

## Supporting Information

### S1 Derivation of results for linear fitness

#### S1.1 Fitness

In the main analysis, we assumed fitness to be linearly dependent on the number of loci adapted to the current environment. Linear fitness measures the Hamming distance (number of mismatched bits)  $d_H$  of  $x$  to the currently selected optimum  $a_j$ ,  $j \in \{1, \dots, k\}$ , for each of the  $k$  blocks (traits) of length  $\ell$ , and the genotype's fitness is directly proportional to the number of matching alleles, defined as

$$f(x) = 1 - \frac{\sum_{B \in \mathcal{B}} d_H(x[B], a[B])}{F_{\max}}, \quad (\text{S1})$$

where  $x[I]$  denotes a bit string (genotype)  $x$  consisting only of the values at the indices  $i \in I \subseteq \{1, \dots, n\}$ , and  $\mathcal{B} = \bigcup_{m=1}^k \{(m-1)\ell + 1, \dots, m\ell\}$  is the index set of all blocks. Note that in the first model, only one block is under selection, while other blocks have undefined target sequences and thus do not contribute to the fitness.  $F_{\max}$  represents the maximum Hamming distance possible between the current genotype and the threat, and thus allows scaling of the fitness between 0 and 1. To scale the fitness equally for all three models, we define  $F_{\max} = \ell$  in the first model and  $F_{\max} = k\ell = n$  in the other two models. Note that in simpler terms, fitness is also directly proportional to the fraction of adapted loci  $F = f = \frac{x}{\ell}$  if only a single trait is under selection, or  $F = f = \frac{X}{n}$  if all traits are under selection.

#### S1.2 Single trait under periodic selection

Here we focus on a single trait encoded by  $\ell$  loci and assume that alleles denoted 1 are adaptive, while alleles denoted 0 are not. Each iteration, one mutation occurs in the genome of length  $n$ . During the strong-selection phase, any mutation occurring in a trait is either positive and fixes in the population within a short time (one iteration) with probability  $p$ , or negative and does not fix in the population. In the presence of selection pressure, the number of adapted loci  $x$  is increasing and the expected increase in fitness—drift—in one iteration is

$$\Delta(x) = p \frac{\ell - x}{n}. \quad (\text{S2})$$

Assuming that steps are small ( $n$  is large), we can approximate the discontinuous process by a continuous (and integrable) path, stating  $\frac{dx}{dt} \approx \Delta(x)$ . Therefore, we can calculate the expected number of adapted alleles at time  $t_1$ :

$$\begin{aligned}
\frac{dx}{dt} &= \frac{p}{n}(\ell - x) \\
\int_{x_0}^{x_1} \frac{dx}{\ell - x} &= \int_{t_0}^{t_1} \frac{p}{n} dt \\
-\log(\ell - x) \Big|_{x_0}^{x_1} &= \frac{p}{n}(t_1 - t_0) \\
\log\left(\frac{\ell - x_0}{\ell - x_1}\right) &= \frac{p}{n}\Delta t \\
\frac{\ell - x_0}{\ell - x_1} &= e^{\frac{p}{n}\Delta t} \\
x_1 &= \ell - (\ell - x_0)e^{-\frac{p}{n}\Delta t} ,
\end{aligned} \tag{S3}$$

where  $x_1$  and  $x_0$  denote the number of adapted alleles at time  $t_1$  and  $t_0$ , respectively, and  $\Delta t = t_1 - t_0$ . The expected gain of adaptive alleles is thus

$$\Delta^{\Delta t}(x) = x_1 - x_0 = (\ell - x_0)(1 - e^{-\frac{p}{n}\Delta t}) . \tag{S4}$$

In the absence of selection, all mutations within the trait are effectively neutral and fix with a probability of  $1/N$ . The expected gain of alleles 1 under no selection pressure is given by the difference between 0 alleles mutating and fixing in the population,  $\frac{\ell-x}{Nn}$ , and alleles 1 mutating to 0 and fixing,  $\frac{x}{Nn}$ :

$$\begin{aligned}
\frac{dx}{dt} &= \frac{\ell - x}{Nn} - \frac{x}{Nn} \\
&= \frac{\ell - 2x}{Nn} .
\end{aligned} \tag{S5}$$

The expected number of adaptive alleles at time  $t_1$  is

$$\begin{aligned}
\int_{x_0}^{x_1} \frac{dx}{\ell - 2x} &= \int_{t_0}^{t_1} \frac{1}{Nn} dt \\
-\frac{1}{2} \log(\ell - 2x) \Big|_{x_0}^{x_1} &= \frac{1}{Nn}(t_1 - t_0) \\
\log\left(\frac{\ell - 2x_0}{\ell - 2x_1}\right) &= \frac{2}{Nn}\Delta t \\
\frac{\ell - 2x_0}{\ell - 2x_1} &= e^{\frac{2}{Nn}\Delta t} \\
x_1 &= \frac{\ell}{2} - \left(\frac{\ell}{2} - x_0\right) e^{-\frac{2}{Nn}\Delta t} .
\end{aligned} \tag{S6}$$

Thus, the expected change in the number of adapted loci for arbitrary  $\Delta t$  is

$$\Delta^{A t}(x) = x_1 - x_0 = (1 - e^{-\frac{2At}{Nn}}) \left( \frac{\ell}{2} - x_0 \right). \quad (\text{S7})$$

Equation (S3) shows that the number of adapted alleles converges to  $\ell$  in the presence of selection, while equation (S5) shows that in its absence it converges to  $\ell/2$ , which is expected, as all alleles are neutral in the absence of selection.

If we assume that a trait is periodically under selection pressure for  $\tau_1$  iterations but the selection is then absent for  $\tau_0$  iterations, we can find the maximum expected number of adapted alleles (at the end of the selection period) and its minimum (at the end of the no-selection period), denoted by  $x_{\max}$  and  $x_{\min}$ , respectively, and thus their magnitude  $x_{\Delta}$ :

$$\begin{aligned} x_{\max} &= \ell - (\ell - x_{\min})e^{-\frac{\rho}{n}\tau_1} \quad \text{and} \\ x_{\min} &= \frac{\ell}{2} - \left( \frac{\ell}{2} - x_{\max} \right) e^{-\frac{2}{Nn}\tau_0}. \end{aligned}$$

Defining  $A = e^{-\frac{\rho\tau_1}{n}}$  and  $B = e^{-\frac{2\tau_0}{Nn}}$  and solving the system of equations leads to

$$x_{\max} = \frac{\frac{1}{2}A(1-B) + (1-A)}{1-AB} \ell, \quad (\text{S8})$$

$$x_{\min} = \frac{\frac{1}{2}(1-B) + (1-A)B}{1-AB} \ell, \quad (\text{S9})$$

and the magnitude of oscillations is

$$x_{\Delta} = x_{\max} - x_{\min} = \frac{(1-A)(1-B)}{1-AB} \ell. \quad (\text{S10})$$

The fraction of adapted alleles is easily obtained by dividing the number of adapted alleles by the maximum possible number of adapted alleles  $\ell$ .

To find the maximum time required for the population to climb the fitness peak (all alleles are adapted), we use the variable drift theorem and the expected progress to the optimum when a trait is under selection (S2). Theorem 1 (see Methods; Johannsen 2010) applies to the decreasing the number of zeros  $y = \ell - x$  (the number of remaining mutations that need to be accumulated), thus,  $h(y) = \frac{\rho y}{n}$ :

$$\begin{aligned}
T_{\text{opt}} &\leq \frac{1}{h(1)} + \int_1^\ell \frac{1}{h(y)} dy \\
&\leq \frac{n}{p} + \int_1^\ell \frac{n}{py} dy \\
&\leq \frac{n}{p} (1 + \log \ell) ,
\end{aligned} \tag{S11}$$

where we assumed a worst-case scenario, no adapted loci at the beginning, or  $T_{\text{opt}} \leq \frac{n}{p}(1 + \log \frac{\ell}{2})$  if we assumed that half of the loci were adapted by chance.

To find the maximum expected time required for the population to get to the proximity of the fitness peak (for instance, 90% alleles adapted), we use generalised version of the variable drift theorem (A2):

$$\begin{aligned}
T_{90} &\leq \frac{1}{h(a)} + \int_a^\ell \frac{1}{h(y)} dy \\
&\leq \frac{n}{pa} + \int_a^\ell \frac{n}{py} dy \\
&\leq \frac{n}{p} \left( \frac{1}{a} + \log \frac{\ell}{a} \right) ,
\end{aligned} \tag{S12}$$

assuming that the required distance from the peak is  $a = 0.1\ell$

$$\leq \frac{n}{p} (10 + \log 10) , \tag{S13}$$

To find the time it takes to lose adaptation completely (from 100% of adapted alleles to 50%), we find the time necessary to gain  $\ell/2$  zeros in the trait. In each iteration, the expected gain of zeros is  $\Delta y = \frac{\ell - 2y}{Nn} = h(y)$ . Now we substitute  $z = \ell/2 - y$  and use the variable drift theorem, where  $h(z) = \frac{2z}{Nn}$ :

$$\begin{aligned}
T_{\text{max}} &\leq \frac{1}{h(a)} + \int_a^b \frac{1}{h(z)} dz \\
&\leq \frac{Nn}{2} + \int_1^{\ell/2} \frac{Nn}{2z} dz \\
&\leq \frac{Nn}{2} + \frac{Nn}{2} \log \frac{\ell}{2} \\
&\leq \frac{Nn}{2} \left( 1 + \log \frac{\ell}{2} \right) ,
\end{aligned} \tag{S14}$$

where  $a = 1$  is the last step before reaching  $y = (1/2)\ell$  and  $b = \ell/2$  is the maximum number of zeros we have to accumulate.

## S1.3 Multiple traits under periodic selection

We consider the following three scenarios of time dependent fitness landscapes:

1. Scenario 1: There is a single optimal response to all threats; adaptation to any given threat is independent of adaptation to any other threat (Figure S1A).
2. Scenario 2: Threats have different optimal responses, but adaptations to any two threats overlap in all except two traits (Figure S1B).
3. Scenario 3: Threats have conflicting optimal responses; better adaptation to one threat implies worse adaptation to *all* other threats.

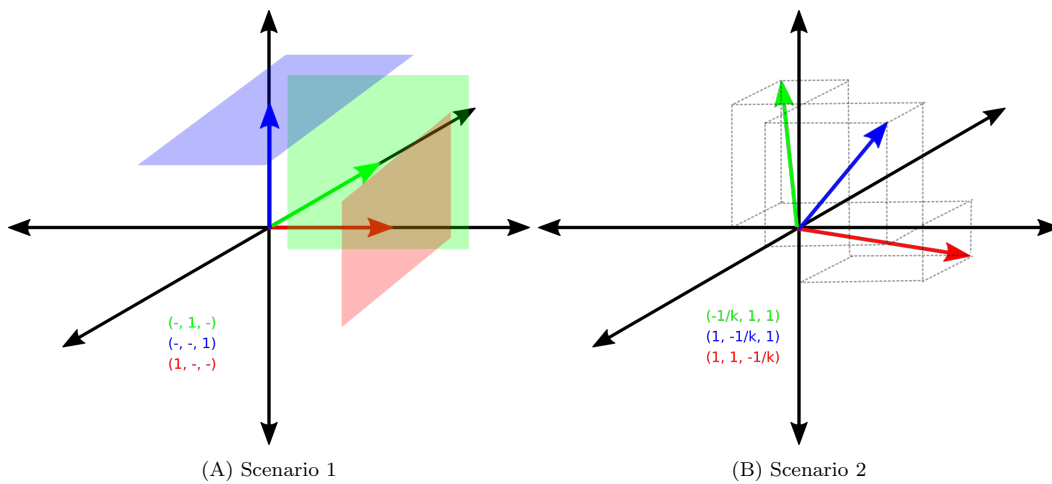


Fig. S1: Scheme of the first two scenarios. Different colors represent different directions of selection. In the first scenario, the optimum is a plane, defined only by a single trait. In the second scenario, the optimum is only one point, a tip of an arrow.

We implement these scenarios as follows: let, for all  $i$ ,  $g_i: \{0, 1\}^i \rightarrow \mathbf{R}$  be a *monotone* function, that is, we assume, for all  $x, y \in \{0, 1\}^i$  with  $\forall j \leq i: x_j \leq y_j$ , that  $g_i(x) \leq g_i(y)$ . For each model, we define a collection  $(f_i)_{i \leq k}$  of  $k$  fitness functions on  $\{0, 1\}^n$  (or, for Model 3, on  $\{1, \dots, k\}^n$ ), where  $k$  is a parameter of the model; we suppose that  $k$  divides  $n$  and write  $k\ell = n$ .

1. Scenario 1: For  $i \leq k$  and all  $x \in \{0, 1\}^n$ ,

$$f_i(x) = g_\ell\left(x[\{1 + i\ell, \dots, (i + 1)\ell\}]\right).$$

Note that each  $f_i$  only depends on a single part of the bit string, and the parts on which the different  $f_i$  depend on are disjoint. The all-1 bit string is optimal for each  $i$ .



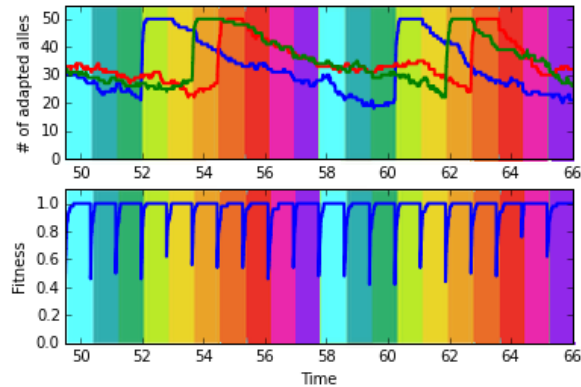


Fig. S3: The number of adapted loci and fitness varies in time. Different background colours represent different environments ( $k = 10$ ). Upper figure: number of adapted loci of randomly selected three traits. If a trait is under selection, all loci quickly adapt. However, if no selection pressure is applied, adaptation is slowly lost. Bottom figure: fitness or fraction of loci that are adapted.

$$f_{\min} = \frac{\frac{1}{2}(1-B) + (1-A)B}{1-AB}, \quad (\text{S15})$$

$$f_{\max} = \frac{\frac{1}{2}A(1-B) + (1-A)}{1-AB}, \quad (\text{S16})$$

and the magnitude of the oscillations is

$$f_{\Delta} = \frac{\frac{1}{2}(1-A)(1-B)}{1-AB}, \quad (\text{S17})$$

where  $A = e^{-\frac{p\tau}{n}}$  and  $B = e^{-\frac{2(k-1)\tau}{Nn}}$ .

Furthermore, equations (8) and (9) derived for the single-trait scenario can be directly used to determine the maximum expected time necessary for a trait to climb the fitness peak or to lose the adaptation completely. Thus, if the environment oscillates with periods longer than  $\frac{n}{p}(1 + \log \ell)$ , the population has enough time to climb the fitness peak. If the period is longer than  $\frac{nN}{2}(1 + \log \frac{3\ell}{2\ell+2})$ , adaptations to individual threats are forgotten and only half of the alleles remain adapted in expectation.

#### *Frequent environmental change*

Another extreme case of environmental change is the environment changing every iteration, i.e., at the same time scale as new mutations appear in the population. To simplify the analysis, we focus at the whole genome at once. In the following theorem, we state the expected level of adaptation (expected number of adapted loci) to which the population converges if the environment changes at the same timescale as new mutations occur

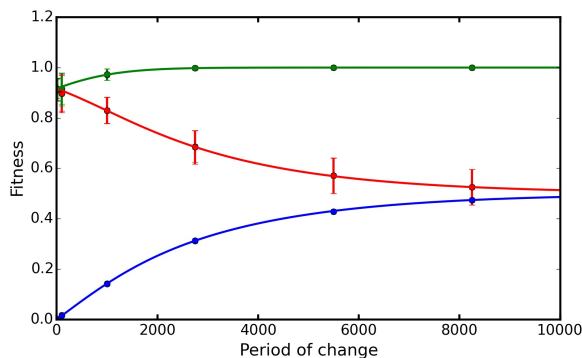


Fig. S4: The dependence of the level of adaptation on the period of environmental change. Green depicts the expected maximum, red the expected minimum, blue the size of oscillations. Lines show analytical results, dots the simulation results. Mean and standard deviation of 100 periods, taken after stable oscillations were achieved.  $k = 10$ ,  $\ell = 50$ ,  $N = 100$ ,  $p = 0.9$ .

in the genome. Furthermore, we provide an estimate of the number of adapted alleles as a function of elapsed time since the beginning of adaptation, assuming no loci were originally adapted. In the proof of the theorem, we first estimate the expected change—drift  $\Delta(X)$ —in the number of adapted alleles across the whole genome, denoted by  $X$ . By finding a threshold value of  $X$  allowing for positive drift, we can determine the number of one bits (adapted alleles) of the whole genome.

**Theorem 5** *Let  $Y(t)$  be the number of 1-bits in the current genome of the SSWM in any iteration  $t \in \mathbf{N}$  when applied to the uncorrelated blocks problem with a constant  $k \geq 2$  number of blocks, where the current block is chosen uniformly at random in every iteration, i.e.,  $\tau = 1$ . Then for any constant  $\varepsilon > 0$ , there exists a constant  $c > 0$  such that*

$$\Pr \left( \max_{1 \leq t \leq e^{cn}} Y(t) \geq (1 + \varepsilon) \frac{n(k-1 + N(k\varepsilon + p))}{2(k-1) + Np} \right) = e^{-\Omega(n)} .$$

Furthermore, for any  $\delta \in (0, 1)$ , SSWM obtains a genotype with at least

$$\frac{n(k-1 + Np(1 + \delta)/2)}{2(k-1) + Np}$$

1-bits in expected time at most

$$\frac{knN\delta}{(1 - \delta)(2(k-1) + Np)} .$$

*Proof* Let  $Y_i(t)$ ,  $i \in [n/k] \cup \{0\}$  be the number of 1-bits in the  $i$ -th block of SSWM at time  $t$ . We apply Hajek's theorem (2.8) to  $Y(t) := \sum_{i=1}^k Y_i(t)$ , i.e., the total number of 1-bits in the bit string, and define  $\Delta(t+1) := Y(t+1) - Y(t)$ .



To check condition (C1), we let  $p$  be the probability that SSWM accepts a new genotype when the fitness has increased by one, and  $1/N$  the probability that SSWM accepts a genotype with identical fitness.

$$\begin{aligned}
\mathbb{E}[\Delta(t+1) | Y(t)] &= \sum_{i=1}^k \left(\frac{1}{N}\right) \left(1 - \frac{1}{k}\right) \left(\frac{n/k - Y_i(t)}{n} - \frac{Y_i(t)}{n}\right) + p \left(\frac{1}{k}\right) \left(\frac{n/k - Y_i(t)}{n}\right) \\
&= \sum_{i=1}^k \frac{k-1 + Np}{Nk^2} - \frac{2(k-1) + Np}{Nkn} Y_i(t) \\
&= \frac{1}{Nk} \left(k-1 + Np - \frac{2(k-1) + Np}{n} Y(t)\right). \tag{S18}
\end{aligned}$$

The first part of equation (S18) describes the probability of a neutral mutation occurring and fixing in the population, while the second part describes the probability of positive mutations occurring in the selected trait and fixing in the population.

Hence, for an arbitrary constant  $\varepsilon > 0$ , if

$$Y(t) \geq \frac{n(k-1 + N(p + k\varepsilon))}{2(k-1) + Np} =: a(n),$$

then the drift is

$$\mathbb{E}[\Delta(t+1) | Y(t)] \leq -\varepsilon.$$

Condition (C2) is trivially satisfied because the number of 1-bits changes by at most one. Assuming that  $Y(0) \leq a(n)$ , Hajek's theorem (2.8) implies for any  $t \geq 0$  that

$$\Pr(Y(t) \geq a(n)(1 + \varepsilon)) = e^{-\Omega(n)}. \tag{S19}$$

Note that  $a(n) > n(1 + \varepsilon)/2$ , hence by a Chernoff bound, the assumption  $Y(0) \leq a(n)$  holds with probability  $e^{-\Omega(n)}$  because the initial genotype is sampled uniformly at random. The first statement now follows by a union bound with respect to the time  $t$ .

For the second statement, it suffices to note that for  $\varepsilon_2 := (1 - \delta)p/(2k)$

$$Y(t) < \frac{n(k-1 + N(p - k\varepsilon_2))}{2(k-1) + Np} =: b(n) \tag{S20}$$

the expected drift from (S18) is bounded by

$$\mathbb{E}[\Delta_{t+1}; Y_t < b(n) | Y_t] > \varepsilon_2. \tag{S21}$$

Hence, the expected time to reach  $b(n)$  1-bits starting from a uniformly chosen genome is by the additive drift theorem at most

$$\mathbb{E} \left[ \frac{b(n) - Y(0)}{\varepsilon_2} \right] = \frac{b(n) - n/2}{\varepsilon_2} = \frac{nN(p - 2k\varepsilon_2)}{\varepsilon_2(4(k-1) + 2Np)} = \frac{knN\delta}{(1-\delta)(2(k-1) + Np)}.$$

A little oversimplified, Theorem 5 implies that the population quickly obtains approximately

$$\approx \frac{n(k-1 + Np)}{2(k-1) + Np}$$

adapted alleles. However, from this level, it takes exponential time to adapt significantly more alleles.

The following proposition states that there is a simple linear relationship between the expected number of adapted alleles and the expected fitness.

**Proposition 1** *Let  $F(t)$  be the fitness and  $Y(t)$  be the number of adapted alleles of SSWM in any generation  $t \in \mathbb{N}$  when applied to the uncorrelated blocks problem, where the current block is chosen uniformly at random in every generation (i.e.,  $\tau = 1$ ). Then*

$$\mathbb{E}[F(t)] = \mathbb{E}[Y(t)]/k. \quad (\text{S22})$$

*Proof* The fitness  $F(t)$  equals the number of adapted alleles in the current block in generation  $t$ . For all  $i \in [k]$ , let  $Y_i(t)$  be the number of adapted alleles in block  $i$  at time  $t$ , and  $Y(t) = \sum_{i=1}^k Y_i(t)$  be the total number of adapted alleles in the genome. Let the random variable  $K(t) \in [k]$  denote the current block in generation  $t$ . Since, the current block is chosen uniformly at random in each generation, the expected fitness conditional on the number of adapted alleles in each block is

$$\mathbb{E}[F(t) \mid Y_1(t), \dots, Y_k(t)] = \sum_{i=1}^k \Pr(K = i) Y_i(t) = \sum_{i=1}^k Y_i(t)/k = Y(t)/k. \quad (\text{S23})$$

Finally, by the tower property of expectation,

$$\mathbb{E}[F(t)] = \mathbb{E}[\mathbb{E}[F(t) \mid Y_1(t), \dots, Y_k(t)]] = \mathbb{E}[Y(t)]/k. \quad (\text{S24})$$

As the environment changes every iteration, all adapted alleles are uniformly distributed across the all traits, resulting in the expected number of adapted alleles in a currently selective trait  $x(t) = \frac{X(t)}{k}$ :

$$x \approx \frac{n\left(\frac{k-1}{N} + p\right)}{k\left(\frac{2(k-1)}{N} + p\right)}. \quad (\text{S25})$$

We can obtain this result also by substituting  $\tau = 1$  into equations (S16) and (S15) and assuming that  $n$  is large enough such that  $A \rightarrow 1$ . Limits of both equations lead to equation (S25).



$$x_1 = \ell - (\ell - x_0)(e^{-\frac{p}{n}(k-1)\tau}) ,$$

$$\Delta^t(x) = (\ell - x_0)(1 - e^{-\frac{p}{n}(k-1)\tau}) ,$$

where  $x_0$  and  $x_1$  denote the number of alleles 1 at the beginning and the end of the period, with selection acting in principal direction.

Similarly, using equation (S27), we can calculate the expected gain of alleles 0 (or rather loss of alleles 1) when a trait experiences selection in the opposite direction during time  $\tau$ :

$$\Delta x = \frac{dx}{dt} = -\frac{p}{n}x$$

$$\int_{x_0}^{x_1} \frac{dx}{x} = \int_{t_0}^{t_0+\tau} -\frac{p}{n} dt$$

$$\log(x) \Big|_{x_0}^{x_1} = -\frac{p}{n}\tau$$

$$x_1 = x_0(e^{-\frac{p}{n}\tau}) . \tag{S28}$$

Expected loss of alleles 1 is thus

$$\Delta^t(x) = x_1 - x_0 = x_0(e^{-\frac{p}{n}\tau} - 1) . \tag{S29}$$

We can find the minimum and the maximum number of ones that each trait is expected to reach by solving the following set of equations

$$x_{\max} = \ell - (\ell - x_{\min})(e^{-\frac{p}{n}(k-1)\tau}) \text{ and}$$

$$x_{\min} = x_{\max}e^{-\frac{p}{n}\tau} .$$

Defining  $A = e^{-\frac{p\tau}{n}}$  and  $B = e^{-\frac{p(k-1)\tau}{n}} = A^{(k-1)}$  and solving the equations leads to

$$x_{\max} = \frac{(1-B)\ell}{1-AB} = \frac{1-A^{k-1}}{1-A^k}\ell \text{ and}$$

$$x_{\min} = \frac{A(1-B)\ell}{1-AB} = \frac{A-A^k}{1-A^k}\ell .$$

Note that the expressions above give us only the minimum and the maximum number of ones in each trait, or, dividing by  $\ell$ , the minimum and maximum fraction. To find the minimum, maximum and the magnitude of fitness oscillations, we cannot simply compare the gain and the loss of alleles in a single trait, as all the

other traits are in various stages of adaptation. Furthermore, one trait is always under selection in the opposite direction, and alleles denoted 0 contribute positively to the fitness and are thus adaptive in this trait. Hence, to find the total fraction of the alleles that are adaptive, we have to sum them up over the number of periods that passed since the change in the selection direction.

The maximum fraction of alleles that are adaptive at the end of each period is

$$\begin{aligned}
f_{\max}(\tau) &= \frac{1}{n} \left[ \left(1 - \frac{A - A^k}{1 - A^k}\right) \ell + \sum_{i=1}^{k-1} \left( \ell + \left( \frac{A - A^k}{1 - A^k} \ell - \ell \right) A^i \right) \right] \\
&= \frac{1}{n} \left[ \left(1 - \frac{A - A^k}{1 - A^k}\right) \ell + (k-1)\ell + \ell \sum_{i=1}^{k-1} \left( \left( \frac{A - A^k}{1 - A^k} - 1 \right) A^i \right) \right] \\
&= \frac{\ell}{n} \left[ k - \frac{A - A^k}{1 - A^k} + \frac{A - A^k}{1 - A^k} \sum_{i=1}^{k-1} A^i - \sum_{i=1}^{k-1} A^i \right] \\
&= \frac{\ell}{n} \left[ k + \frac{A - A^k}{1 - A^k} \left( -1 + \sum_{i=1}^{k-1} A^i \right) - \sum_{i=1}^{k-1} A^i \right] \\
&= \frac{\ell}{n} \left[ k + \frac{A - A^k}{1 - A^k} \left( -1 + \frac{A - A^k}{1 - A} \right) - \frac{A - A^k}{1 - A} \right] \\
&= \frac{\ell}{n} \left[ k - \frac{2(A - A^k)}{1 - A^k} \right] \\
&= 1 - \frac{2}{k} \cdot \frac{A - A^k}{1 - A^k}, \tag{S30}
\end{aligned}$$

where the first term in the first line is the fitness contribution of a trait that is under selection in the opposite direction. Using the same approach, it is possible to calculate the expected minimum fitness, right after the environmental change.

We expect that the trait that was longest under selection pressure in the principal direction will come under selection pressure in the opposite direction. Thus, its fitness contribution will be given only by  $\ell - x_{\max}$  loci. The trait that was under selection in the opposite direction until now will contribute only  $x_{\min}$  loci. Other traits had already from 1 to  $k - 2$  periods of selection in the one direction, thus their contribution can be found by using equation (S3) with a time of  $i \cdot \tau$ , where  $i$  is the number of periods that each trait spent under selection in the principal direction.

$$\begin{aligned}
f_{\min}(\tau) &= \frac{1}{n} \left[ \ell - x_{\max} + x_{\min} + \sum_{i=1}^{k-2} \frac{A - A^k}{1 - A^k} \ell \right] \\
&= \left( \frac{(A - A^k)}{1 - A^k} - \frac{(1 - A^{k-1})}{1 - A^k} + \frac{(kA^{k+1} - 2A^{k+1} - A^k + A^2 - Ak + 2A)}{A(A^k - 1)} + 1 \right) \frac{\ell}{n} \\
&= \frac{\ell (kA^k - 2A^{k-1}(k-2))}{n(A^k - 1)} \\
&= 1 - \frac{2}{k} \cdot \frac{1 - A^{k-1}}{1 - A^k}, \tag{S31}
\end{aligned}$$

where  $A = e^{-\frac{p\tau}{n}}$ . Resulting oscillations in fitness are

$$\begin{aligned}
\Delta f(\tau) &= f_{\max}(\tau) - f_{\min}(\tau) \\
&= 1 - \frac{2}{k} \cdot \frac{A - A^k}{1 - A^k} - 1 + \frac{2}{k} \cdot \frac{1 - A^{k-1}}{1 - A^k} \\
&= \frac{2}{k} \cdot \frac{(1 - A)(1 - A^{k-1})}{1 - A^k}. \tag{S32}
\end{aligned}$$

#### *Frequent environmental change*

To find out what happens if the environment changes frequently, i.e., every iteration, we can substitute  $\tau = 1$  into the equations (S30), (S31) and (S32). However, to get a better idea how the resulting state depends on the number of loci  $\ell$  and traits  $k$ , we assume that  $n \gg p$  and thus  $A \rightarrow 1$  and find the limit of the minimum and maximum fitness/fraction of adapted loci across all traits:

$$\begin{aligned}
\lim_{A \rightarrow 1} f_{\max}(1) &= \lim_{A \rightarrow 1} f_{\min}(1) = \frac{(k-1)^2 + 1}{k^2} \\
&= \frac{(k^2 - 2k + 2)\ell}{kn} = 1 - 2\left(\frac{1}{k} - \frac{1}{k^2}\right). \tag{S33}
\end{aligned}$$

See Theorem 7 for a proof that, after a sufficiently long time, the fraction of adapted alleles converges into the solution above, regardless of the initial state, if the environment changes frequently.

#### *Rare environmental change*

To find the time necessary for the adaptation, we denote the number of alleles matching the current threat (regardless whether they are ones or zeros)  $X$ , and determine the expected change in each iteration

$$\Delta = \frac{(n - X(t))p}{n}. \tag{S34}$$

We define decreasing number of all non-matching alleles  $h(Y) = \frac{Yp}{n}$  and use the variable drift theorem:

$$\begin{aligned} T_{\text{opt}} &\leq \frac{1}{h(1)} + \int_1^{2^\ell} \frac{1}{h(Y)} dY \\ &\leq \frac{n}{p} + \int_1^{2^\ell} \frac{n}{pY} dY \\ &\leq \frac{n}{p} (1 + \log(2^\ell)) , \end{aligned}$$

where we assumed that at the beginning,  $2^\ell$  loci were not adapted, or

$$T_{\text{opt}} \leq \frac{n}{p} (1 + \log n) , \quad (\text{S35})$$

where we assumed that no loci were adapted at the beginning. Thus, the equation above sets a limit to the maximum expected adaptation time in this scenario.

Upon environmental change after this time, 2 traits are expected to be completely maladapted, thus the fitness is reduced by  $2/k$ . See Theorem 9 for the proof.

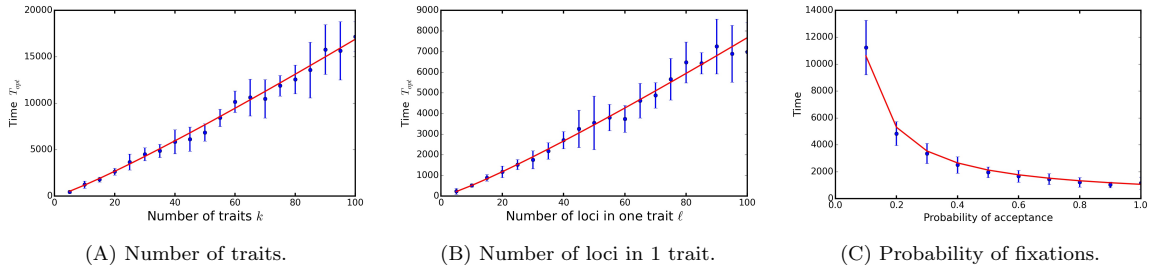


Fig. S7: Time to find the temporal optimum in scenario 2, and its dependence on various parameters. Red lines depict analytical results, blue dots simulation results. Mean and standard deviation of 100 independent trials.

### S1.6 Scenario 3: Adaptations in different environments are completely antagonistic

In this scenario, we assume that all traits are under selection at all times. However, every environment requires a specific response (allele) at each locus, thus there are as many alleles per locus as there are threats. Threats are completely dissimilar, adaptation to one of them means maladaptation to the rest of them (Figure S8).

As all traits are under selection in the same direction, we look at the whole genome at once. The probability of a positive mutation occurring is  $\frac{n-X}{n(k-1)}$ , where  $X$  is the total number of alleles across all traits adapted to the current threat, and the factor  $(k-1)$  comes from the fact that only one in  $(k-1)$  possible mutations at each locus is positive in a given time. As all traits are under selection in the same direction, we can apply the

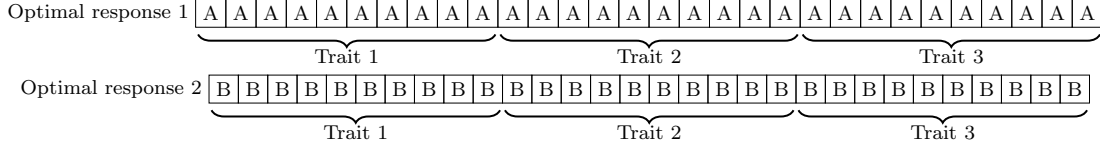


Fig. S8: All traits are under selection at all times. Optimal responses to all threats are not compatible.

same approach as we used for a single trait to the whole genome. Thus, the expected gain of adaptive alleles in each time step is

$$\Delta X = \frac{p(n-X)}{n(k-1)}. \quad (\text{S36})$$

The expected number of adaptive alleles after time period  $\tau$  is

$$\begin{aligned} \frac{dX}{dt} &= \frac{p}{n(k-1)}(n-X) \\ \int_{X_0}^{X_1} \frac{dX}{n-X} &= \int_{t_0}^{t_0+\tau} \frac{p}{n(k-1)} dt \\ \log(n-X) \Big|_{X_0}^{X_1} &= \frac{p}{n(k-1)}(\tau) \\ \log\left(\frac{n-X_0}{n-X_1}\right) &= \frac{p}{n(k-1)}\tau \\ \frac{n-X_0}{n-X_1} &= e^{\frac{p}{n(k-1)}\tau} \\ X_1 &= n - (n-X_0)e^{-\frac{p}{n(k-1)}\tau}, \end{aligned} \quad (\text{S37})$$

where  $X_1$  and  $X_0$  denote the number of adapted alleles at the beginning and the end of the period  $\tau$ , respectively. The expected gain of adaptive alleles is thus

$$\Delta^t(X) = (n-X_0)(1 - e^{-\frac{p}{n(k-1)}\tau}). \quad (\text{S38})$$

Again, we assume that a trait is periodically under selection pressure in one direction for  $\tau$  iterations, but under selection in a different direction (we have  $k$  directions, as there are  $k$  alleles per locus) for  $(k-1)\tau$  iterations, thus the expected change of alleles of a particular type (denoted by  $X$ ) in each time step is

$$\Delta X = -\frac{pX}{n(k-1)} - \frac{X(k-2)}{Nn(k-1)}, \quad (\text{S39})$$

where the first part is a loss due to positive mutations occurring and fixing, while the second part captures the loss of alleles due to neutral mutations to other possible alleles. In time  $(k-1)\tau$ , the change is



$$\begin{aligned}
\frac{dX}{dt} &= -\frac{X}{n(k-1)} \left( p + \frac{k-2}{N} \right) \\
\int_{X_0}^{X_1} \frac{dX}{X} &= -\int_{t_0}^{t_0+(k-1)\tau} \frac{p + \frac{k-2}{N}}{n(k-1)} dt \\
\log(X) \Big|_{X_0}^{X_1} &= -\frac{p + \frac{k-2}{N}}{n(k-1)} (k-1)\tau \\
\log\left(\frac{X_1}{X_0}\right) &= -\frac{p + \frac{k-2}{N}}{n} \tau \\
\frac{X_1}{X_0} &= e^{-\frac{p + \frac{k-2}{N}}{n} \tau} \\
X_1 &= X_0 e^{-\frac{p + \frac{k-2}{N}}{n} \tau}, \tag{S40}
\end{aligned}$$

where  $X_1$  and  $X_0$  denote the number of type X alleles at the beginning and the end of the period, when this allele was not suitable for the environment.

The expected loss of adaptive alleles is thus

$$\Delta^t(X) = X_0 - X_0 e^{-\frac{p + \frac{k-2}{N}}{n} \tau} = X_0 (1 - e^{-\frac{p + \frac{k-2}{N}}{n} \tau}). \tag{S41}$$

We can find the maximum expected number of adapted alleles in the whole genome (at the end of the selection period) and its minimum (at the end of the no-selection period), denoted by  $X_{\max}$  and  $X_{\min}$ , respectively, and thus their magnitude  $X_{\Delta}$ :

$$\begin{aligned}
X_{\max} &= n - (n - X_{\min}) e^{-\frac{p}{n(k-1)} \tau} \text{ and} \\
X_{\min} &= X_{\max} (e^{-\frac{p + \frac{k-2}{N}}{n} \tau}).
\end{aligned}$$

Defining  $A = e^{-\frac{p\tau}{n(k-1)}}$  and  $B = e^{-\frac{pN + k - 2}{Nn} \tau}$  and solving the system of equations leads to

$$X_{\max} = \frac{1 - A}{1 - AB} n \text{ and} \tag{S42}$$

$$X_{\min} = \frac{(1 - A)B}{1 - AB} n, \tag{S43}$$

and the magnitude of oscillations is

$$X_{\Delta} = \frac{(1 - A)(1 - B)}{1 - AB} n. \tag{S44}$$

The total fraction of adapted loci can be found by dividing the results above by  $n$ , as we were looking at the whole genome.

### Rare environmental change

As before, we use variable drift theorem to find the maximum expected time to adapt all loci across all traits.

Defining  $h(Y) = \frac{pY(t)}{n(k-1)}$ ,

$$\begin{aligned} T_{\text{opt}} &\leq \frac{1}{h(1)} + \int_1^n \frac{1}{h(Y)} dY \\ &= \frac{(k-1)n}{p} + \int_1^n \frac{(k-1)n}{pY} dY \\ &= \frac{(k-1)n}{p} (1 + \log n), \end{aligned} \quad (\text{S45})$$

where we assumed the worst case scenario, when no adaptive alleles are present at the beginning. After this time, it is expected that all loci are adapted to the current threat, and if the environment changes, the population is completely maladapted to the environment.

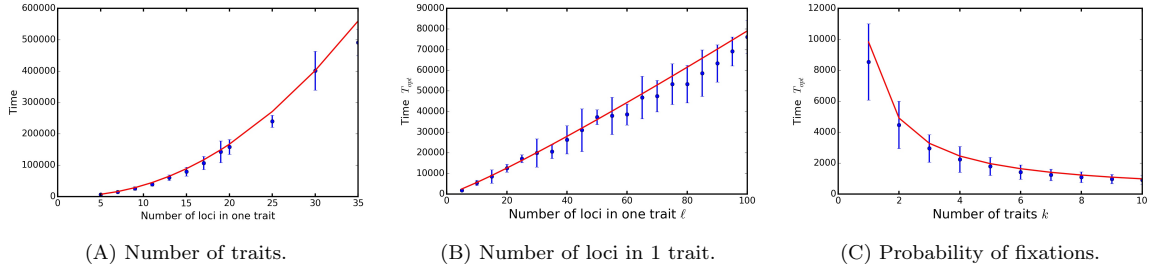


Fig. S9: Time to find the temporal optimum in scenario 3, and its dependence on various parameters. Red lines depict analytical results, blue dots simulation results. Mean and standard deviation of 100 independent trials.

## S2 Adding stochasticity to environmental change

To simplify the calculations above, we assumed that the environment changes periodically and different threats follow in the same order. However, as our results are expectations, they apply to more general scenarios as well, where different threats arise in random order. We still assume that they are all equally likely and of the same length. In such a case, each environment repeats in expectation every  $(k-1)\tau$  iterations, and our results hold. However, the variance in the minimum and the maximum fraction of adapted alleles is increased.

Figure S10 shows analytical results (solid line) and simulations of threats arising in random order.

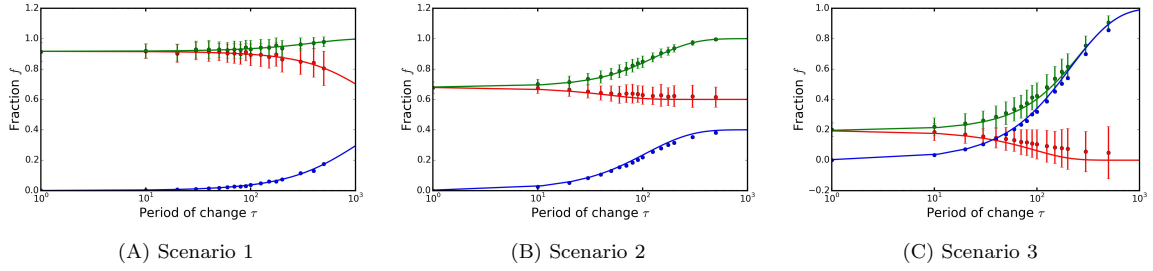


Fig. S10: Minimum (red), maximum (green) and magnitude of the fitness oscillations (blue) in all three models, when environments change in random order. Lines depict analytical calculations, dots mean and standard deviation of 200 periods taken after stable oscillations were achieved.

### S3 Generalized fitness landscape—non-linear fitness

Here, we generalize our results by relaxing assumptions on the fitness landscapes. We assume the fitness to be an arbitrary monotone function increasing with the size of the mutation effects, and thus larger mutations are more likely to get fixed in the population. Several cases of epistasis can be incorporated into the model.

We develop a general framework for the analysis of an arbitrary monotone fitness function, then work out another specific saturating fitness function.

#### S3.1 Probability of a given state

The following lemma is due to [Randall \(2006\)](#) and will be used in the upcoming proofs. It says that, after a mixing time of at most  $\tau(\varepsilon)$ , the probability to be in either state of a two-state Markov chain is only by  $\varepsilon$  from its stationary distribution. This lemma is useful to determine the fraction of adapted alleles in all three scenarios and is independent of the fitness function, as it only deals with probabilities of fixations.

**Lemma 1** *Assume a two-state Markov chain (Figure S11) with transition probabilities  $x$  and  $y$ . For all  $t \in \mathbf{N}$ , let  $x(t)$  and  $y(t)$  be the probabilities of being in state 0 and 1 at time  $t$ , respectively, and let  $x^* = \lim_{t \rightarrow \infty} x(t)$  and  $y^* = \lim_{t \rightarrow \infty} y(t)$ . Then*

$$x^* = \frac{y}{x+y} \text{ and}$$

$$y^* = 1 - x^* .$$

Further, for  $\varepsilon > 0$ , let  $\tau(\varepsilon)$  denote the first point in time such that, for all  $t \geq \tau(\varepsilon)$ ,  $|x(t) - x^*| \leq \varepsilon$  and  $|y(t) - y^*| \leq \varepsilon$ , and let  $p^* = \min\{x^*, y^*\}$ . Then

$$\tau(\varepsilon) = O\left(\frac{1}{x+y} \log\left(\frac{1}{p^* \varepsilon}\right)\right) .$$

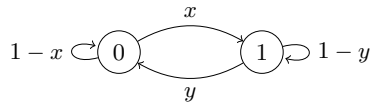


Fig. S11: Markov chain with two states, representing the value of any bit.

In the lemma above, state 0 means that a position has a specific value, and state 1 that it is *not* this specific value. The lemma then states that the transition probabilities  $x$  and  $y$  are (after a certain mixing time) very close to the limit probabilities of being in state 1 or 0, respectively.

### S3.2 Saturating fitness

In this example, we assume that the fitness landscape is saturating due to some kind of epistasis, with adaptive mutations having diminishing fitness effects where new adaptive mutations contribute less to the trait value than the previous ones resulting in fitness gain diminishing with the number of adapted loci in each trait. Note that fitness contributions across traits are additive:

$$f(x) = 1 - \frac{\sum_{B \in \mathcal{B}} 2^{d_H(x[B], a[B])}}{F}, \quad (\text{S46})$$

where  $F = k \cdot 2^\ell$ . Note that the fitness here is scaled to go from 0 to  $1 - 1/F$ .

We derive our results for extreme scenarios of environmental change, when the environment changes frequently, every iteration, or rarely, after the population fully adapted to the current threat. While analytical calculations only deal with these special cases, numerical simulations provide insight into scenarios with intermediate frequencies of environmental change.

Further, we assume that the probability of fixation is given by the fitness contribution, thus the probability of fixation of the first positive mutation is the largest, denoted  $p_{\max}$ , and the probability of the fixation of the last positive mutation is the smallest, denoted  $p_1$ . Neutral mutations fix with probability  $p_0 = 1/N$ .

### S3.3 Scenario 1: Selection acting at different traits in different environments

For saturating fitness

$$f(x) = 1 - \frac{\sum_{B \in \mathcal{B}} 2^{d_H(x[B], a[B])}}{F}, \quad (\text{S47})$$

we use Lemma 1 to derive bounds on the expected fraction of alleles that are adapted. The transition probability  $x$  to mutate from allele 0 to allele 1 is  $\frac{p_x}{nk} + \frac{(k-1)p_0}{nk}$ , where the first term is the probability that the locus is currently under selection, mutates and is fixed with probability given by probability  $p_x$  dependent on its contribution, while the second term is the probability that it mutates when the trait is not under selection

(neutral mutation). This transition probability can be bounded by

$$\frac{1}{nk}(p_1 + (k-1)p_0) \leq x \leq \frac{1}{nk}(p_{\max} + (k-1)p_0) . \quad (\text{S48})$$

Mutation from allele 1 to allele 0 can occur only if no selection is present, and is thus given as  $y = \frac{k-1}{nk}p_0$ . According to Lemma 1, we get the probability  $x^*$  that a locus is adapted

$$\frac{p_1 + (k-1)p_0}{2(k-1)p_0 + p_{\max}} \leq x^* \leq \frac{p_{\max} + (k-1)p_0}{2(k-1)p_0 + p_1} . \quad (\text{S49})$$

If we assume the linear scenario,  $p_1 = p_{\max}$ , and the expected probability that the locus is adapted (which is equal to the fraction of adapted alleles) goes to 1 for small  $k$  and to 0.5 with increasing  $k$ , which is in agreement with our previous calculations.

From equation (S49), we can derive bounds on the expected fitness  $F$ . If  $p_0 < p_1 \ll p_{\max}$ , the upper bound on the fraction of adapted alleles approaches 1. On the other hand, the lowest fraction of adapted alleles is expected when  $p_0 \approx p_1 \approx p_{\max}$ , setting the lower bound of the expected alleles to be  $> 0.5$ . Thus, the expected fitness is

$$2^\ell - 2^{\ell/2} \leq F \leq 2^\ell \quad (\text{S50})$$

or, if we want to express it as scaled fitness,

$$1 - 2^{-\ell/2} \leq F \leq 1 . \quad (\text{S51})$$

We now bound the maximal fitness that can be obtained in the case of saturating fitness. Following Section S3.2, the fitness at time  $t$  is given by

$$F(t) = 1 - \frac{2^{\ell - Y_i(t)}}{k2^\ell} = 1 - \frac{1}{k2^{Y_i(t)}} , \quad (\text{S52})$$

where  $Y_i(t)$  is the number of 1-bits in the ‘active block’ in iteration  $t$ . We assume that the fixation probabilities of positive mutations are monotonically decreasing in the fitness, and at most  $p_{\max}$ .

**Theorem 6** *Let  $F(t)$  be the saturating fitness of the SSWM in any iteration  $t \in \mathbf{N}$  when applied to the uncorrelated blocks problem with a constant  $k \geq 2$  number of blocks,  $p_{\max}$  be the largest probability of fixation of a positive mutation, and where the current block is chosen uniformly at random in every iteration, i.e.,  $\tau = 1$ . Then, for any constant  $\varepsilon > 0$ , there exists a constant  $c > 0$  such that*

$$\Pr \left( \max_{1 \leq t \leq e^{cn}} F(t) \geq 1 - \frac{1}{k2^{a(n)(1+\varepsilon)}} \right) = e^{-\Omega(n)} , \quad (\text{S53})$$

where

$$a(n) := \frac{n(k-1 + N(p_{\max} + k^2\varepsilon))}{k(2(k-1) + Np_{\max})}. \quad (\text{S54})$$

*Proof* We use the same notation and ideas as in the proof of Theorem 5. In addition, we define for each block  $i \in [k]$ , the drift in the number of adapted alleles in the block, by

$$\Delta_i(t+1) := Y_i(t+1) - Y_i(t). \quad (\text{S55})$$

Using similar derivations as in the proof of Theorem 5, we get

$$\mathbb{E}[\Delta_i(t+1) \mid Y_i(t)] \leq \frac{k-1 + Np_{\max}}{Nk^2} - \frac{2(k-1) + Np_{\max}}{Nkn} Y_i(t).$$

Hence, for any constant  $\varepsilon > 0$ , if

$$Y_i(t) \geq \frac{n(k-1 + N(p_{\max} + k^2\varepsilon))}{k(2(k-1) + Np_{\max})} =: a(n), \quad (\text{S56})$$

then the drift is

$$\mathbb{E}[\Delta_i(t+1) \mid Y_i(t)] \leq -\varepsilon. \quad (\text{S57})$$

Note that  $a(n) \geq (n/k)(1 + \varepsilon)/2 = \ell(1 + \varepsilon)/2$ , hence, by a Chernoff bound, the assumption  $Y(0) \leq a(n)$  holds with probability  $e^{-\Omega(n)}$ , because the initial genotype is chosen uniformly at random. Condition (C1) is therefore satisfied on the interval  $a(n) \leq Y(t) \leq a(n)(1 + \varepsilon)$ . Condition (C2) is trivially satisfied because  $Y_i(t)$  changes by at most one in each iteration. Hajek's theorem (2.8) now implies for any  $t \geq 0$  that

$$\Pr(Y_i(t) \geq a(n)(1 + \varepsilon)) = e^{-\Omega(n)}. \quad (\text{S58})$$

Furthermore, a union bound over all the blocks and time iterations  $0 \leq t \leq e^{cn}$  yield

$$\Pr\left(\max_{0 \leq t \leq e^{cn}} \max_{1 \leq i \leq k} Y_i(t) \geq a(n)(1 + \varepsilon)\right) \leq ke^{cn} e^{-\Omega(n)} = e^{-\Omega(n)}, \quad (\text{S59})$$

assuming that  $c > 0$  is a sufficiently small constant. This now yields the statement of the theorem, because

$$\Pr\left(\max_{0 \leq t \leq e^{cn}} F(t) \geq 1 - 1/(k2^{a(n)(1+\varepsilon)})\right) \leq \Pr\left(\max_{0 \leq t \leq e^{cn}} \max_{1 \leq i \leq k} Y_i(t) \geq a(n)(1 + \varepsilon)\right). \quad (\text{S60})$$

## S3.4 Scenario 2: Selection acting at all traits, with partial overlap between different environments

We formalize the model 2 described above by defining a set  $A \subseteq \{0, 1\}^n$ ,  $|A| = k$  of  $k$  different optima  $a_j$  ( $j \in \{1, \dots, k\}$ ) defined as follows:

$$a_j = 1^{(j-1)\ell} 0^\ell 1^{(n-j)\ell} .$$

Note that for each bit position, there is only one  $a_j$  that has a 0 at that position.

*Frequent environmental change*

We first focus on a case when the environment changes every iteration.

Using Lemma 1, we show that, after some time  $T = \Omega(n \log(nk))$ , the population in the SSWM regime reaches a state where the probability of being adapted is (almost; in the limit it is exactly) the probability of a trait being under selection pressure. It says that if a position is optimal with probability  $y$ , then, in the limit, the probability of having an optimal value at that position is  $y$  as well.

**Lemma 2** *Consider SSWM optimizing a monotone function  $f$  that changes its optimum each iteration. After at least  $\Omega(n/(p_{\max}) \log(nkp_{\max}/p_1))$  iterations, for each  $i \in \{1, \dots, n\}$ , for the probability  $x^*$  to have a 0 at bit position  $i$ , we have*

$$\frac{1}{k} \cdot \frac{p_1}{p_{\max}} \leq x^* \leq \frac{1}{k} \cdot \frac{p_{\max}}{p_1} ,$$

and, for the probability  $y^*$  to have a 1 at bit position  $i$ , we have

$$\left(1 - \frac{1}{k}\right) \frac{p_{\max}}{p_1} \leq y^* \leq \left(1 - \frac{1}{k}\right) \frac{p_1}{p_{\max}} .$$

*Proof* We model the event of bit  $i$  being 0 or 1 as a two-state Markov chain as depicted in Figure S11. State 0 means that the current bit is 0, and state 1 means that the current bit is 1. We are now going to estimate the probabilities  $x$  and  $y$  of how likely it is to change from one state to the other.

First, consider  $x$ , i.e., the probability of bit  $i$  being flipped from 0 to 1. Hence, bit  $i$  has to be chosen for mutation by SSWM and the result has to be accepted. The probability of mutating bit  $i$  is  $1/n$ . Since  $\Delta f$  cannot be 0 in this setting, the probability to accept such a mutation is comprised of the probability that the current optimum has a 1 at position  $i$ , and of the fixation probability, which is at least  $p_1$  and at most  $p_{\max}$ .

Thus, we get

$$\frac{p_1}{n} \left(1 - \frac{1}{k}\right) \leq x \leq \frac{p_{\max}}{n} \left(1 - \frac{1}{k}\right) . \tag{S61}$$

For  $y$ , we can argue analogously: Bit  $i$  has to be flipped, the momentary optimum has to have a 0 at bit  $i$ , and the offspring has to be accepted. Hence, we have

$$\frac{p_1}{n} \cdot \frac{1}{k} \leq y \leq \frac{p_{\max}}{n} \cdot \frac{1}{k}. \quad (\text{S62})$$

By applying Lemma 1, we end up with

$$\begin{aligned} \frac{1}{k} \cdot \frac{p_1}{p_{\max}} &\leq x^* \leq \frac{1}{k} \cdot \frac{p_{\max}}{p_1}, \\ \left(1 - \frac{1}{k}\right) \frac{p_{\max}}{p_1} &\leq y^* \leq \left(1 - \frac{1}{k}\right) \frac{p_1}{p_{\max}}, \text{ and} \\ \tau(\varepsilon) &= O\left(\frac{n}{p_{\max}} \log\left(\frac{k}{\varepsilon} \cdot \frac{p_{\max}}{p_1}\right)\right). \end{aligned}$$

If we choose  $\varepsilon = \Omega(1/\text{poly}(n))$ , we get  $\tau(\varepsilon) = O(n/(p_{\max}) \log(nkp_{\max}/p_1))$ . That means that we can get polynomially close to the stationary distribution of the Markov chain after a mixing time of  $\Omega(n/(p_{\max}) \log(nkp_{\max}/p_1))$ .

The lemma generalizes our previous results (S33), where we stated what fraction of alleles is expected to be adapted if the environment changes every iteration. If we assume that the probability of accepting a positive mutation is the same, regardless of the fitness contribution (or that all alleles contribute equally to the fitness),  $p_{\max} = p_1$ , we obtain exactly the same results as previously in section S1.5: Equations (S61) and (S62) show that  $x = 1/k$  and  $y = 1 - 1/k$ . As we want zeros in 1 trait, and ones in  $(k-1)$  traits, the total fraction of adapted alleles is

$$f = \frac{1}{n} \left( \frac{1}{k} \ell + \frac{k-1}{k} (k-1) \ell \right) = \frac{(k^2 - 2k + 2) \ell}{kn} = 1 - 2 \left( \frac{1}{k} - \frac{1}{k^2} \right).$$

The following theorem states that, after a sufficiently long time ( $t_{\text{mix}}$ ), the number of adapted loci converges to the solution given by (S63) if we assume equal contributions of fitness. The probabilities bound how likely it is that there is a point in time (during  $t^*$  rounds; at least  $t_{\text{mix}}$ ) such that the total number of adapted loci deviates by a constant factor from  $(1 \pm \varepsilon)k^* \ell$ , where  $k^* = \frac{k^2 - 2k + 2 + \varepsilon k - \varepsilon}{k}$ . Since  $\varepsilon$  can be arbitrarily close to 0 (not dependent on  $n$  and  $k$ ), the number of adapted loci is basically the solution given above.

**Theorem 7** Consider SSWM optimizing  $f_1$ , changing its current optimum  $a_j$  every iteration. Let  $s_t$  denote the current solution of SSWM in iteration  $t$ , and let  $k^*(u, v) = k - (u+1) + (u+v)/k$ . After at least  $t_{\text{mix}} = \Omega(n/(p_1) \log(nk))$  iterations, for any  $\varepsilon = \Omega(1/\text{poly}(n)) < 1$  and any  $t^* \geq t_{\text{mix}}$ , it holds, for any constant  $\delta > 0$ ,

$$\Pr\left(\exists t, t_{\text{mix}} \leq t \leq t^*: f_1(s_t) \geq (1 + \delta)(1 + \varepsilon) \ell k^*(1 - \varepsilon, 1)\right) \leq (t^* - t_{\text{mix}} + 1) e^{-\frac{\delta^2 \ell k^*(1 + \varepsilon, 1 + \varepsilon)}{3}},$$

and, for any constant  $0 < \delta < 1$ ,

$$\Pr\left(\exists t, t_{\text{mix}} \leq t \leq t^*: f_1(s_t) \leq (1 - \delta)(1 - \varepsilon) \ell k^*(1, 1)\right) \leq (t^* - t_{\text{mix}} + 1) e^{-\frac{\delta^2 \ell k^*(1 - \varepsilon, 1 - \varepsilon)}{2}}.$$



*Proof* In the following, let  $x'$  be  $x^*$  from Lemma 2 with a factor of  $1 \pm \varepsilon$  denoting the difference to its limit, i.e.,  $x' = (1 \pm \varepsilon)x^* = (1 \pm \varepsilon) \cdot 1/k$ . Note that  $p_{\max} = p_1$  because we optimize  $f_1$ .

Let  $t^* \geq t_{\text{mix}}$ . We will only bound the probability of  $f_1(s_t)$  deviating too much for any single  $t$  with  $t_{\text{mix}} \leq t \leq t^*$ . The statement then follows by a union bound over all possible values of  $t$ .

First, we bound  $\Pr(f_1(s_t) \geq (1+\delta)(1+\varepsilon)\ell k^*(1-\varepsilon, 1)) \leq \Pr(f_1(s_t) \geq (1+\delta)c\ell k^*(c, c))$  via a Chernoff bound, where we assume  $x' = c/k$  with  $c \in \{1+\varepsilon, 1-\varepsilon\}$ . Note that then  $\mathbb{E}[f_1(s_t)] = n/(k)x' + n(k-1)/(k) \cdot (1-x') = \ell x' + (k-1)\ell(1-x') = \ell k^*(c, c) \leq c\ell(x^* + (k-1)(1-cx^*)) = c\ell k^*(c, 1)$ .

We get

$$\Pr\left(f_1(s_t) \geq (1+\delta)\ell k^*(c, c)\right) \leq e^{-\frac{\delta^2 \ell k^*(c, c)}{3}} \leq e^{-\frac{\delta^2 \ell k^*(1+\varepsilon, 1+\varepsilon)}{3}}.$$

Second, we bound  $\Pr(f_1(s_t) \leq (1-\delta)(1-\varepsilon)\ell k^*(1, 1)) \leq \Pr(f_1(s_t) \leq (1-\delta)\ell k^*(c, c))$ , for  $0 < \delta < 1$ , analogously. We get

$$\Pr\left(f_1(s_t) \leq (1-\delta)\ell k^*(c, c)\right) \leq e^{-\frac{\delta^2 \ell k^*(c, c)}{2}} \leq e^{-\frac{\delta^2 \ell k^*(1+\varepsilon, 1+\varepsilon)}{2}}.$$

The following theorem considers diminishing fitness gain of new adaptive alleles in each trait. It states that with high probability, the fitness is at least  $(k-1)2^\ell$ .

**Theorem 8** Consider SSWM optimizing  $f_2$  with  $\ell = o(kp_1/p_{\max})$  and  $k = \omega(p_{\max}/p_1) \cap o(2^\ell)$ , changing its optimum every iteration. Let  $s_t$  denote the current solution of SSWM in iteration  $t$ . After at least  $t_{\text{mix}} = \Omega(n/(p_{\max}) \log(nkp_{\max}/p_1))$  iterations, we get

$$\Pr\left(\exists t, t_{\text{mix}} \leq t \leq t^*: f_2(s_t) \geq k \cdot 2^\ell - o(2^\ell)\right) \leq (t^* - t_{\text{mix}} + 1) \left( O\left(\frac{\ell p_{\max}}{4^\ell p_1}\right) + e^{-\Theta(\ell)} \right)$$

and, for any constant  $\delta$  with  $0 < \delta \leq k-1$ ,

$$\Pr\left(\exists t, t_{\text{mix}} \leq t \leq t^*: f_2(s_t) \leq k \cdot 2^\ell - (1+\delta)2^\ell\right) \leq (t^* - t_{\text{mix}} + 1) O\left(\frac{\ell p_{\max}}{4^\ell p_1}\right).$$

*Proof* In the following, we are going to use  $x^* = \Theta(c/k)$ , where  $c \in [p_1/p_{\max}, p_{\max}/p_1]$ , and  $y^* = 1 - x^*$  from Lemma 2 instead of  $x^* \pm 1/\text{poly}(n)$  and  $y^* \pm 1/\text{poly}(n)$  as the probabilities of being having a 0 or a 1 at any bit position, respectively, after  $t_{\text{mix}}$  rounds of SSWM because the  $\Theta$  incorporates these offsets.

We are now going to look at the expected fitness and bound it after  $t_{\text{mix}}$  time has passed. Let  $a_j$  be an arbitrary optimum, and let  $t \geq t_{\text{mix}}$ . Again, as in the proof of Theorem 7, we only prove the probabilities for a single  $t$ . The probabilities stated in the theorem then follow by applying a union bound.

$$\begin{aligned} \mathbb{E}[f_2(s_t)] &= \mathbb{E} \left[ k \cdot 2^\ell - \sum_{B \in \mathcal{B}} 2^{d_H(s_t[B], a_j[B])} \right] \\ &= k \cdot 2^\ell - \sum_{B \in \mathcal{B}} \mathbb{E} \left[ 2^{d_H(s_t[B], a_j[B])} \right]. \end{aligned}$$

$2^{d_H(s_t[B], a_j[B])}$  is a random variable whose distribution is dependent on  $B$ : If  $B$  is the block  $B_z$  of  $a_j$  containing only zeros,  $d_H(s_t[B_z], a_j[B_z])$  is going to be very big because  $s_t[B_z]$  contains 0s only with probability  $\Theta(c/k)$ . On the other hand, this will lead to  $d_H(s_t[B], a_j[B])$  being small for all other blocks since they contain almost only 1s anyway. We first look at all blocks  $B$  but  $B_z$ . In this case, the Hamming distance increases if there is a 0 at a bit position in  $s_t[B]$ .

$$\begin{aligned} \mathbb{E} \left[ 2^{d_H(s_t[B], a_j[B])} \right] &= \sum_{i=0}^{\ell} 2^i \binom{\ell}{i} (x^*)^i (y^*)^{\ell-i} \\ &= (2x^* + y^*)^\ell \\ &= (1 + x^*)^\ell. \end{aligned}$$

We get  $(1 + x^*)^\ell \geq 1$  and  $(1 + x^*)^\ell \leq e^{x^* \ell} = e^{\Theta(\frac{c\ell}{k})} = O(1)$ , because we assume  $\ell = o(kp_1/p_{\max})$ . Hence,  $(1 + x^*)^\ell = \Theta(1)$  and thus

$$\mathbb{E} \left[ 2^{d_H(s_t[B], a_j[B])} \right] = \Theta(1).$$

For the second case, we are going to focus on  $s[B_z]$ . With an analogous calculation (swapping  $x^*$  and  $y^*$ ) and noting that  $(1 + y^*)^\ell \geq (2 - \Theta(c/k))^\ell \geq (1 - o(1))2^\ell$ , because  $k = \omega(p_{\max}/p_1)$ , we get

$$(1 - o(1))2^\ell \leq \mathbb{E} \left[ 2^{d_H(s_t[B_z], a_j[B_z])} \right] \leq 2^\ell,$$

where the upper bound follows trivially from all bits being set incorrectly.

Note that the results hold for an arbitrary  $a_j$ . Overall we get

$$\begin{aligned} \mathbb{E}[f_2(s_t)] &\geq k \cdot 2^\ell - 2^\ell - \Theta(k) \geq k \cdot 2^\ell - (1 + o(1))2^\ell \text{ and} \\ \mathbb{E}[f_2(s_t)] &\leq k \cdot 2^\ell - (1 - o(1))2^\ell - \Theta(k) \leq k \cdot 2^\ell - (1 - o(1))2^\ell, \end{aligned}$$

since we assume  $k = o(2^\ell)$ .

Now we first bound the probability that  $\sum_{B \in \mathcal{B}'} 2^{d_{\text{H}}(s_t[B], a_j[B])}$  does not deviate too strongly from its mean  $\Theta(k)$ , where  $\mathcal{B}' = \mathcal{B} \setminus \{B_z\}$ , i.e., that it is in  $o(2^\ell)$ . We do so by using Chebyshev's inequality. For calculating the variance, we have

$$\text{Var} \left( \sum_{B \in \mathcal{B}'} 2^{d_{\text{H}}(s_t[B], a_j[B])} \right) = \mathbb{E} \left[ \left( \sum_{B \in \mathcal{B}'} 2^{d_{\text{H}}(s_t[B], a_j[B])} \right)^2 \right] - \mathbb{E} \left[ \sum_{B \in \mathcal{B}'} 2^{d_{\text{H}}(s_t[B], a_j[B])} \right]^2 .$$

The minuend can be split up into two cases: one, where the random variables are independent, and the other, where they are not. This results in

$$\begin{aligned} \mathbb{E} \left[ \left( \sum_{B \in \mathcal{B}'} 2^{d_{\text{H}}(s_t[B], a_j[B])} \right)^2 \right] &= \sum_{B \in \mathcal{B}'} \sum_{\substack{B' \in \mathcal{B}' \\ B' \neq B}} \mathbb{E} \left[ 2^{d_{\text{H}}(s_t[B], a_j[B])} \right] \mathbb{E} \left[ 2^{d_{\text{H}}(s_t[B'], a_j[B'])} \right] + \\ &\quad \sum_{B \in \mathcal{B}'} \mathbb{E} \left[ 4^{d_{\text{H}}(s_t[B], a_j[B])} \right] . \end{aligned}$$

Substituting this in our equation for the variance leaves us with

$$\text{Var} \left( \sum_{B \in \mathcal{B}'} 2^{d_{\text{H}}(s_t[B], a_j[B])} \right) = \sum_{B \in \mathcal{B}'} \left( \mathbb{E} \left[ 4^{d_{\text{H}}(s_t[B], a_j[B])} \right] - \mathbb{E} \left[ 2^{d_{\text{H}}(s_t[B], a_j[B])} \right]^2 \right) .$$

Using the binomial theorem, we can expand  $(1+a)^b = \sum_{i=0}^b a^i \binom{b}{i}$  and we get

$$\begin{aligned} \mathbb{E} \left[ 4^{d_{\text{H}}(s_t[B], a_j[B])} \right] - \mathbb{E} \left[ 2^{d_{\text{H}}(s_t[B], a_j[B])} \right]^2 &= (1 + 3x^*)^\ell - (1 + x^*)^{2\ell} \\ &= 1 + 3x^*\ell + O((x^*\ell)^2) - \left( 1 + 2x^*\ell + O((x^*\ell)^2) \right) = \Theta(x^*\ell) = \Theta\left(\frac{c\ell}{k}\right) , \end{aligned}$$

where  $O((x^*\ell)^2) = o(x^*\ell)$ , because  $x^*\ell = o(cp_1/p_{\max}) = o(1)$ , due to our assumptions. This results in

$$\text{Var} \left( \sum_{B \in \mathcal{B}'} 2^{d_{\text{H}}(s_t[B], a_j[B])} \right) = \Theta(c\ell) .$$

According to Chebyshev's inequality, we can now bound

$$\Pr \left( \left| \sum_{B \in \mathcal{B}'} 2^{d_{\text{H}}(s_t[B], a_j[B])} - \Theta(k) \right| \geq \Omega(2^\ell) = \Omega\left(\sqrt{c\ell} \frac{2^\ell}{\sqrt{c\ell}}\right) \right) \leq \mathcal{O}\left(\frac{c\ell}{4^\ell}\right) \leq \mathcal{O}\left(\frac{\ell p_{\max}}{4^\ell p_1}\right) .$$

For the upper concentration bound, we have to bound the probability of  $\mathbb{E} \left[ 2^{d_{\text{H}}(s_t[B_z], a_j[B_z])} \right]$  taking values in  $o(2^\ell)$ . We do not have to bound the probability of it getting too large for the lower concentration bound because we already made the maximally pessimal assumption of  $2^\ell$  in that case.

To calculate the desired probability, we use a Chernoff bound to show that it is unlikely that  $\omega(1)$  bits in  $B_z$  are set incorrectly, i.e., 1. Note that the resulting fitness would then be in  $2^{\ell - \omega(1)} = o(2^\ell)$ . Let  $X_z$  denote

the number of 0s in  $B_z$ , then  $E[X_z] = y^* \ell = \Theta(\ell)$  because  $x^* = o(1)$  due to our assumptions. We get

$$\Pr\left(X_z \leq o(\ell) = o(1)\Theta(\ell) = \left(1 - (1 - o(1))\right)\Theta(\ell)\right) \leq e^{-\frac{(1-o(1))^2 \Theta(\ell)}{2}} = e^{-\Theta(\ell)}.$$

Note that the upper concentration bound on  $\sum_{B \in \mathcal{B}'} 2^{d_H(s_t[B], a_j[B])}$  is an upper bound for this case as well. Hence, by a union bound over both events, the proof is completed.

### Rare environmental change

The following theorem looks at the fitness of the population upon environmental change that occurred after a long time  $t_{\text{mix}} \geq (2n/p_1) \ln n$ , and states that at least 2 traits will be completely maladapted, both in the case of linear and saturating fitness. We show that  $t_{\text{mix}}$  iterations are enough for SSWM to fully optimize for the current optimum  $a_j$  with probability at least  $1 - 1/n$ . If the optimum then changes to another optimum, this will result in a change of fitness from two traits, as they will be completely maladapted. Thus, the fraction of the lost fitness in both cases is  $2/k$ .

The terms  $1 - 1/n^a$  and  $1 - 1/k^a$  follow from SSWM fully optimizing for  $a_j$  during an interval of  $t_{\text{mix}}$  iterations (i.e., not failing at least once during  $a$  tries) and from the new optimum being different from the current one (i.e., not getting the same optimum during  $a$  tries), respectively.

**Theorem 9** Consider SSWM optimizing  $f_1$  or  $f_2$ , changing its current optimum  $a_j$  only after at least  $t_{\text{mix}} \geq 2n/(p_1) \ln n$  iterations. Let  $s_t$  denote the current solution of SSWM in iteration  $t$ . For any  $a \in \mathbf{N}$ , we have

$$\begin{aligned} \Pr\left(\exists t \leq a \cdot t_{\text{mix}} : f_1(s_t) \leq \overbrace{k^\ell}^{=n} - 2^\ell\right) &\geq \left(1 - \frac{1}{n^a}\right) \left(1 - \frac{1}{k^a}\right) \text{ and} \\ \Pr\left(\exists t \leq a \cdot t_{\text{mix}} : f_2(s_t) \leq k \cdot 2^\ell - 2 \cdot 2^\ell\right) &\geq \left(1 - \frac{1}{n^a}\right) \left(1 - \frac{1}{k^a}\right). \end{aligned}$$

*Proof* This proof makes use of drift theory. Hence, we define a potential over the process and then determine its expected hitting time.

Let  $X_{t'}$  denote the number of incorrectly set bits of  $s_{t'}$  (with respect to the current optimum  $a_j$ ) at time point  $t'$ , and assume that  $a_j$  has not been reached yet. Note that  $a_j$  has been reached if  $X_{t'} = 0$ , i.e.,  $X_{t'} < 1$ . We are going to bound the expected progress of  $X_{t'}$  and, thus, the expected time it takes until SSWM fully optimizes for  $a_j$ . Note that  $X_{t'+1} \leq X_{t'}$  holds because we cannot get worse in fitness.

$$E[X_{t'} - X_{t'+1} \mid X_{t'}] = E[X_{t'} - X_{t'+1} \mid X_{t'}, X_{t'} > X_{t'+1}] \geq \frac{X_{t'}}{n} \cdot p_1,$$

as we have a chance of  $X_{t'}/n$  to mutate one incorrectly set bit, and accept the mutation with probability at least  $p_1$ . The resulting change in potential is always 1, as we can only change exactly one bit.

Using the multiplicative drift theorem (Theorem 3), we bound the expected time  $T$  until  $X_t = 0$ , given that SSWM started with an individual having  $O(n)$  bits set incorrectly at an earlier point in time  $t''$ :

$$\mathbb{E}[T \mid X_{t''}] \leq \frac{1 + \ln(X_{t''})}{\frac{p_1}{n}} \leq 2 \frac{n}{p_1} \ln n .$$

We now upper-bound the probability that SSWM will *not* have fully optimized for  $a_j$  in  $t_{\text{mix}}$  iterations, using Theorem 4. By choosing  $c = \ln n$ , we get

$$\Pr \left( T > 2 \frac{n}{p_1} \ln n \geq \frac{c + \ln X_{t''}}{\frac{p_1}{n}} \mid X_{t''} \right) \leq e^{-\ln n} = \frac{1}{n} .$$

This concludes the proof.

### S3.5 Scenario 3: Adaptations in different environments are completely antagonistic.

#### *Frequent environmental change*

In the following lemma, we state and prove the probability of having a specific allele at each locus if the environment changes frequently. We define  $p_1$  to be the smallest and  $p_{\text{max}}$  to be the largest probability of a positive mutation fixing in the population, while  $p_0$  is the probability of a neutral mutation fixing. The theorem states that in the case of equal fitness contribution of all mutations ( $p_1 = p_{\text{max}}$ ), the probability that a given allele is adapted to the current optimum is  $1/k$ . For the more general scenario ( $p_1 \neq p_{\text{max}}$ ), we give a probability interval of having a particular fraction of alleles adapted to the current optimum.

**Lemma 3** *Consider SSWM with  $p_{\text{max}} \leq kp_1 + (k-1)(k-2)p_0$  optimizing a monotone function  $f$  that changes its optimum each iteration. After at least  $\Omega\left(nk/(p_{\text{max}} + (k-2)p_0) \log\left(nk(p_{\text{max}} + (k-2)p_0)/(p_1 + (k-2)p_0)\right)\right)$  iterations, for each  $i \in \{1, \dots, n\}$ , for the probability  $x^*$  to have a specific value  $j \in \{1, \dots, k\}$  at position  $i$ , we have*

$$\frac{1}{k} \cdot \frac{p_1 + (k-2)p_0}{p_{\text{max}} + (k-2)p_0} \leq x^* \leq \frac{1}{k} \cdot \frac{p_{\text{max}} + (k-2)p_0}{p_1 + (k-2)p_0}$$

and, for the probability  $y^*$  to have another value at position  $i$ , we have

$$1 - \frac{1}{k} \cdot \frac{p_{\text{max}} + (k-2)p_0}{p_1 + (k-2)p_0} \leq y^* \leq 1 - \frac{1}{k} \cdot \frac{p_1 + (k-2)p_0}{p_{\text{max}} + (k-2)p_0} .$$

*Proof* This proof is similar to the one of Lemma 2. We are, again, going to use Lemma 1 and consider a two-state Markov chain (cf. Figure S11). Consider a value  $j \in \{1, \dots, k\}$ . State 0 of the Markov chain means that component  $i$  of the momentary solution is  $j$ , and state 1 means that the component is not  $j$ .

Consider  $x$ , i.e., the probability that component  $i$  is not  $j$ , given that it was  $j$ . For this to happen, component  $i$  has to be chosen for mutation, mutated to another value than  $j$ , and the current optimum must not be  $a_j$ , since else the mutated individual would not be accepted.

Assuming that the current optimum is not  $a_j$ , the mutated individuals gets accepted with probability at least  $p_1$  and at most  $p_{\max}$  if the new value of the mutated component is the same as the current optimum, and it gets accepted with probability  $p_0$  if the value is different from the current optimum. Hence, we get

$$\begin{aligned} x &\geq \frac{k-1}{k} \cdot \frac{1}{n} \cdot \frac{1}{k} p_1 + \frac{k-1}{k} \cdot \frac{1}{n} \cdot \frac{k-2}{k} p_0 = \frac{k-1}{k} \cdot \frac{1}{n} \left( \frac{1}{k} p_1 + \frac{k-2}{k} p_0 \right) \text{ and} \\ x &\leq \frac{k-1}{k} \cdot \frac{1}{n} \left( \frac{1}{k} p_{\max} + \frac{k-2}{k} p_0 \right). \end{aligned}$$

Analogously, we can compute  $y$  as follows:

$$\begin{aligned} y &\geq \frac{1}{k} \cdot \frac{1}{n} \cdot \frac{1}{k} p_1 + \frac{k-2}{k} \cdot \frac{1}{n} \cdot \frac{1}{k} p_0 = \frac{1}{k} \cdot \frac{1}{n} \left( \frac{1}{k} p_1 + \frac{k-2}{k} p_0 \right) \text{ and} \\ y &\leq \frac{1}{k} \cdot \frac{1}{n} \left( \frac{1}{k} p_{\max} + \frac{k-2}{k} p_0 \right). \end{aligned}$$

Applying Lemma 1 leads to

$$\begin{aligned} \frac{1}{k} \cdot \frac{p_1 + (k-2)p_0}{p_{\max} + (k-2)p_0} &\leq x^* \leq \frac{1}{k} \cdot \frac{p_{\max} + (k-2)p_0}{p_1 + (k-2)p_0}, \\ 1 - \frac{1}{k} \cdot \frac{p_{\max} + (k-2)p_0}{p_1 + (k-2)p_0} &\leq y^* \leq 1 - \frac{1}{k} \cdot \frac{p_1 + (k-2)p_0}{p_{\max} + (k-2)p_0}, \text{ and} \\ \tau(\varepsilon) &= O\left( \frac{nk}{p_1 + (k-2)p_0} \log\left( \frac{k}{\varepsilon} \cdot \frac{p_{\max} + (k-2)p_0}{p_1 + (k-2)p_0} \right) \right), \end{aligned}$$

where  $x^* \leq 1$  if  $p_{\max} \leq kp_1 + (k-1)(k-2)p_0$ .

For any  $\varepsilon = \Omega(1/\text{poly}(n)) < 1$ , we get  $\tau(\varepsilon) = O\left( nk/(p_1 + (k-2)p_0) \log\left( nk(p_{\max} + (k-2)p_0)/(p_1 + (k-2)p_0) \right) \right)$ .

The following theorem states that if all new positive mutation contribute equally to the fitness and fix with equal probability ( $p_1 = p_{\max}$ ), the expected number of adapted loci is  $\ell$ , thus a  $1/k$  fraction of all loci, regardless of the trait they belong to.

**Theorem 10** *Consider SSWM optimizing  $f_1$ , changing its current optimum  $a_j$  every iteration. Let  $s_t$  denote the current solution of SSWM in iteration  $t$ , and let  $k^*(u, v) = k - (u+1) + (u+v)/k$ . After at least  $t_{\text{mix}} = \Omega(nk/(p_1 + (k-2)p_0) \log(nk))$  iterations, for any  $\varepsilon = \Omega(1/\text{poly}(n)) < 1$  and any  $t^* \geq t_{\text{mix}}$ , it holds, for any constant  $\delta > 0$ ,*

$$\Pr\left(\exists t, t_{\text{mix}} \leq t \leq t^*: f_1(s_t) \geq (1+\delta)(1+\varepsilon)\ell k^*(1-\varepsilon, 1)\right) \leq (t^* - t_{\text{mix}} + 1)e^{-\frac{\delta^2 \ell k^*(1+\varepsilon, 1+\varepsilon)}{3}}$$

and, for any constant  $0 < \delta < 1$ ,

$$\Pr\left(\exists t, t_{\text{mix}} \leq t \leq t^*: f_1(s_t) \leq (1 - \delta)(1 - \varepsilon)\ell k^*(1, 1)\right) \leq (t^* - t_{\text{mix}} + 1)e^{-\frac{\delta^2 \ell k^*(1 + \varepsilon, 1 + \varepsilon)}{2}}.$$

*Proof* This proof is completely analogous to the one from Theorem 7, the only difference being the mixing time. Because  $p_{\text{max}} = p_1$  when optimizing  $f_1$ , we get  $x^* = 1/k$ . From then on, all following calculations are exactly the same because the limit distribution is the same.

The following theorem states that if the fitness contribution of new positive mutations diminishes and, as a consequence, they are less likely to fix in the population ( $p_1 < p_{\text{max}}$ ), after a sufficiently long time  $t_{\text{mix}}$ , the expected fitness of the population is concentrated around  $k(1 - o(1))2^\ell$ , where  $o(1)$  describes a term that goes to 0 as  $n$  goes to infinity.

**Theorem 11** Let  $d = (p_{\text{max}} + (k - 2)p_0)/(p_1 + (k - 2)p_0)$ . Consider SSWM optimizing  $f_2$  with  $\ell = o(kd^{-1})$  and  $k = \omega(d)$ , changing its current optimum  $a_j$  every iteration. Let  $s_t$  denote the current solution of SSWM in iteration  $t$ . After at least  $t_{\text{mix}} = \Omega(nk/(p_{\text{max}} + (k - 2)p_0) \log(nkd))$  iterations, for any  $\varepsilon = \Omega(1/\text{poly}(n)) < 1$  and any  $t^* \geq t_{\text{mix}}$ , it holds, for any constant  $\delta > 0$ ,

$$\Pr\left(\exists t, t_{\text{mix}} \leq t \leq t^*: f_2(s_t) \geq k(1 - o(1))2^\ell\right) \leq (t^* - t_{\text{mix}} + 1)e^{-\Theta(\ell)}$$

and, for any constant  $0 < \delta < 1$ ,

$$\Pr\left(\exists t, t_{\text{mix}} \leq t \leq t^*: f_2(s_t) \leq (1 - \delta)2^{\ell-1} \frac{\ell}{d}\right) \leq (t^* - t_{\text{mix}} + 1)O\left(\frac{d}{\ell}\right).$$

*Proof* This proof is similar to the one of Theorem 8. We assume that already  $t_{\text{mix}}$  rounds have passed. Let  $x'$  be an approximation of  $x^*$  up to a factor of  $1 \pm \varepsilon$  for any  $\varepsilon = \Omega(1/\text{poly}(n)) < 1$ , i.e.,  $x' = c/k$ , where  $c \in [(1 - \varepsilon)d^{-1}, (1 + \varepsilon)d]$ . Further, let  $y' = 1 - x'$ . As before, we only provide the calculations for a single  $t \geq t_{\text{mix}}$ . The Theorem then follows by applying a union bound.

Let  $a_j$  be an arbitrary optimum. We then get:

$$\begin{aligned} \mathbb{E}[f_2(s_t)] &= \mathbb{E}\left[k \cdot 2^\ell - \sum_{B \in \mathcal{B}} 2^{d_{\text{H}}(s_t[B], a_j[B])}\right] \\ &= k \cdot 2^\ell - \sum_{B \in \mathcal{B}} \mathbb{E}\left[2^{d_{\text{H}}(s_t[B], a_j[B])}\right]. \end{aligned}$$

As in the proof of Theorem 8, we want to bound  $\mathbb{E}\left[2^{d_{\text{H}}(s_t[B], a_j[B])}\right]$ . For this, note that  $2^{d_{\text{H}}(s_t[B], a_j[B])}$  is a binomially distributed random variable with success probability  $y'$ , i.e., with probability  $y'$ , a single value is set

incorrectly. Thus, we get

$$\begin{aligned}
\mathbb{E} \left[ 2^{d_{\text{H}}(s_t[B], a_j[B])} \right] &= \sum_{i=0}^{\ell} 2^i \binom{\ell}{i} (y')^i (x')^{\ell-i} \\
&= (2y' + x')^{\ell} \\
&= (1 + y')^{\ell} \\
&= (2 - x')^{\ell} \\
&= \sum_{i=0}^{\ell} \binom{\ell}{i} 2^{\ell-i} (-x')^i,
\end{aligned}$$

where we used the binomial theorem twice and that  $x' + y' = 1$ . Expanding the first two terms of the sum leads to

$$(2 - x')^{\ell} = 2^{\ell} - 2^{\ell-1}(x'\ell) + \sum_{i=2}^{\ell} \binom{\ell}{i} 2^{\ell-i} (-x')^i.$$

We first upper-bound this term. Note that  $x'\ell = o(1)$ , due to our assumptions. Thus,  $(x'\ell)^{i+1} = o((x'\ell)^i)$  for all  $i > 1$ .

$$\begin{aligned}
(2 - x')^{\ell} &\leq 2^{\ell} - 2^{\ell-1}(x'\ell) + \Theta(x'\ell) \sum_{i=0}^{\ell-2} 2^i (x'\ell)^i \\
&\leq 2^{\ell} - 2^{\ell-1}(x'\ell) + o(1)2^{\ell-1}(x'\ell) \\
&= 2^{\ell} - (1 - o(1))2^{\ell-1}(x'\ell).
\end{aligned}$$

For our lower bound, we proceed analogously:

$$\begin{aligned}
(2 - x')^{\ell} &\geq 2^{\ell} - 2^{\ell-1}(x'\ell) - \Theta((x'\ell)^{\ell/2-1}) \sum_{i=0}^{\ell-2} 2^i (x'\ell)^i \\
&\geq 2^{\ell} - 2^{\ell-1}(x'\ell) - o(1)2^{\ell-1}(x'\ell) \\
&= 2^{\ell} - (1 + o(1))2^{\ell-1}(x'\ell).
\end{aligned}$$

Combining both cases, we get:

$$2^{\ell} - (1 + o(1))2^{\ell-1}(x'\ell) \leq \mathbb{E} \left[ 2^{d_{\text{H}}(s_t[B], a_j[B])} \right] \leq 2^{\ell} - (1 - o(1))2^{\ell-1}(x'\ell).$$

This results in the following bounds for the expected fitness of  $s_t$ :

$$k(1 - o(1))2^{\ell-1}(x'\ell) \leq \mathbb{E}[f_2(s_t)] \leq k(1 + o(1))2^{\ell-1}(x'\ell).$$



For the lower concentration bound, we want to apply Chebyshev's inequality, as in the proof of Theorem 8. Deriving the variance is completely analogous to that proof, hence we have

$$\text{Var} \left( \sum_{B \in \mathcal{B}} 2^{d_{\text{H}}(s_t[B], a_j[B])} \right) = \sum_{B \in \mathcal{B}} \left( \mathbb{E} \left[ 4^{d_{\text{H}}(s_t[B], a_j[B])} \right] - \mathbb{E} \left[ 2^{d_{\text{H}}(s_t[B], a_j[B])} \right]^2 \right).$$

We now bound the difference to bound the variance, using the binomial theorem multiple times, as we did before.

$$\begin{aligned} \mathbb{E} \left[ 4^{d_{\text{H}}(s_t[B], a_j[B])} \right] - \mathbb{E} \left[ 2^{d_{\text{H}}(s_t[B], a_j[B])} \right]^2 &= (1 + 3y')^\ell - (1 + y')^{2\ell} \\ &= (4 - 3x')^\ell - (2 - x')^{2\ell} \\ &= 4^\ell - 3 \cdot 4^{\ell-1}(x'\ell) \pm o(1)4^\ell(x'\ell) \\ &\quad - (4^\ell - 4^\ell(x'\ell) \pm o(1)4^\ell(x'\ell)) \\ &= \Theta(4^\ell(x'\ell)). \end{aligned}$$

This gives us

$$\text{Var} \left( \sum_{B \in \mathcal{B}} 2^{d_{\text{H}}(s_t[B], a_j[B])} \right) = \Theta(k \cdot 4^\ell(x'\ell)) = \Theta(4^\ell c\ell).$$

We now bound the probability of  $\sum_{B \in \mathcal{B}} 2^{d_{\text{H}}(s_t[B], a_j[B])}$  getting into the dimensions of  $k(1 + \delta)2^{\ell-1}(x'\ell) \geq (1 + \delta)2^{\ell-1}(\ell/d)$ , where  $\delta > 0$  is a constant. Since the expected value of  $\sum_{B \in \mathcal{B}} 2^{d_{\text{H}}(s_t[B], a_j[B])}$  is in the order of  $(1 \pm o(1))2^{\ell-1}(x'\ell)$ , the difference to that has to be in the order of  $\delta k 2^{\ell-1}(x'\ell) = \Omega(k \cdot 2^\ell(x'\ell)) = \Omega(2^\ell c\ell)$ .

$$\begin{aligned} \Pr \left( \left| \sum_{B \in \mathcal{B}} 2^{d_{\text{H}}(s_t[B], a_j[B])} - k(1 + o(1))2^{\ell-1}(x'\ell) \right| \geq \Omega(2^\ell c\ell) = \Omega(2^\ell \sqrt{c\ell} \sqrt{c\ell}) \right) &\leq O\left(\frac{1}{c\ell}\right) \\ &\leq O\left(\frac{d}{\ell}\right). \end{aligned}$$

For the upper concentration bound, let  $X_w$  denote the number of values in a single block  $B \in \mathcal{B}$  that differ from the current optimum, i.e., the number of wrong values. Only if the value of  $X_w$  for each block is sufficiently small, the expected fitness of  $s_t$  can be in the order of  $(k - o(1))2^\ell$ . To get to this value, per block,  $X_w$  has to be in the order of  $o(\ell)$  since then the contribution of this block subtracts at most  $2^{o(\ell)}$  from the fitness. We use a Chernoff bound to bound this probability. Note that  $\mathbb{E}[X_w] = y'\ell = \Theta(\ell)$  because  $x' = o(1)$ , due to our assumptions.

$$\Pr \left( X_w \leq o(\ell) = o(1)\Theta(\ell) = \left(1 - (1 - o(1))\right)\Theta(\ell) \right) \leq e^{-\frac{(1 - o(1))^2 \Theta(\ell)}{2}} = e^{-\Theta(\ell)}.$$

The upper bound follows from only considering a single block.

*Rare environmental change*

In the following theorem, we show that  $t_{\text{mix}} \geq (2nk/p_1) \ln n$  iterations are enough for SSWM to fully optimize for the current optimum. If the optimum then changes to another optimum, all loci will be maladapted, both in the case of linear and saturating fitness.

**Theorem 12** *Consider SSWM optimizing  $f_1$  or  $f_2$ , changing its current optimum  $a_j$  only after at least  $t_{\text{mix}} \geq 2nk/(p_1) \ln n$  iterations. Let  $s_t$  denote the current solution of SSWM in iteration  $t$ . For any  $a \in \mathbf{N}$ , we have*

$$\begin{aligned} \Pr\left(\exists t \leq at_{\text{mix}} : f_1(s_t) = 0\right) &\geq \left(1 - \frac{1}{n^a}\right) \left(1 - \frac{1}{k^a}\right) \text{ and} \\ \Pr\left(\exists t \leq at_{\text{mix}} : f_2(s_t) = 0\right) &\geq \left(1 - \frac{1}{n^a}\right) \left(1 - \frac{1}{k^a}\right). \end{aligned}$$

*Proof* This proof is similar to the one of Theorem 9, and we are going to use the same notation. We get

$$\mathbb{E}[X_{t'} - X_{t'+1} \mid X_{t'}] = \mathbb{E}[X_{t'} - X_{t'+1} \mid X_{t'}, X_{t'} > X_{t'+1}] = \frac{X_{t'}}{n} \frac{1}{k} p_1,$$

where the  $1/k$  factor is due to the mutation choosing the correct out of the  $k$  different values.

Using the multiplicative drift theorem, we bound the expected time  $T$  until  $X_{t'} = 0$ , given that SSWM started with an individual having  $O(n)$  components set incorrectly at an earlier point in time  $t^*$ :

$$\mathbb{E}[T \mid X_{t^*}] \leq \frac{1 + \ln(X_{t^*})}{\frac{p_1}{nk}} \leq 2 \frac{nk}{p_1} \ln n.$$

Bounding the probability of SSWM *not* fully optimizing for  $a_j$  completes the proof:

$$\Pr\left(T > 2 \frac{nk}{p_1} \ln n \geq \frac{\ln n + \ln X_{t''}}{\frac{p_1}{nk}} \mid X_{t''}\right) \leq e^{-\ln n} = \frac{1}{n}.$$

## S3.6 Simulations of multitrait scenarios with saturating fitness

Simulations for saturating fitness for a range of  $\tau$  are shown below. We carried out simulations for small values of  $k = 5$  and  $\ell = 10$ , as well as larger ones with  $k = 10$  and  $\ell = 20$ . Both cases used threats changing in random order. In the first case, we did not see any qualitative difference between the effect of saturating and linear fitness functions (see Figure 7). However, in the second case, we observed that the achieved level of adaptation was greatly reduced and differed from the analytical results obtained for the linear fitness function, even when a lower probability of fixation was assumed (Figure S12).

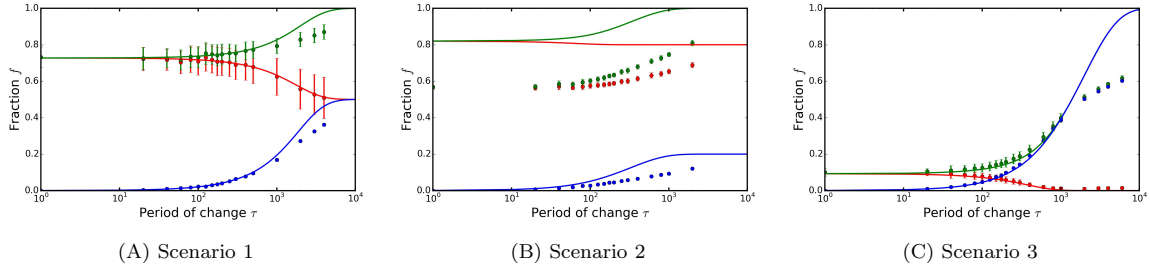


Fig. S12: Dependence of the level of adaptation (fraction of adapted alleles) on the period of environmental change. Green depicts the expected maximum, red the expected minimum, blue the size of oscillations. Dots depict simulation results. Mean and standard deviation of 200 periods, taken after stable oscillations were achieved.  $k = 10$ ,  $\ell = 20$ ,  $N = 100$ . Lines depict analytical results for the linear scenario assuming A)  $p = 0.15$ , B)  $p = 0.6$ , C)  $p = 0.9$ .

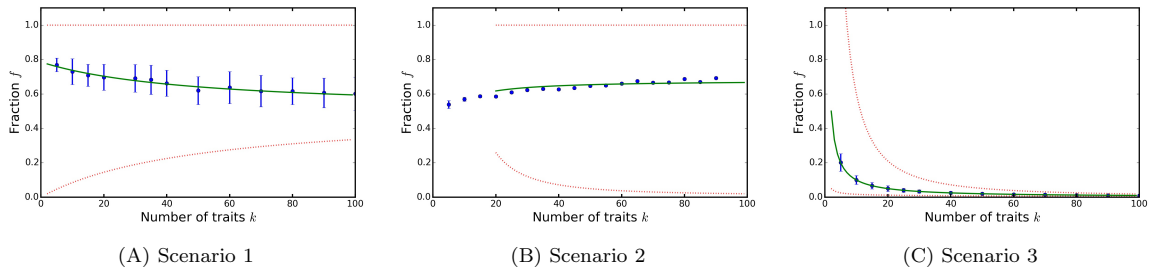


Fig. S13: Dependence of the level of adaptation (fraction of adapted alleles) on the number of traits. Blue dots depict simulation results. Mean and standard deviation of 200 trials.  $\ell = 20$ ,  $N = 100$ . Red dotted lines depict lower and upper bounds. Green lines are fitted using the lower bounds and probability of fixation A)  $p_{1\text{eff}} = 0.78$ , B)  $p_{1\text{eff}} = 0.68$ , C)  $p_{1\text{eff}} = 1$ .

### S3.7 Summary of model assumptions

As mentioned throughout the main article and the supplementary material, we made several assumptions in order to derive our results. We summarise them here again to assist the reader.

The model assumes the following:

- Monomorphic population with constant size  $N$ .
- Haploid genome of length  $n$ . It is not necessary that  $n$  is the total size of the genome, but that  $n$  is the total number of loci under consideration. However, we assume that mutation rate is  $1/n$ .
- Strong selection and probability of fixation of positive mutations ( $p$ ).
- Mutations are rare when compared with generation time and the time necessary for the fixation of positive mutations.
- Generation time is short compared to frequency of environmental changes
- Each trait is affected by multiple loci  $\ell$ . Fitness is affected by  $k$  multiple traits (subject to scenarios), and  $k\ell = n$ .

### S3.8 Simulations

All simulations were programmed in Python. The code is available on GitHub under <https://goo.gl/k7eqzX>.

#### *Main simulations*

We carried out 3 main simulations, that were identical for each scenario except for: definitions of genotypes (biallelic loci in the first two scenarios,  $k$  alleles in the third one); corresponding mutation definitions; and the calculation of fitness.

*Simulations for variable  $\tau$*  The aim of these simulations was to find the expected minimum and the maximum level of adaptation (fitness, or fraction of adapted alleles) when environment changes every  $\tau$  iterations. After initialization, the population was allowed to adapt in a fluctuating environment for sufficiently long time, until it reached stable oscillations in fitness. This time depended on  $k$  and  $\ell$ , as longer and more numerous traits took longer to adapt to this stable level. After stabilization, the minimum level of adaptation (just after environmental change) and the maximum level (just before the change) were recorded. Means for both the minimum and the maximum levels of adaptation were calculated from 200 records.

*Simulations of frequent environmental change* We run simulations for frequent environmental change, when environment changes every iteration  $\tau$ , for varying parameters  $k$  and  $\ell$ . After initialization, the population was allowed to adapt in a frequently changing environment for a sufficiently long time, until it reached a stable level of adaptation. This time depended on  $k$  and  $\ell$ , as longer and more numerous traits took longer to adapt to this stable level. After stabilization, values of the level of adaptation were recorded for 1000 cycles (iterations). Calculated mean was compared to analytical results.

*Simulations of rare environmental change* The aim of these simulations was to find the time necessary to achieve complete adaptation to the given environment. After initialization, the population was allowed to adapt in a stable environment using SSWM algorithm (A.1), for as long as it was necessary to achieve the full adaptation. Due to the stochasticity of the SSWM algorithm, we simulated 100 trials for each given parameter set. The number of iterations was recorded for each trial and mean was compared to the analytically calculated expectations.

#### *Generalizations*

*Stochastic environment - generalization* In our main simulations, environment varied in a regular manner (different threats followed a defined order). To make the simulations more realistic, we added stochasticity into the order of threats and simulated variable  $\tau$  and frequent environmental change as described above.

*Saturating fitness generalization* In the final generalization, we replaced linear fitness function in each scenario by the saturating one, as described in section S3.2. Then we carried out simulations for variable  $\tau$ , rare and frequent environmental change, as described above.

### S3.9 Extinction simulations

As we discussed in the main manuscript, our theoretical results suggest that under some circumstances, rapid environmental fluctuations can prevent population from extinction, that would occur if the environmental changes were less frequent. This is most likely when long time period lead to high fitness loss upon environmental change, such as in Scenario 3. Below, we simulate and analyse a few examples of this scenario. Simulations below are intended to serve as an illustration and a proof that such scenarios may occur. We do not provide extensive analysis of such events, as it is out of scope of our manuscript. However, we list detailed description of additional parameters that should be investigated in future studies below.

We simulated evolving populations in Scenario 3 with linear fitness as described above. However, population size was not kept constant, but changing according to the population fitness in a given time. If the fitness was above a given threshold  $Thr$ , population increased by 1, if it was below, it decreased by 1 and remained the same otherwise. Furthermore, population size change affected the probability of fixation of new mutations. For each parameter set, we simulated 20 times 50 trials and recorded the fraction of simulations that lead to extinction for a given parameter set. Examples of simulation runs (evolving fitness and changing population size) are shown in figure S14. Note that the time scale is in iterations, thus, this change of the population size is very slow in generation time.

Figure S15 A shows the dependence of the extinction rate on  $\tau$  for different values of  $k$  and  $\ell$ , assuming threshold for population growth rate  $Thr = 1/(k + 2)$ . As predicted, populations are more likely to become extinct if the environmental change is slow. If the environmental change is frequent, populations can survive in the changing environment. Figure S15 B shows the dependence of the extinction rate on threshold  $Thr$ . A small change in the threshold leads to dramatically increased extinction rate. However, frequent environmental change enable at least some populations to survive.

Below, we list multiple functions and variables that affect the resulting simulations and should be investigated in detail in the future studies.

- Initial size and the level of adaptation of the population: If the initial population size is too small, or the initial level of adaptation is too small, extinction is more likely to occur as the population does not have time to adapt before becoming extinct. In our simulations, we used initial population size of 100 individuals.
- Carrying capacity: If the population reaches the carrying capacity of the environment, it can no longer grow even if the population is fully optimized for the given condition. Upon environmental change, decreased

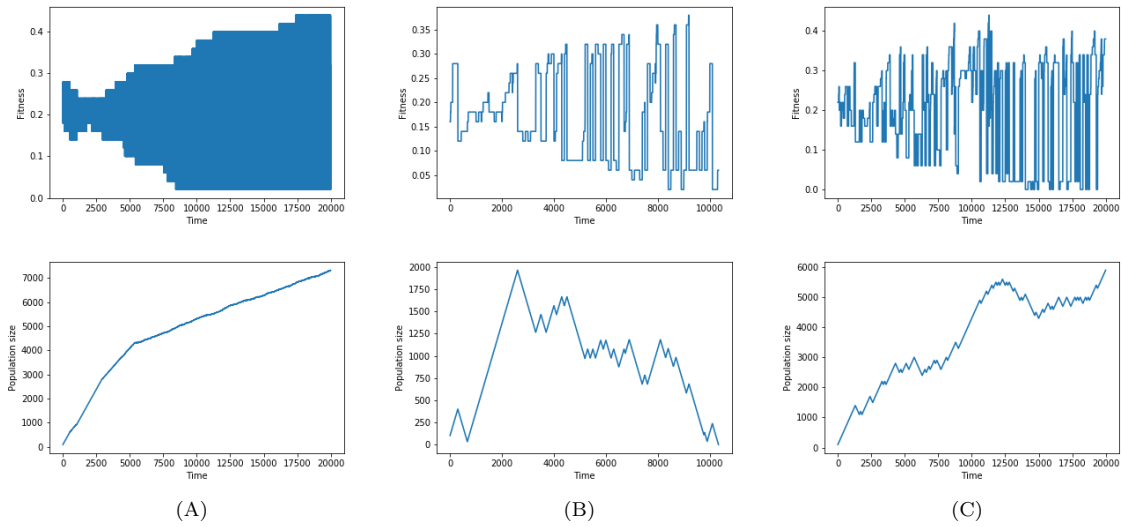


Fig. S14: Examples of simulation of evolving population. Fluctuating fitness (top) and changing population size (bottom).  $k = 5$ ,  $\ell = 10$ ,  $Thr = 1/(k + 2)$ . Starting population size  $N_0 = 100$ . A:  $\tau = 1$ , B:  $\tau = 100$ , C:  $\tau = 100$

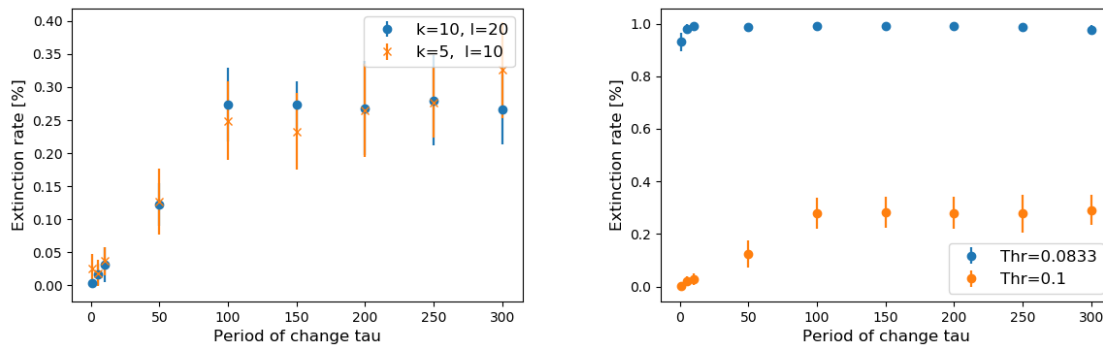


Fig. S15: Extinction rate depends on the length of the period  $\tau$ , as well as growth rate function. Starting population size  $N_0 = 100$ .

fitness will cause the population shrink, until it adapts sufficiently. However, if the carrying capacity is small, it can become extinct before adapting. Larger carrying capacity will create a buffer and may prevent population from extinction. We expect that surviving in an environment with a small carrying capacity will require more frequent environmental changes. In our simulations we considered unlimited carrying capacity of the environment.

- Dependence of the population growth rate on fitness: Fitness as defined in our model depends on the number of loci adapted to the current environment. It is necessary to determine how this definition translates into the number of offspring, or population growth rate. In our simulation, we used the simplest definition: If the fitness was about a given threshold, population increased by 1, while if it was below, it decreased by

- 1, otherwise it remained the same. This threshold was set to  $1/(k + 2)$ . However, many other functions are possible and reasonable to use, for instance growth rate proportional to fitness.
- Dependence of population on the size of the population. We assumed constant population growth rate, thus linear growth of the population. Exponential, or logistic growth would be reasonable options to use, depending on the modeled species.

### S3.10 Available data

Complete simulations described above take long time and need multiple repetitions. Therefore, partial results of the simulations are available upon request. These raw data are available as text files and contain complete information from each trial: fitness and fractions of adapted alleles, total number of alleles of different types, and many other, for each iteration of each trial.