What is knowable about past demography? - The limited scope of genomic data analysis.

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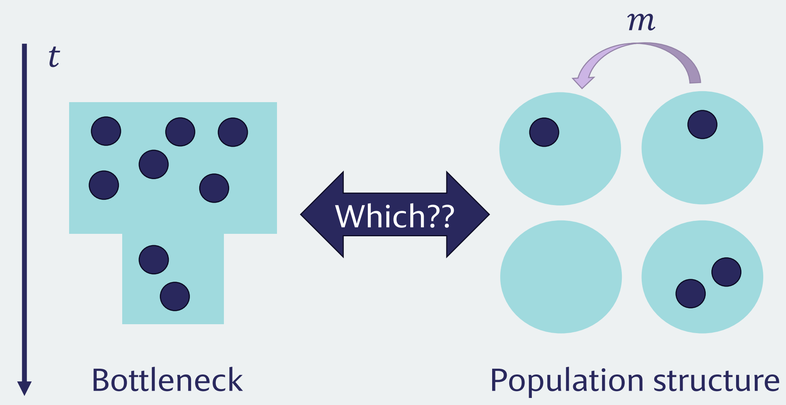
Introduction

Demographic inference tools (e.g. MSMC2) can reveal a population's history. However, the signal produced by the analysis of a **genomic sample from a structured population can be mistaken for a bottleneck** [1, 2].

So, is your inferred population crash actually evidence of population structure?

We provide simple guidelines to help decide.



Methods

ms prime Simulations [3]

ts kit Analysis [4]

MSMC2 Demographic inference [5]

Don't get misled – quantifying the distortions of N_e estimates produced by population substructure

Here we derive simple formulae describing the false history of a recent crash in population size produced by population substructure.

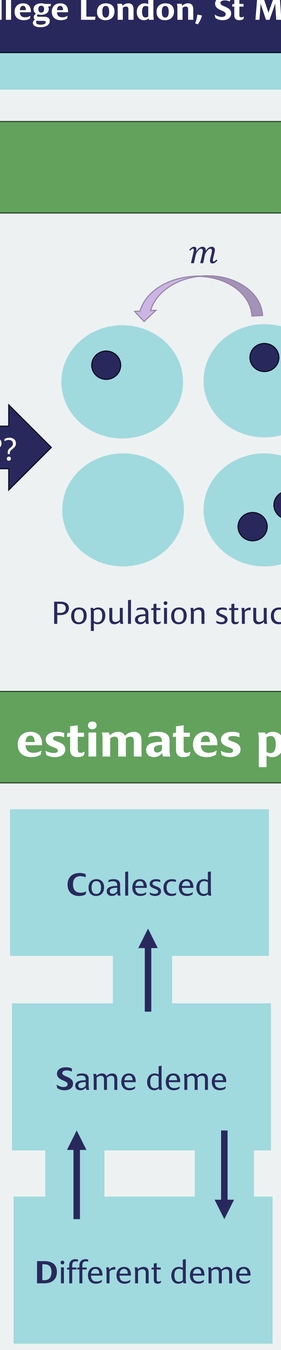
Rate of apparent crash

$$q \approx e^{t\left(-\frac{1}{2N}-\frac{2m}{d-1}\right)}$$

Inflation of N_e estimate

$$N_e = \frac{N}{p}$$

Where $p = \frac{p\left(1-\frac{1}{2N}-2m\right)+(1-p)\frac{2m}{d-1}}{1-\frac{p}{2N}}$

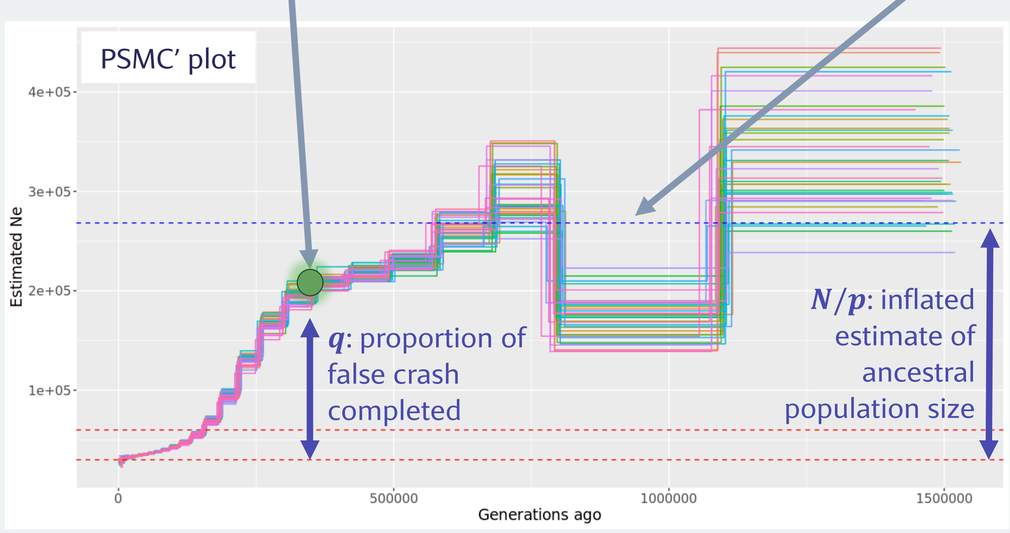


An **ODE** provides the full **shape** of the curve.

$$\frac{dS(t)}{dt} = -2mS(t) - \frac{S(t)}{2N} + \frac{2mD(t)}{d-1}$$

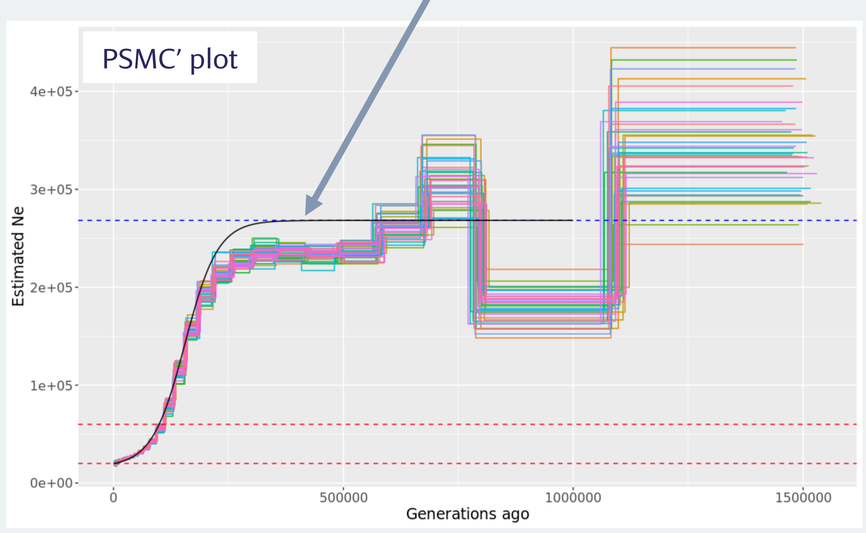
$$\frac{dD(t)}{dt} = 2mS(t) - \frac{2mD(t)}{d-1}$$

$$\frac{dC(t)}{dt} = \frac{S(t)}{2N}$$



Simulation parameters

Number of demes (d)	Population size in deme (N)	Total migration rate (m)
2	30,000	1.07e-6
3	20,000	1.11e-6

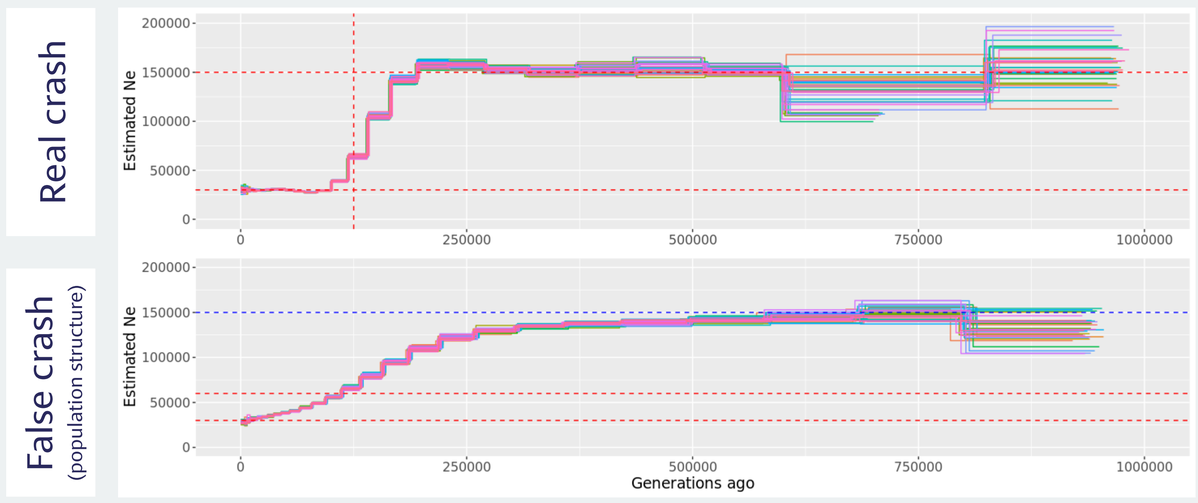


The simple rules and the black curve accurately describe the coalescent rates (equivalent to $1/2N_e$) in the simulations of the subdivided populations that generated these data – so **mathematical models and simulations agree**. However, notice that the algorithm for inferring N_e shows **systematic deviations** from this curve.

More promisingly, the estimates from the **recent past can be more readily interpreted**.

OVERALL: Any one curve could be the result of population structure displaying changes in N_e, however an evolutionary geneticist can make use of their **knowledge of biologically reasonable parameter values** (m, d, N) to distinguish between the different interpretations.

Distinguishing between bottleneck and substructure



Formally, this idea can be implemented by **Approximate Bayesian Computation** to distinguish between the two cases. It will require **informative priors** based on the timing and size of population decline and subdivision for the specific model system.

Conclusions

The effect of population substructure has straightforward effects on the **shape** of the N_e curve in recent time.

Inference tools **overestimate the ancestral coalescence rate** – but why?

Idea in action – **ABC and informative priors**

References

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Acknowledgments

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