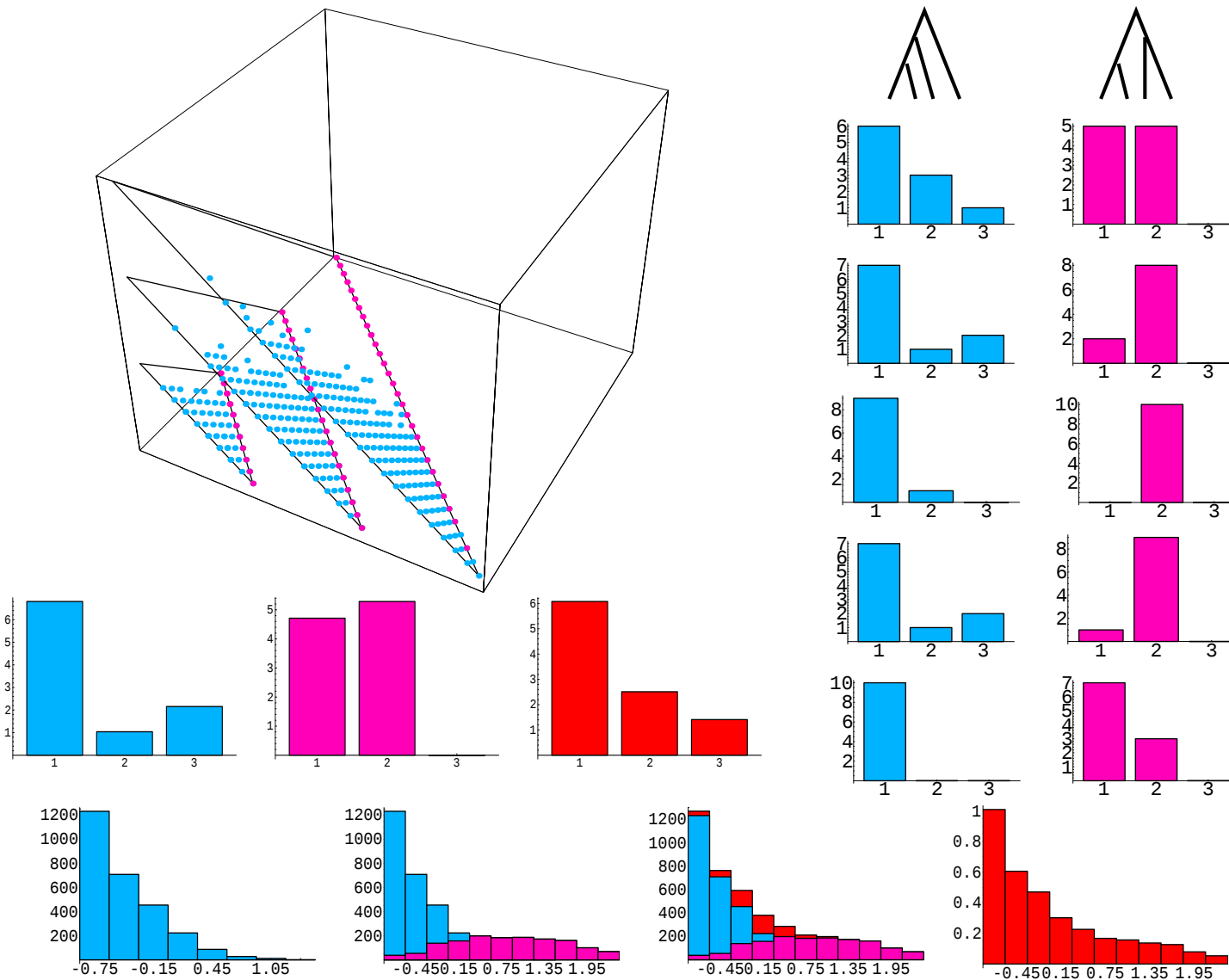
where, the initial state is $(f_1, X^{\otimes}(x)) = ((0, 0, \dots, 1), x^{\otimes})$ and the final absorbing state is

$$(f_n, (0, 0, \dots, 0)) = ((n, 0, \dots, 0), (0, 0, \dots, 0)).$$

Maximum *Aposteriori* Estimates of θ and ν by $\sum$ over $f \in F_n^c(x^*)$

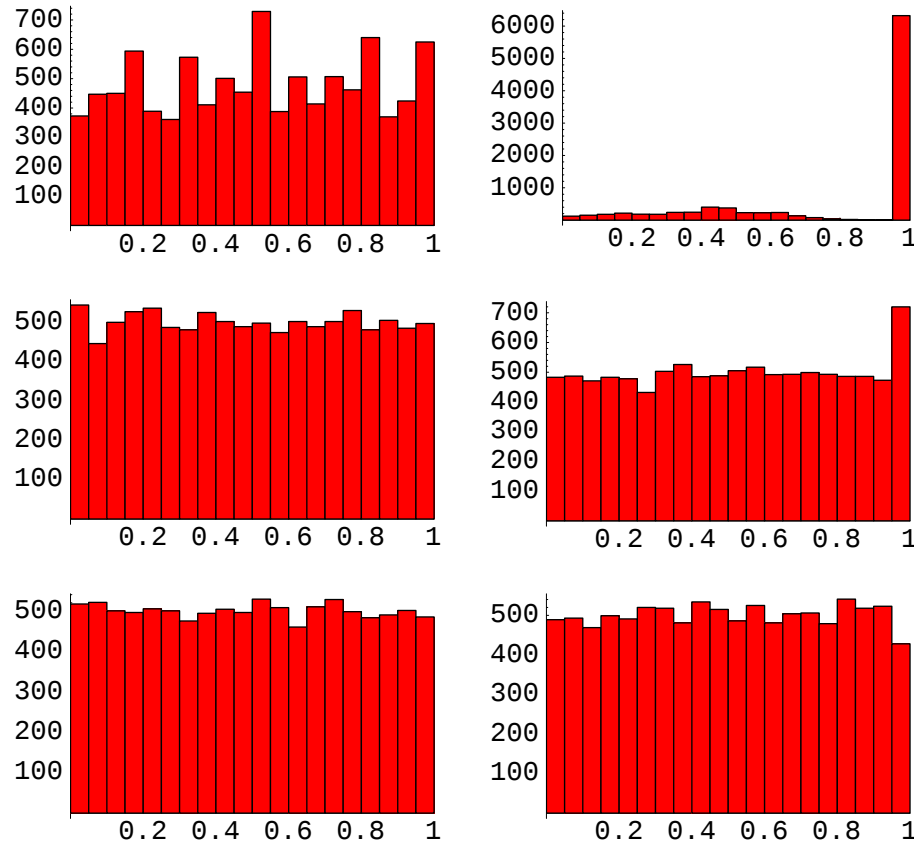
n	$\hat{\nu}$			$\hat{\theta}$			$(\hat{\theta}, \hat{\nu})$	
	$\sqrt{se}$	bs	$C_{99\%}$	$\sqrt{se}$	bs	$C_{99\%}$	$C_{99\%}$	$Qrt(\check{\mathcal{K}})$
4	46	30	42	43	30	53	98	{0.061, 0.079, 0.13}
5	32	19	42	31	22	63	96	{0.074, 0.098, 0.16}
6	31	18	41	35	23	69	93	{0.082, 0.11, 0.17}
7	34	19	48	32	20	68	87	{0.090, 0.12, 0.21}
8	26	12	66	21	11	72	92	{0.098, 0.14, 0.26}
9	27	12	65	18	10	70	93	{0.097, 0.14, 0.21}
10	23	11	64	17	10	66	95	{0.091, 0.14, 0.30}

Topological Unfolding of SFS and Tajima's D when $n = 4$

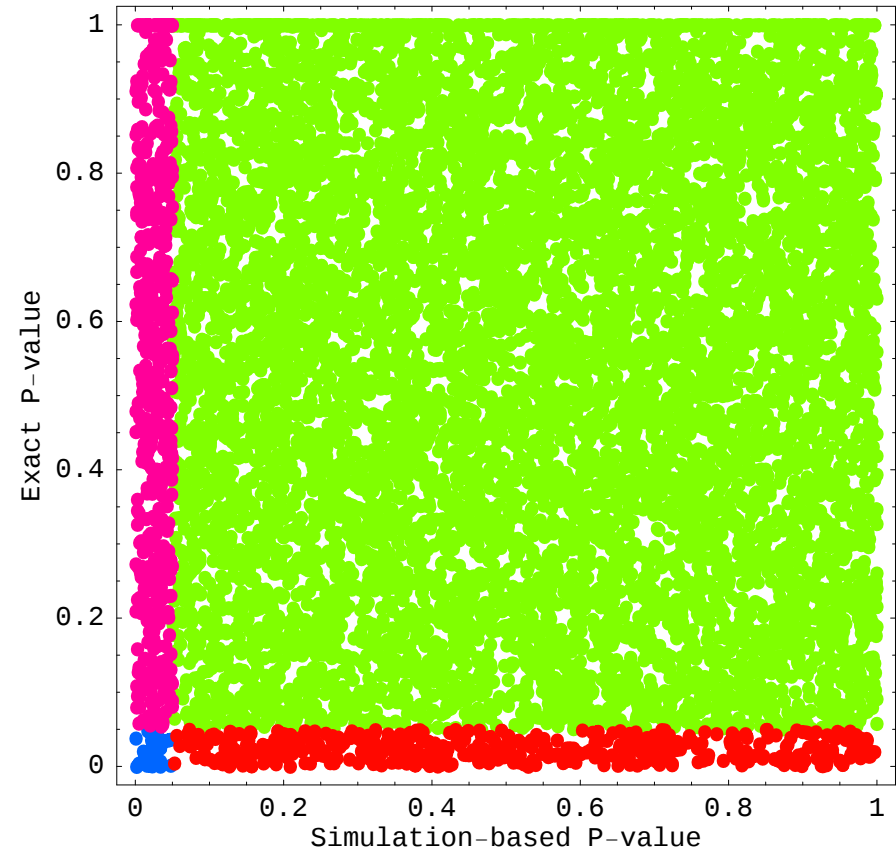


Simulated Vs. Gen. Fisher's Exact Test with Tajima's D

P-values for Simulated Vs. Exact Tajima's D Test ($\theta = 1, 10, 50$)



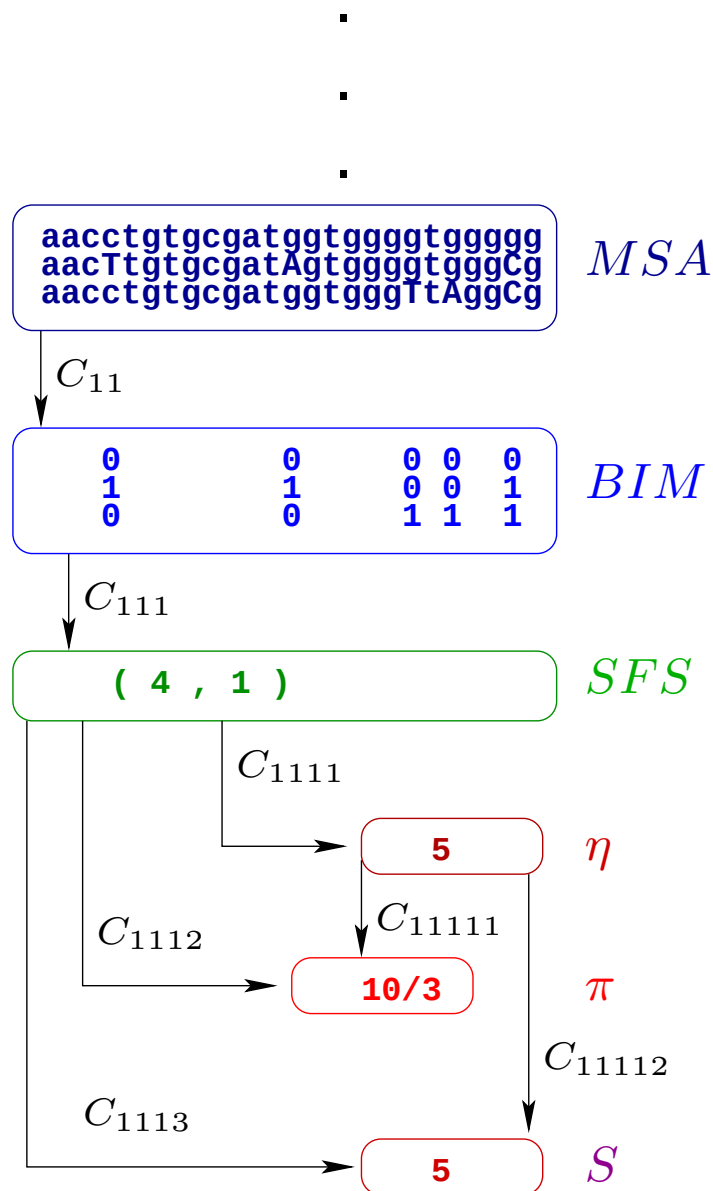
Simulated Vs. Exact Tajima's D Test (corr. = -0.0045)



Left panel: Distribution of p-values from the simulated test (left) and the generalized Fisher's exact test (right) for three values of $\theta = \{1, 10, 50\}$ per 1000 bp with $n = 30$.

Right panel: The almost zero correlation of p-values between the two tests.

Summary



- Limits on Inference from Finest Empirical Resolutions
- Inference from Coarser Site Frequency Spectrum is Possible via a Collapsed Kingman's n -coalescent Markov chain
- Algebraic Geometry is useful to infer from classical summaries of SFS.
- MSEs are smaller – the exponential growth model
- Helps speed-up intensive SIS methods (Particle filtering on Experiment Graph)
- Topological unfolding of SFS and $D \Rightarrow$ Tree-less Genome Scans are essentially meaningless
- A Decision-theoretic formalism – partially-ordered coalescent experiments graph
- Possible to generalize
- Saves electricity and slows down global warming!

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