## **Supporting Information**

## Multi-locus analysis of genomic time series data from experimental evolution

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## Text S1

Here we provide proofs of the theoretical results mentioned in the **Methods** section of the main text.

**Lemma 1.** To order  $O(r + \frac{1}{2N})$ ,

$$\mathbb{E}_{\pi} Z_{t}^{(i)} = z^{(i)} + \epsilon_{i} trc_{0} \left( 1 - \frac{t-1}{4N} \right)$$
$$\mathbb{E}_{\pi} (r Z_{t}^{(i)} Z_{t}^{(j)}) = \frac{r}{2N} \left[ z^{(i)} z^{(j)} (2N-t) + t z^{(i)} \mathbf{1} \{ i = j \} \right]$$
$$\mathbb{E}_{\pi} (r Z_{t}^{(i)} C_{t}) = \frac{r}{2N} \left[ z^{(i)} c_{0} (2N-3t) + \frac{t}{2} \left( (1-\epsilon_{i}) z^{(1)} z^{(4)} - (1+\epsilon_{i}) z^{(2)} z^{(3)} \right) \right].$$

*Proof of Lemma 1.* By direct computation using the moment generating function of the multinomial distribution, we find that

$$\mathbb{E}_{\pi}(Z_{t}^{(i)} \mid \mathbf{Z}_{t-1}) = Z_{t-1}^{(i)} + \epsilon_{i}rC_{t-1}$$

$$\mathbb{E}_{\pi}(rZ_{t}^{(i)}Z_{t}^{(j)} \mid \mathbf{Z}_{t-1}) = rZ_{t-1}^{(i)}Z_{t-1}^{(j)} \left(1 - \frac{1}{N}\right) + Z_{t-1}^{(i)}\mathbf{1}\{i = j\} + O(r^{2} + 1/N^{2})$$

$$\mathbb{E}_{\pi}(rC_{t}Z_{t}^{(i)} \mid \mathbf{Z}_{t-1}) = \frac{r}{N} \Big[ Z_{t-1}^{(i)}C_{t-1}(N-3) + \frac{1}{2} \left( (1 - \epsilon_{i})z^{(1)}z^{(4)} - (1 + \epsilon_{i})z^{(2)}z^{(3)} \right) \Big] + O(r^{2} + 1/N^{2}).$$

The results now follow by induction.

**Corollary 2.** To order  $O(r + \frac{1}{2N})$ ,

$$\mathbb{E}_{\pi} \left( Z_{t}^{(i)} Z_{t}^{(j)} \right) = z^{(i)} z^{(j)} + \epsilon_{i} \epsilon_{j} trc_{0}(\epsilon_{i} z^{(i)} + \epsilon_{j} z^{(j)}) + \frac{t}{2N} \left( -z^{(i)} z^{(j)} \mathbf{1}_{\{i \neq j\}} + z^{(i)} (1 - z^{(j)}) \mathbf{1}_{\{i = j\}} \right)$$
$$\frac{rt}{2N} \left\{ \frac{1}{2} \left( t + 1 - |\epsilon_{i} - \epsilon_{j}| \right) \left( z^{(1)} z^{(4)} + z^{(2)} z^{(3)} \right) - \epsilon_{i} \epsilon_{j} c_{0} (2t - 1) (\epsilon_{i} z^{(i)} + \epsilon_{j} z^{(j)}) - \frac{1}{8} |\epsilon_{i} + \epsilon_{j}| \left[ c_{0} (\epsilon_{i} + \epsilon_{j}) (t + 1) \mathbf{1}_{\{i \neq j\}} + 4t \left( (\epsilon_{i} + 1) z^{(2)} z^{(3)} + (1 - \epsilon_{i}) z^{(1)} z^{(4)} \right) \right] \right\}.$$

Proof of Corollary 2. The formula is obtained by considering the conditional expectation  $\mathbb{E}_{\pi}(Z_t^{(i)}Z_t^{(j)} \mid \mathbf{Z}_{t-1})$ , inducting on t and checking cases for i and j. We illustrate the proof for the case i = j = 1 and omit the lengthy but routine computations used to check the remaining cases. (A Mathematica notebook which checks all cases is available from the authors upon request.) With i = j = 1 we have

$$\mathbb{E}_{\pi}\left[\left(Z_{t}^{(1)}\right)^{2} \left| \mathbf{Z}_{t-1}\right] = \frac{1}{N} \left[Z_{t-1}^{(1)}(1 - Z_{t-1}^{(1)}) - rC_{t-1}\left(1 - 2Z_{t-1}^{(1)}\right)\right] - rC_{t-1}Z_{t-1}^{(1)} + O(r^{2} + 1/N^{2}).$$

This yields the claim for t = 1. Taking expectation and applying the preceding lemma, we find that

$$\mathbb{E}_{\pi}\left[\left(Z_{t}^{(1)}\right)^{2}\right] = \frac{1}{N}\left[z_{1} - trc_{0} + (N-1)\mathbb{E}_{\pi}\left(Z_{t-1}^{(1)}\right)^{2} - 2rz_{1}\left(c_{0}(N-3t+3) + (t-1)z_{4}\right)\right] + O(r^{2} + 1/N^{2}).$$

Applying the inductive hypothesis, we obtain

$$\mathbb{E}_{\pi}\left[\left(Z_{t}^{(1)}\right)^{2}\right] = \frac{1}{N}\left[z_{1} - trc_{0} + z_{1}\left(t - 1 + (n - t + 1)z_{1} - (t - 1)(t - 2)rz_{4}\right) - (t - 1)rc_{0}\left[\frac{t}{2} + 2\left(n - 2t + 3\right)z_{1}\right] - z_{1}^{2} + 2trc_{0}z_{1} - 2rz_{1}\left(c_{0}(n - 3t + 3) + (t - 1)z_{4}\right)\right] + O(r^{2} + 1/N^{2}),$$

which agrees with the claim after some simplification.