Ancestries of a Recombining Diploid Population:

towards a theoretical union of behavioural ecology and population genetics

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Insights from the field

Ancestries of Recombining Diploid Populations

Insights from field work in November 2011

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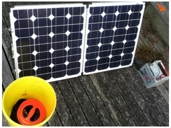
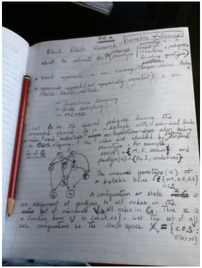




POA — Genetics + Science

Black Robin Research

want to estimate (θ). P(observed phenotype | parameters in model of inheritance, pedigree, founding genotypes)

- Exact approach is via Cannings–Thompson–Skolnick Peeling
- approximate approach (but asymptotically consistent) is via Monte Carlo methods.
  - Importance Sampling
  - Gibbs Sampling
  - MCMC

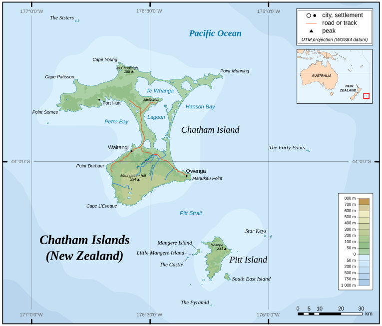
Let G be the observed pedigree during the managed period. G is a digraph with individual birds as nodes and ~~marriage edges~~ ~~or copulation edges~~ edges leading to each offspring. The nodes are identified by observed sex and phenotype. For example, $sex(v_i) \in \{M, F, \text{unkown}\}$ and $phenotype(v_i) \in \{0, 1, \text{undefined}\}$

Eg of G

The unobserved $genotype(v_i)$ at a biallelic locus $\in \{aa, aA, AA\} =: S$

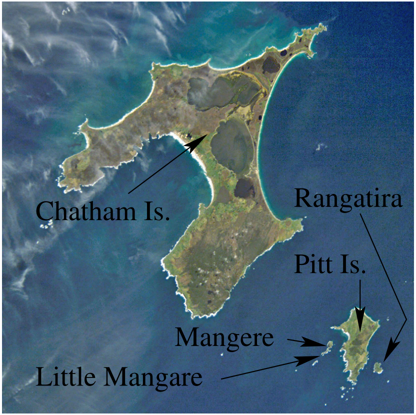
A configuration or state x ~~of G~~ is an assignment of genotypes to all nodes in the ~~vertex~~ set of individuals V i.e. all nodes in G. Thus x is a function from V to $\{aa, aA, AA\}$. Let the set of all such configurations be the state space $\mathbb{X}_\pi = \{x \in S^V : \pi(x) > 0\}$

Map of Antarctica / Chatham Islands (New Zealand)



- The Chatham Islands lie 800 kms east of Christchurch.
- Two main islands – Chatham Island and Pitt Island

Chatham Islands (New Zealand)

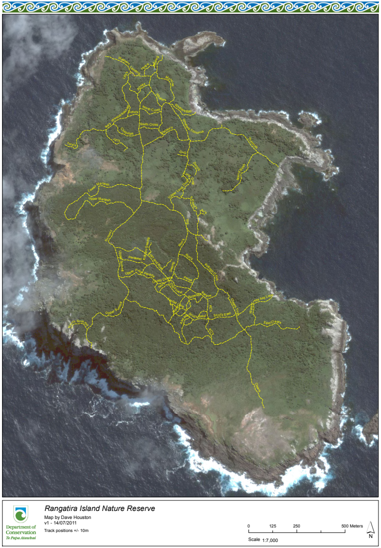


- Many smaller islands – including Little Mangere, Mangere and Rangatira
- The islands have only emerged above sea level in the last 4 million years and are part of the Chathams rise connected below ocean to NZ.
- The climate is cool and wet with salt-laden winds all year round.

Chatham Islands (New Zealand)

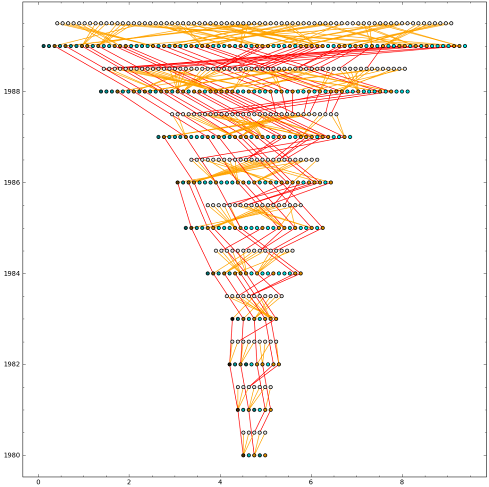
Rangatira Island

- is the third largest island in the Chatham Islands
- covers an area of 218 hectares (539 acres)
- is a gazetted nature reserve since 1953
- is now home to many endemic species
- is home to black robins – saved from near extinction by team led by Don Merton in the 1980s



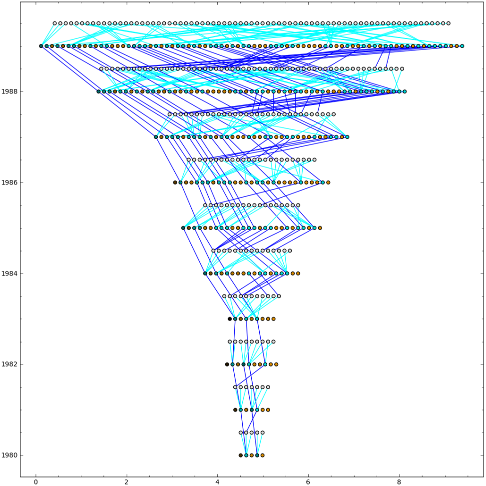
A Chatham island Black Robin in Rangatira today

Temporal Pedigrees with Overlapping Generations



Female Population Tree during Field Conservation in 1980s

Temporal Pedigrees with Overlapping Generations



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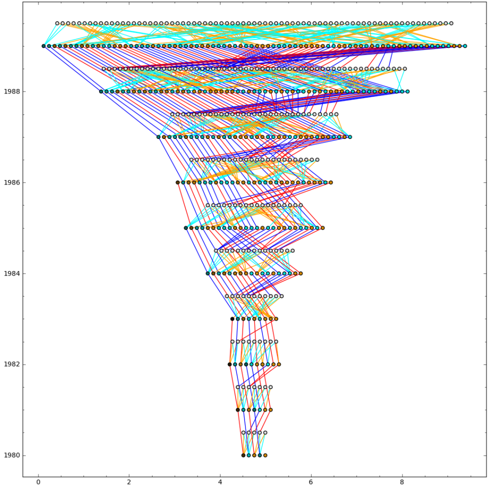

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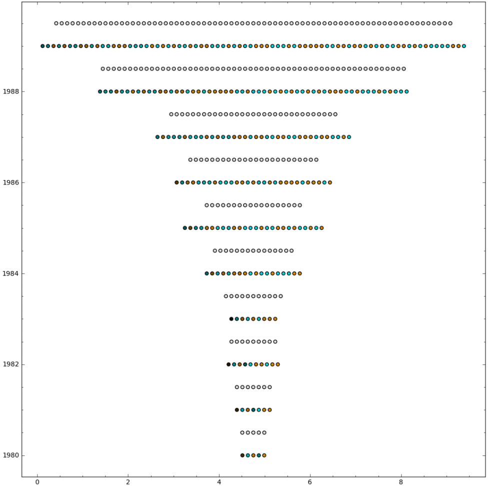
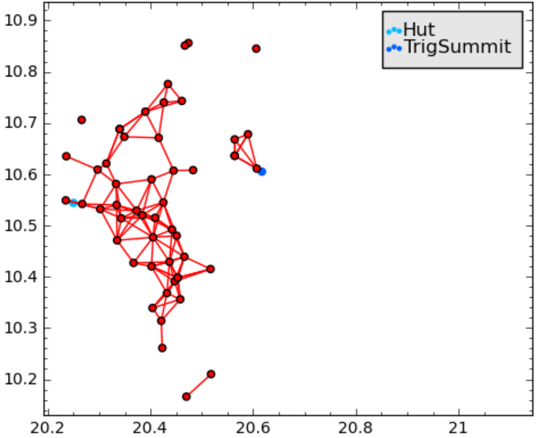


Coalescent Sub-Pedigree of the 1989 population $\Longrightarrow$ Part ARDP

Male Territory Graphs by year



2009 (eye-balled by a ball graph)

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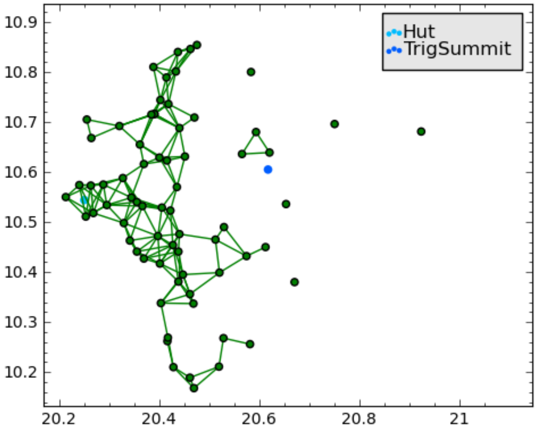

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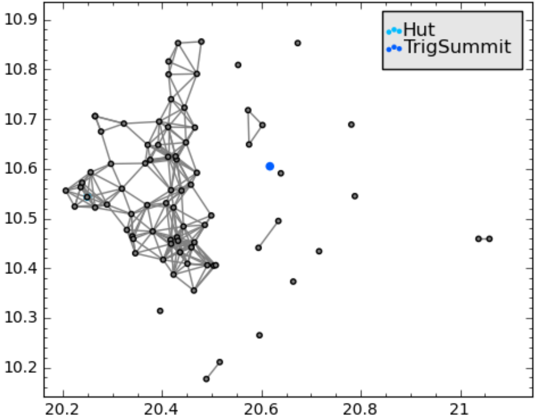
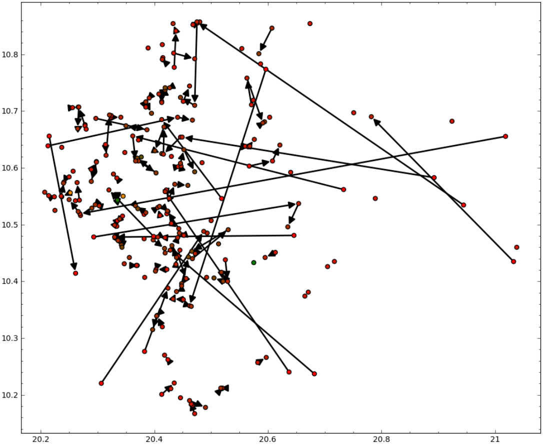
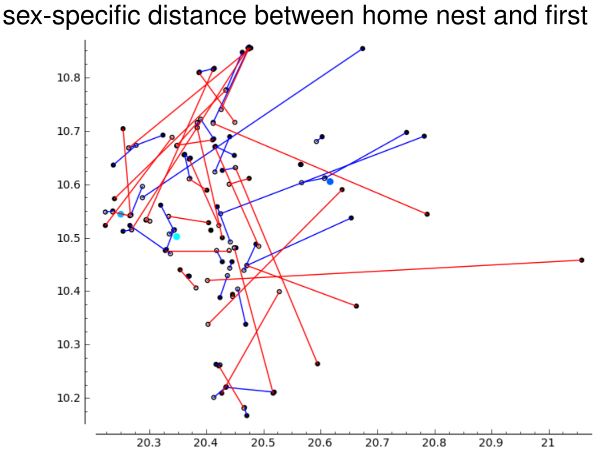


2011 (eye-balled by a ball graph)

Male Territorial Dynamics – yearly nest site relocation

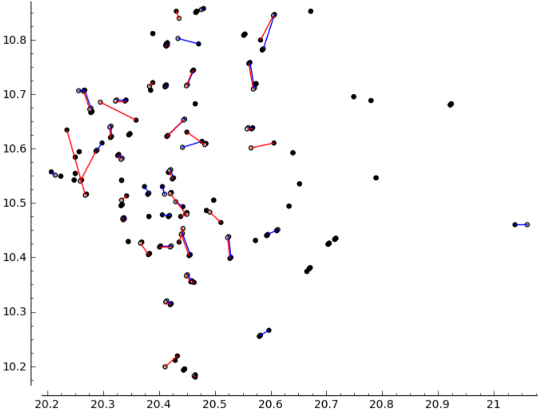


Male / Female yearly nest to nest distance



Male / Female yearly nest to nest distance

sex-specific distance between nest at age ≥ 1 and next nest



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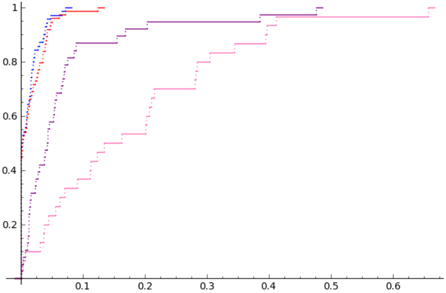
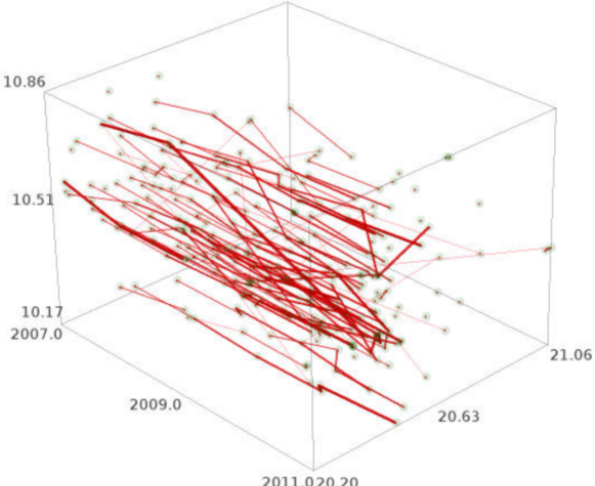


- Permutation Test to Reject H_0 : male dist = female dist (10^5 MC samples)
- Strongly reject H_0 for home to first nest (pv = 0.00025)
- Fail to reject H_0 for nest at age ≥ 1 to next nest (pv = 0.14)

male / female distance from home nest to first nest
male / female distance from nest at age $\geq$ 1 to next nest

Need Models of Spatio-temporal Behavioural Population Pedigrees



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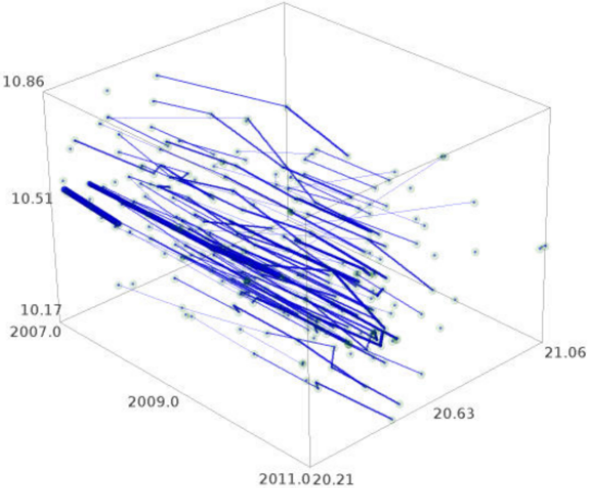

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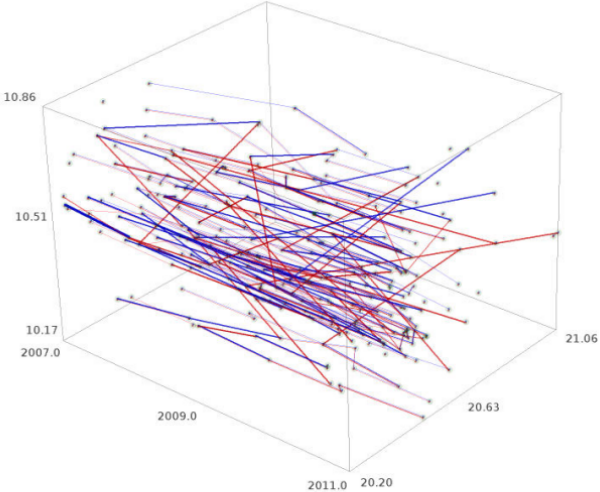

parametric families of behavioural pedigree processes

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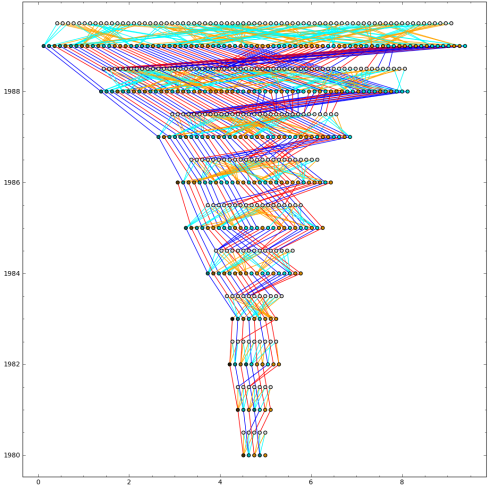
- **CORE MODEL** *(Dominating discrete skeletal measure)*: Coalescent with Recombination inside "A Well-stirred Urn of Self-Fertile Hermaphrodites"

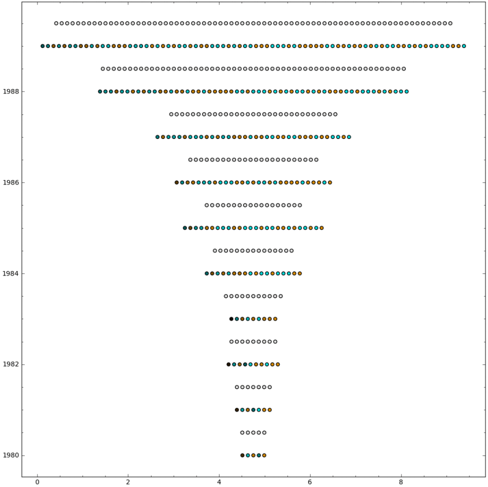
Part ARDP

Ancestries of Recombining Diploid Populations

Raazesh Sainudiin, Bhalchandra Thatte, and Amandine Véber,
Journal of Mathematical Biology, January 2016, Volume 72, Issue
1-2, pp 363–408.



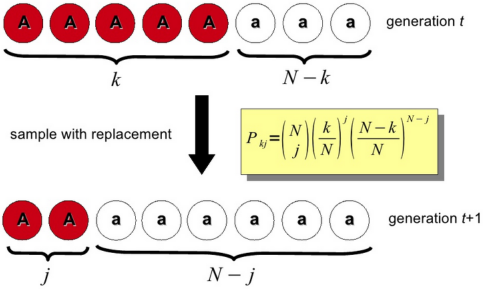
Motivation: Diploid Population Pedigree (forwards in time)



Coalescent Sub-Pedigree (backwards in time) “inheritance topology of diploid zygotes?”

Three Notions of Molecular continuums within W-F Population Pedigrees

One *r* to rule them all!



Wright-Fisher Model (forwards in time)

where $r = 0$ is the probability of recombination per locus per meiotic generation

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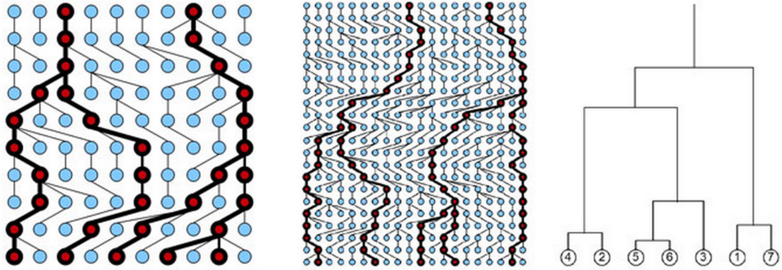

Wright-Fisher Genealogy with Large N $\Longrightarrow$ Kingman's Coalescent Tree for small *n* (backwards in time)

where *r* is the probability of recombination per locus per meiotic generation ($r = 0$ for Kingman's model)

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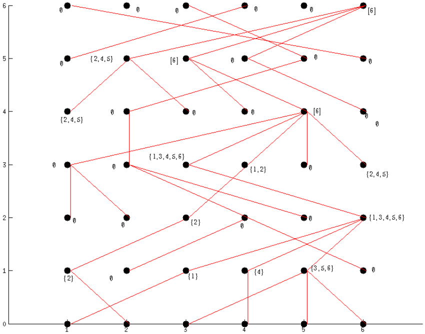

(1) Kingman's Discrete Genealogy at a non-recombining locus with $r = 0$ (forwards in time)

Observe: Time to most recent ancestor (TMRCA) = 4 (can you locate the MRCA?)

Three Notions of Molecular continuums within W-F Population Pedigrees

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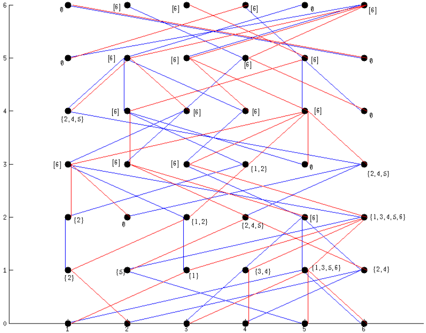

(2) Chang's Discrete Pedigree as the Genealogy of an always-recombining locus with $r = 1$ (forwards in time)

Observe: Time to most recent ancestor (TMRCA) = 2 (can you locate the MRCA? how about other CAs?)

Observe: Time to be or not to be (TTBONTB) = 5 (can you say why?)

Three Notions of Molecular continuums within W-F Population Pedigrees

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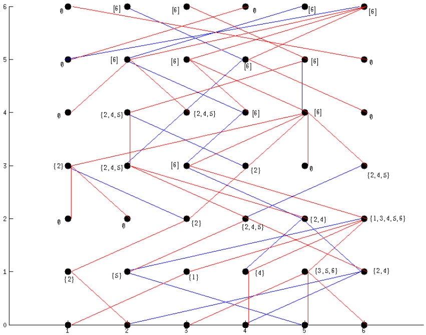


(3) Hudson-Griffiths Discrete Ancestral Recombination Graph at a recombining locus with $0 < r < 1$ (fwds in time)
SIMPLEST UNIFICATION PROBLEM: What is TMRCA and TTBONTB for any r?

(NOT for $rN =: \rho > 0$, where $r \to 0$ and $N \to \infty$, the Griffiths-Husdon limit)

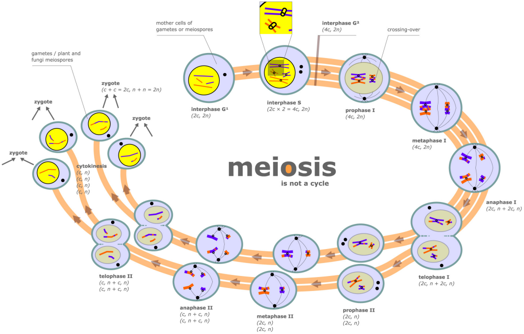
Unifying these three notions of molecular ancestry

Consider the **ancestral graphs** of these three genealogical processes for a given sample taken today (backwards in time).

- Uni-parental Ancestry of sample : Kingman's Discrete Genealogy at a non-recombining locus (1982)
- Bi-parental Ancestry of sample : Chang's Discrete Pedigree (1999)
- Uni/Bi-parental Ancestry of sample: Hudson-Griffiths Discrete Ancestral Recombination Graph (1983-1989)

Unifying these three notions of molecular ancestry

consistent with the zygotic topology in sync with meiosis:



This unification was an open problem since 1983

This topologically consistent notion of diploid ancestry (RS, Thatte & Veber, 2015) in a common probability space is a pre-requisite for more realistic models of population pedigree processes, including:

- non-overlapping generations

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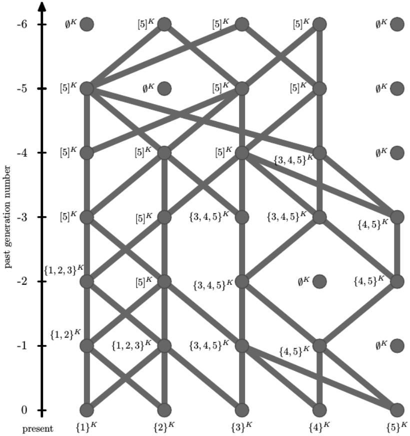
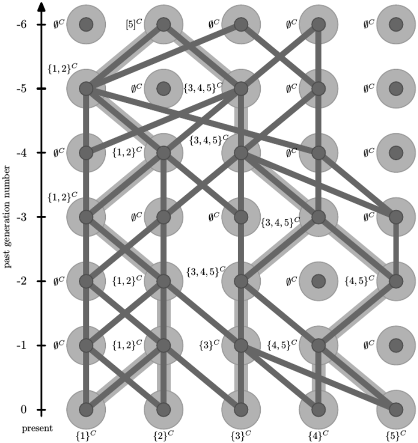
- dioecious (non-hermaphroditic) diploidy
- gender-specific behavioural effects on spatio-temporal pedigree through which genes flow under natural selection...
- etc. (think of Florida Scrub Jay, feral cat populations, heroms of Mujahidiin warlords post Soviet withdrawal in 1980s)



karyotic ancestral graph of a bi-parental Wright-Fisher population with five eukaryotic individuals

Can you find the MRC-karyotic-A (MRCkA)? TMRCkA? TT-karyotically-BONTB (TTkBONTB)?

Chang's Main results say that TMRCkA and TTkBONTB $\sim O(\log_2(n))$, where $n =$ population size



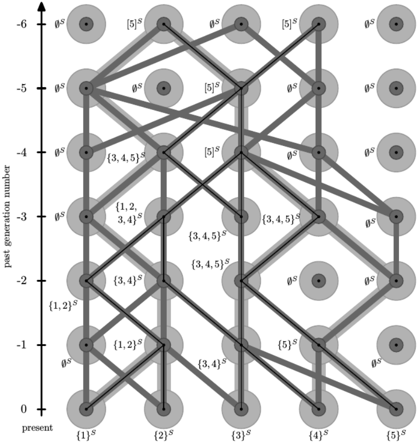
Zygotic pedigree containing the cytoplasmic tree (Kingman's discrete coalecent) and karyotic ancestral graph of a

bi-parental Wright-Fisher population

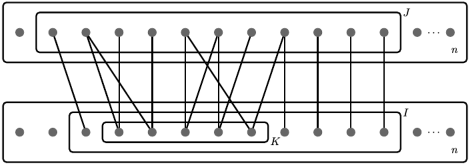
Can you find the MRC-cytoplasmic-A (MRCcA)? TMRCcA?

Kingman's Main results say that TMRCcA and TTcBONTB $\sim$ $O(n)$, where $n =$ population size

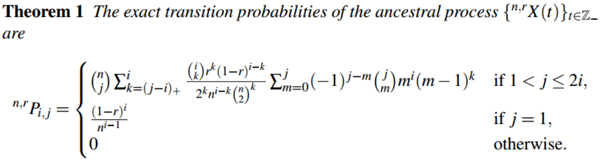
so: $O(\log_2(n))$ versus $O(n)$ is a huge difference!



Putting it all together: Zygotic, cytoplasmic, karyotic and sub-karyotic ancestral graphs (discrete ARGs of Hudson and Griffiths) of a bi-parental Wright-Fisher population with five eukaryotic diploid individuals



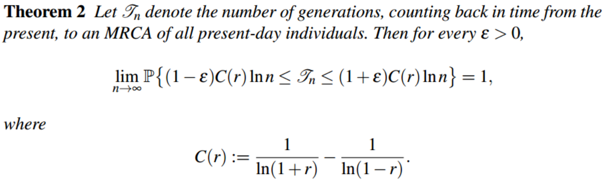
Combinatorial Structure Diagram



Theorem 1 *The exact transition probabilities of the ancestral process* $\{{}^{n,r}X(t)\}_{t\in\mathbb{Z}_-}$ *are*

$$ {}^{n,r}P_{i,j} = \begin{cases} \binom{n}{j}\sum_{k=(j-i)_+}^{i} \frac{\binom{i}{k} r^k (1-r)^{i-k}}{2^k n^{i-k} \binom{n}{2}^k} \sum_{m=0}^{j} (-1)^{j-m} \binom{j}{m} m^i (m-1)^k & \text{if } 1 < j \leq 2i, \\ \frac{(1-r)^i}{n^{i-1}} & \text{if } j = 1, \\ 0 & \text{otherwise.} \end{cases} $$

Kingman-Chang-Hudson-Griffiths Unified Ancestral Chain



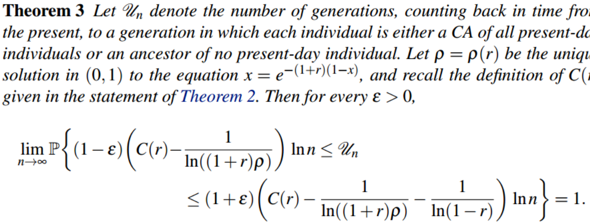
Theorem 2 *Let $\mathscr{T}_n$ denote the number of generations, counting back in time from the present, to an MRCA of all present-day individuals. Then for every $\varepsilon > 0$,*

$$\lim_{n\to\infty} \mathbb{P}\left\{(1-\varepsilon)C(r)\ln n \leq \mathscr{T}_n \leq (1+\varepsilon)C(r)\ln n\right\} = 1,$$

where

$$C(r) := \frac{1}{\ln(1+r)} - \frac{1}{\ln(1-r)}.$$

Time to MRCA for a possibly recombining locus with intra-locus recombination probability per non-overlapping meiotic generation in a population of *n* diploid individuals.



Theorem 3 *Let $\mathscr{U}_n$ denote the number of generations, counting back in time from the present, to a generation in which each individual is either a CA of all present-day individuals or an ancestor of no present-day individual. Let $\rho = \rho(r)$ be the unique solution in $(0,1)$ to the equation $x = e^{-(1+r)(1-x)}$, and recall the definition of $C(r)$ given in the statement of Theorem 2. Then for every $\varepsilon > 0$,*

$$\lim_{n\to\infty} \mathbb{P}\left\{(1-\varepsilon)\left(C(r) - \frac{1}{\ln((1+r)\rho)}\right)\ln n \le \mathscr{U}_n \le (1+\varepsilon)\left(C(r) - \frac{1}{\ln((1+r)\rho)} - \frac{1}{\ln(1-r)}\right)\ln n\right\} = 1.$$

Time to Be or Not to Be for a possibly recombining locus with intra-locus recombination probability per non-overlapping meiotic generation in a population of *n* diploid individuals.

Proof ideas

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- For Thm 1: Just count the integers in the numerator and denominator of the rational probabilities
    - counting Wright-Fisher constrained bipartite graphs from the combinatorial diagram
- For Theorems 2 and 3:
    - carefully partitioning the time-axis into six distinct n-asymptotic regimes

$$\left[0, \oplus \frac{2\log\log n}{\log(1+r)}, \oplus \frac{\log n}{\log(1+r)}, \oplus \log\log n, \oplus \log\log n, \oplus - \frac{\log n}{\log(1-r)}, \oplus \frac{-2\log\log n}{\log(1-r)}\right]$$

and applying the right tools from below:

- $\approxeq$ the $\#$(descendants / non-descendants of individual I_i), binomial RVs, by a GW branching process with Poisson($1 + / - r$) offspring distribution (start/end)
- Bernstein $\neq$'s for the Binomial RVs away from start/end
- standard branching process results from Athreya & Ney

Conclusions

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- PLAN: continue to work with FSJ @CornellLab’O (2016)

Thank you!

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