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It doesn't always pay to be fit: success landscapes

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Abstract
Landscapes play an important role in many areas of biology, in which biological lives are deeply entangled. Here we discuss a form of landscape in evolutionary biology which takes into account (1) initial growth rates, (2) mutation rates, (3) resource consumption by organisms, and (4) cyclic changes in the resources with time. The long-term equilibrium number of surviving organisms as a function of these four parameters forms what we call a success landscape, a landscape we would claim is qualitatively different from fitness landscapes which commonly do not include mutations or resource consumption/changes in mapping genomes to the final number of survivors. Although our analysis is purely theoretical, we believe the results have possibly strong connections to how we might treat diseases such as cancer in the future with a deeper understanding of the interplay between resource degradation, mutation, and uncontrolled cell growth.

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Guest Editors: Robert Austin, Shyamsunder Erramilli, Sonya Bahar

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1 Introduction

Never say "first." Somebody has always been there before you. One of the authors, RHA, got into hot water at a talk he was giving among experts on protein folding. He pointed out that it wasn't the protein folding experts, or even his thesis advisor Hans Frauenfelder (who has definitely been one of the pioneers of the concept of protein energy landscapes [1–3]), who has been the "first" to exploit the concept of landscapes in biology. We hope Professor Frauenfelder will not be upset to hear that one of the *very early* exponents of the utility of landscapes in quantitative evolutionary biology was Sewall Wright with his idea of fitness landscapes [4].

Others in this volume will give Hans Frauenfelder the credit he deserves for protein energy landscapes, so let's take a walk several levels up in biological complexity and look at fitness landscapes. Simply put, a fitness landscape as originally defined was a map between variations in the genotype of an organism and variations in the growth rate, for a given environment [5]. Peaks in a fitness landscape represent genotypes which give the highest growth rates, and valleys represent the lowest growth rates, even negative growth [6]. In some sense, a fitness landscape is inverted from the normal physicist's free-energy landscape such as for proteins, where low-lying free energies are most likely places for a protein structure, so beware. Wright showed how evolutionary dynamics could be graphically visualized on a fitness landscape by movement on the landscape as the genome changed [4].

Wright analyzed how genetic heterogeneity and metapopulation numbers could explain many aspects of evolution, including the speed of evolution and the way population substructure and genetic drift could allow evolution from a lower to a higher peak of the fitness landscape.

But in this article, we will be most concerned with the *limitations* of Wright's fitness landscape in understanding evolutionary dynamics, and propose the replacement of the fitness landscape with the success landscape. Unlike a fitness metric which values reproduction rates we will stress that a high growth rate also can result in more resource consumption, thus there is a cost for too high a fitness. This implies that high reproduction rates can get selected out due to the subsequent degradation of resources with time. Further, we will discuss how mutations can be both too fast and too slow depending on growth rates and resource impacts, highlighting the hidden complexities in Wright's intuitively appealing fitness landscape.

As we noted, fitness is defined by biologists as the reproduction rate of an organism: the faster you reproduce, the more fit you are [6]. The fundamental act of reproduction of offspring in biology means that after a discrete time step $\Delta t = 1$, or generation, an individual will be replaced by a number of w individuals:

$$N(t + 1) = wN(t) , \tag{1}$$

where w is defined as the absolute fitness. If $w > 1$, then a population has a higher fitness and conversely if $w < 1$, then the population will decrease with time and is doomed. In the continuum limit of time, we can approximate:

$$\partial_t N(t) = gN(t) , \tag{2}$$

where we identify the growth rate to be $g = \ln(w)$ [7]. For $w \to 0$ then $g \to -\infty$.

Of course growth can't go on forever, even for Ponzi schemes [8]. Natural environments have limited resources, and the *logistic* model of population growth incorporates

this fact. As the population grows toward the carrying capacity, effectively birth rates decline or death rates increase. The simplest differential equation that expresses this self-limiting growth is called the logistic equation [9]. In the simplest form of the logistic equation, the initial growth rate is modified by a fixed number N_c, the individual carrying capacity of the environment:

$$\partial_t N = g\left(1 - \frac{N}{N_c}\right)N \,, \tag{3}$$

This can be solved analytically to get:

$$N(t) = \frac{N(0)e^{gt}}{1 - \frac{N(0)}{N_c}(1 - e^{gt})} \,. \tag{4}$$

$N(t)$ is a sigmoidal curve: the initial portion of the curve is exponential in time with growth rate g (assuming $N(0) \ll N_c$) but folds over as the carrying capacity N_c of the environment is reached, with final growth rate at $t \to \infty$ approaching 0. Note that for the logistic equation as written having greater fitness simply increases the rate at which you reach the carrying capacity, but it does not change the carrying capacity N_c!

Of course, having a fixed carrying capacity is far too simple. It assumes that the carrying capacity N_c of the environment is some number, that the fitness w of the species does not change with the number of individuals $N(t)$, that the growth occurs in a spatially uniform environment and completely ignores genetic evolution, which would make w a function of both time and the number of individuals as the genotype changes in response to random mutations and stress-induced mutations.

As we stated, an important early idea which improved upon simple logistic growth was the fitness landscape of Wright in [4]. Figure 1 shows Wright's simplified model. In this model, only two genes are present as the x and y axes, but related mutational patterns exist within a metapopulation (a large population consisting of many small related populations). The metapopulation, representing a heterogenous but interconnected genetic space, then maps onto a complex fitness landscape.

There is a great deal of information in Fig. 1. A key panel is the upper right corner, Fig. 1C, which represents Wright's realization that if the environment changes, as shown by the different fitness contours from center Subfigure 1B, that a highly adapted population is in extreme danger of going extinct since it is so far from the new genetic fitness maximum. We will not extensively discuss in this paper the lower right-hand corner, Fig. 1F, which represents Wright's mechanism of enhanced evolution via a heterogenous genomic distribution of quasi-species.

While Wright's approach is clearly better than the simplest logistic equation, in that it allows fitness to vary with individuals within the metapopulation (shown in his panel Fig. 1F , his approach assumes that only a pre-existing heterogenous genomic distribution given by m_i can sustain a metapopulation with rapid environmental change. Wright was deeply concerned with evolution dynamics from a purely genetic level [10].

However, in terms of resources surely more individuals/area must degrade the local environment, and thus the carrying capacity must be a function in the case of a metapopulation of the number of agents n_i in the i-th subpopulation, and even influence the mutation rate due to high stresses as resources decline [11]. The interplay between resources, populations that exploit the resources, and evolution remains a very difficult problem [12].
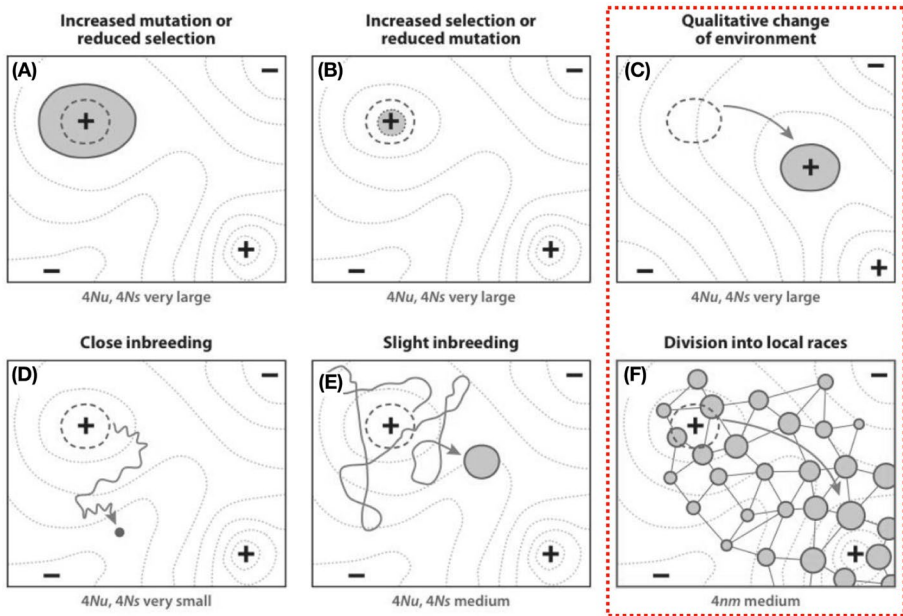
Fig. 1 The fitness landscape as a function of two genes as a function of population size N, mutation rate u and selection pressure s (adapted from Wright [4]). We only concern ourselves here with panel (**C**) and (**F**)

However, we cannot ignore the problem of resource exploitation for it is certainly true that organisms DO degrade and exploit their resources, they must to survive. Thus, there must be another important landscape beneath the fitness landscape, the "deformable" resource landscape, very broadly defined, whose surface can be changed by externally imposed elements and the time and spatially dependent density of the organisms.

The number of dimensions in these landscapes is also a major factor. For a complex organism such as *Homo sapiens*, each multi-dimensional (20,000 dimensions corresponding to 20,000 genes) voxel of Wright's "fitness" landscape (genetic) maps from a high-dimensional resource landscape. The resource landscape is basically a collective metabolomic landscape but has other aspects as well as those which control how gene phenotypes determine the ultimate number of surviving agents.

This sounds horribly complicated, and it is, but one should not give up! Many of the dimensions (genes) are really points as per fixed N_c values in the logistic equation, i.e., mutating them has little effect. Presumably we can derive some useful features of these landscapes by considering only a few dimensions that are dominant in determining survival.

2 Theoretical considerations of toy success landscapes

We assume four factors determine success: (1) growth, (2) the commonly assumed genetic variations (mutations), (3) the not so commonly assumed exploitation of resources by organisms, and (4) the very rarely considered time-dependent externally

imposed resource changes. Externally imposed global resource changes which are then modified by organism exploitation we call changes in the *environmental state*.

Thus, environmental state changes are here broadly defined to capture those where access to, e.g., nutrients change with a cyclicity of seconds, hours, months, or years in most niches on the surface of Earth, as well as within the human body. It is fair to assume that in all environments on Earth where there is enough labile carbon to sustain ecosystems with complex trophic paths, and therefore high biodiversity, the nutrient landscape is fluctuating with some rhythm, or several [13]. For example, the El Nino phenomenon limits the up-welling of nutrient-rich bottom water off the west coast of South America with an interval of a couple of years, whereas microalgae that produce oxygen in the day and respire it at night changes the shallow benthic marine environment on a daily basis. Similarly, oxygen concentrations fluctuate within the human body over seconds (affected by, e.g., intense muscle work), hours (affected by, e.g., sleep), and years (affected by aging). A contrasting setting is the deep continental biosphere, where the chemical landscape is relatively stable but the carbon cycle also so slow such that a complex foodweb is unfeasible [14, 15].

We consider a single "toy" gene in which a given sequence of basepairs is represented by a point on a finite-size one-dimension $\theta \in [0, 2\pi]$ (see Fig. 2A). While a more thorough mathematical model for the genetic space should be higher dimensional and equipped with Hamming-like distance metric [16] (see Fig. 2B), this simple model can still capture many essential features of the success landscape. For every sequence θ, the resultant number density n_θ can have discrete values for the maximum growth-rate g_θ and the over-population constraint N_θ^c:

$$\partial_t n_\theta = g_\theta \left(1 - \frac{N}{N_\theta^c}\right) n_\theta , \ N = \oint n_\theta d\theta . \tag{5}$$

Mutations turn the sequence from θ into θ' with rate $r_{\theta \to \theta'}$:
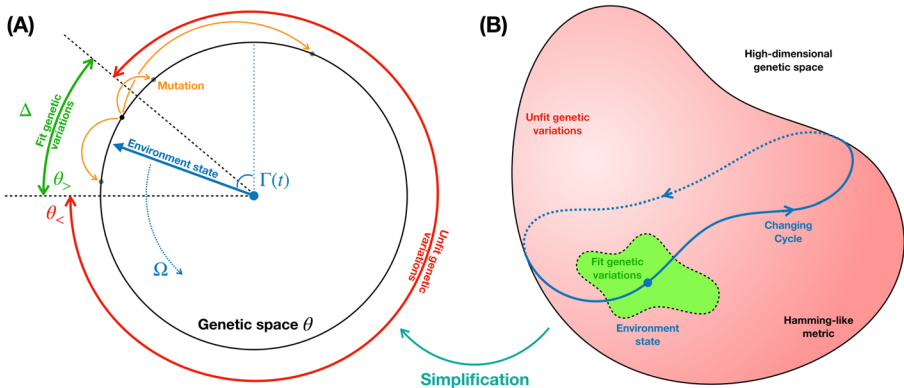

Fig. 2 (**A**) A toy model of genetic variation on a temporal-changing environment. In genetic space θ, for every environment state Γ there is a region of fit genetic variation $\theta \in [\Gamma - \Delta/2, \Gamma + \Delta/2]$ while the rest is unfit. (**B**) A more realistic model of genetic variation on a temporal-changing environment, in which the genetic space is high-dimensional and equipped with a Hamming-like metric

$$\partial_t n_\theta = g_\theta \left(1 - \frac{N}{N_\theta^c}\right) n_\theta$$
$$+ \oint r_{\theta' \to \theta} n_{\theta'} d\theta' - \oint r_{\theta \to \theta'} n_\theta d\theta' \; . \tag{6}$$

We represent the external environment by the state Γ and the amount of resource R, which determines growth-rates and the over-population constraint:

$$\partial_t n_\theta = g_{\theta,\Gamma} \left(1 - \frac{N}{N_{\theta,R}^c}\right) n_\theta$$
$$+ \oint r_{\theta' \to \theta} n_{\theta'} d\theta' - \oint r_{\theta \to \theta'} n_\theta d\theta' \; . \tag{7}$$

To keep things simple, we assume every environment state can be associated with a position Γ in the genetic space, so that for any environment state there is a region of size Δ consisting of fit genetic variations $\theta_> \in [\Gamma - \Delta/2, \Gamma + \Delta/2]$ where $g_{\theta_>,\Gamma} > 0$ while the rest of the genetic space is unfit $g_{\theta_<,\Gamma} < 0$.

At the simplest level, we can assume a cyclic variation in the environmental state, which we assume rotates at a rate Ω. In this way, we build in an advantage to mutations: a low mutation rate may punish an organism if the environment changes too rapidly so that gene sequences that once provided fitness are no longer useful in the new environment. This is our attempt to capture the essence of Wright's challenge to overly specialized genetic populations as depicted in Fig. 1C. Figure 2 shows the interaction between the environment state and the genetic space.

For further simplification, we assume that the mutations can turn any sequence into another at the same rate $r_{\theta' \to \theta''} = r/2\pi$, the growth-rates for fit genetic variation $g_{\theta_>,\Gamma} = g$ (corresponds to fitness $w_{\theta_>,\Gamma} = e^g$) and for unfit genetic variation $g_{\theta_<,\Gamma} \to -\infty$ (corresponds to fitness $w_{\theta_<,\Gamma} = 0$) so that unfit individuals die out quickly thus $n_{\theta_<} \to 0$, therefore the non-trivial dynamics only happen inside the genetically fit region:

$$N = \oint n_\theta d\theta = \int_{\Gamma - \Delta/2}^{\Gamma + \Delta/2} n_{\theta_>} d\theta_> \; . \tag{8}$$

Resource dynamics are modeled here to provide a toy description of the map from the resource landscape, originally called the carrying capacity above, to the success landscape in the spirit of Wright. We assume a linear relationship, serving as a first-order approximation [17, 18], between the over-population constraint and the resource:

$$N_{\theta,R}^c = \alpha R \; , \tag{9}$$

where $N_{\theta,0}^c = 0$ when there is no resource and $N_{\theta,R_c}^c = \alpha R_c$ when the amount of resource is maximum.

We model how the population influences the environment, for example through the consumption of resource:

$$R = R_c - \oint \beta_\theta n_\theta dn_\theta \; , \tag{10}$$

where the influence β_θ of individuals with genetic variation θ depends on the number of offspring w_θ it can produce. As a consequence of energy conservation, we will assume the following first-order approximation:

$$\beta_\theta = \beta w_\theta = \beta e^{g_\theta} . \tag{11}$$

The more offspring an individual can have, the more fit it is but at the cost of consuming more resource for reproduction. For unfit individuals, they cannot survive the environment state, cannot consume resources hence die out instantly.

To understand how Eq. (10) emerges, consider an environment with resource recovery dynamics [19, 20]:

$$\partial_t R = -\frac{R_c - R}{\tau} - \oint \kappa_\theta n_\theta d\theta , \tag{12}$$

where $1/\tau$ is the environment recovery rate and $\kappa_\theta = \kappa w_\theta = \kappa e^{g_\theta}$ is the consumption rate of an agents with gene variation θ. If τ is a small time-scale in the evolutionary dynamics (for example, as the system is reaching stationary), the change in R can happen very fast so that we can treat it as a background field:

$$\partial_t R \to 0 \Rightarrow R \approx R_c - \oint \tau \kappa_\theta n_\theta dn_\theta , \tag{13}$$

which is the same as Eq. (10) after we make the identification $\beta = \tau\kappa$.

In summary, after all the above simplifications, the population dynamics in our crude toy model is given by:

$$\partial_t n_\theta = G_\theta n_\theta + \oint \frac{r}{2\pi} n_{\theta'} d\theta' - \oint \frac{r}{2\pi} n_\theta d\theta' , \tag{14}$$

where for the fit sub-population:

$$G_{\theta_>} = g\left(1 - \frac{N}{\alpha\left(R_c - \beta e^g N\right)}\right) , \tag{15}$$

and for the unfit sub-population:

$$G_{\theta_<} \to -\infty . \tag{16}$$

This model basically describes environmental degradation.

We define *success* as maximizing the stationary number of survivors:

$$S = \frac{N_{st}}{N_{R_c}^c} , \tag{17}$$

where N_{st} is the stationary number of survivors and $N_{R_c}^c = \alpha R_c$ is the maximum carrying capacity.

2.1 Success in an unchanging environmental state and a constant resource

This is closest to the conventional models. For a fixed environment state $\Gamma = \Gamma_0$ and unchanging resource that always stays at the maximum amount $R = R_c$, from Eq. (14) we have:

$$\partial_t n_{\theta_>} = g\left(1 - \frac{N}{N_{R_c}^c}\right) n_{\theta_>} + r\frac{N}{2\pi} - rn_{\theta_>} \ . \tag{18}$$

At the stationary level, we have $\partial_t n_\theta^{st} = 0$, therefore:

$$\begin{aligned} 0 &= g\left(1 - \frac{N_{st}}{N_{R_c}^c}\right) n_{\theta_>}^{st} + r\frac{N_{st}}{2\pi} - rn_{\theta_>}^{st} \\ \Rightarrow n_{\theta_>}^{st} &= \frac{N_{st}}{2\pi} \frac{1}{1 - \frac{g}{r}\left(1 - \frac{N_{st}}{N_{R_c}^c}\right)} \ . \end{aligned} \tag{19}$$

Integrating $\int_{\Gamma_0 - \Delta/2}^{\Gamma_0 + \Delta/2} d\theta_>$ for both sides gives:

$$\begin{aligned} N_{st} &= \Delta \frac{N_{st}}{2\pi} \frac{1}{1 - \frac{g}{r}\left(1 - \frac{N_{st}}{N_{R_c}^c}\right)} \\ \Rightarrow S &= \frac{N_{st}}{N_{R_c}^c} = 1 - \frac{r}{g}\left(1 - \frac{\Delta}{2\pi}\right) \ . \end{aligned} \tag{20}$$

Note that for the unphysical value $S < 0$, the stationary solution corresponds to extinction of the population $N_{st} = 0$ thus $S = 0$.

Figure 4A describes the success surface for an environment with unchanging environment state and constant resource. Intuitively, it is clear that a slow growth rate is not a good strategy here since the resources are not diminished by increasing organisms, and that high mutation rates are also not a good strategy since you are most likely to arrive at a less fit genome.

2.2 Success in an unchanging environment state but a dynamic resource

Here, resources can be exploited, but there is no external drive to change the overall environmental state. For a fixed environment state $\Gamma = \Gamma_0$ but with a dynamical resource, which is influenced by the number of agents, to take into account the backreaction from the environment, followed from Eq. (10) we replace N_c with $N_R^c = \alpha R$ where $R = R_c - \beta e^g N_{st}$ in Eq. (20):

$$\begin{aligned} N_{st} &= \left(N_{R_c}^c - \alpha\beta e^g N_{st}\right)\left(1 - \frac{r}{g}\left(1 - \frac{\Delta}{2\pi}\right)\right) \\ \Rightarrow S &= \frac{N_{st}}{N_{R_c}^c} = \frac{1}{\left(1 - \frac{r}{g}\left(1 - \frac{\Delta}{2\pi}\right)\right)^{-1} + \alpha\beta e^g} \ . \end{aligned} \tag{21}$$

Note that for un-physical values $S < 0$ and $S > 1/\alpha\beta e^g$ (corresponds to negative resource $R < 0$), the stationary (infinite time) solution corresponds to extinction of the population $N_{st} = 0$.

Figure 4B describes the success surface for an environment with unchanging environment state and dynamical resource. Note that here high growth rates are at a disadvantage since they exploit resources and depress the carrying capacity, and mutations again represent a risky bet. Thus, compared to Fig. 4A turning on resource exploitation reduces the advantages to growth.

2.3 Success in a changing environment state but fixed resource

Here, there is no exploitation of resources by organisms but the external environment changes, in our simplified case periodically. For a time-changing environment state $\Gamma(t) = \Omega t$ but non-dynamic resource, we change to the co-moving environmental frame:

$$\theta_\Omega = \theta - \Omega t \,, \; \partial_t n_{\theta - \Omega t} = \partial_t n_{\theta_\Omega} - \Omega \partial_{\theta_\Omega} n_{\theta_\Omega} \,. \tag{22}$$

From Eq. (14), the population dynamics in genetic space is given by:

$$\partial_t n_{\theta_\Omega^>} - \Omega \partial_{\theta_\Omega^>} n_{\theta_\Omega} = \\ g\left(1 - \frac{N}{N_{R_c}^c}\right) n_{\theta_\Omega^>} + r\frac{N}{2\pi} - r n_{\theta_\Omega^>} \,. \tag{23}$$

At stationary times, we have $\partial_t n_{\theta_\Omega}^{st} = 0$, therefore:

$$-\Omega \partial_{\theta_\Omega^>} n_{\theta_\Omega}^{st} = g\left(1 - \frac{N_{st}}{N_{R_c}^c}\right) n_{\theta_\Omega^>}^{st} + r\frac{N_{st}}{2\pi} - r n_{\theta_\Omega^>}^{st} \,. \tag{24}$$

Define:

$$\Xi = 1 - \frac{g}{r}\left(1 - \frac{N_{st}}{N_{R_c}^c}\right) \,, \tag{25}$$

from the boundary condition at the co-moving front $n_{+\Delta/2}^{st} \to 0$ we can solve (24):

$$n_{\theta_\Omega^>}^{st} = \frac{N_{st}}{2\pi} \frac{1 - \exp\left(\frac{(\theta_\Omega^> - \Delta/2)r\Xi}{\Omega}\right)}{\Xi} \tag{26}$$

Figure 3 shows the survivor distribution on genetic space as the population adapts to the changing environment in the co-moving frame.

Integrating $\int_{-\Delta/2}^{+\Delta/2} d\theta_\Omega^>$ for both sides gives:
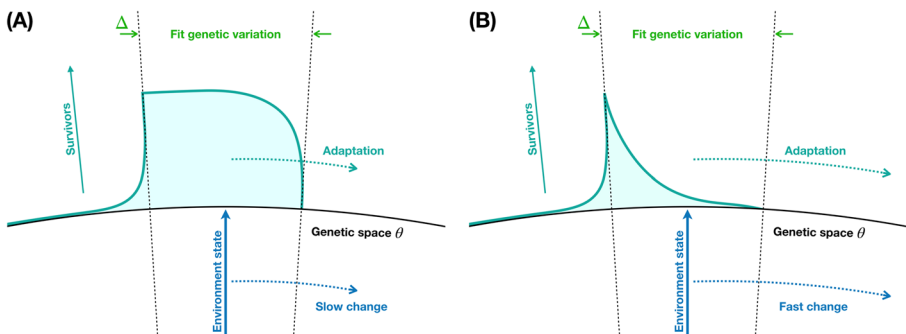

Fig. 3 The survivor profile on genetic space as the population adapts to the changing environment: (**A**) When the change is slow. (**B**) When the change is fast
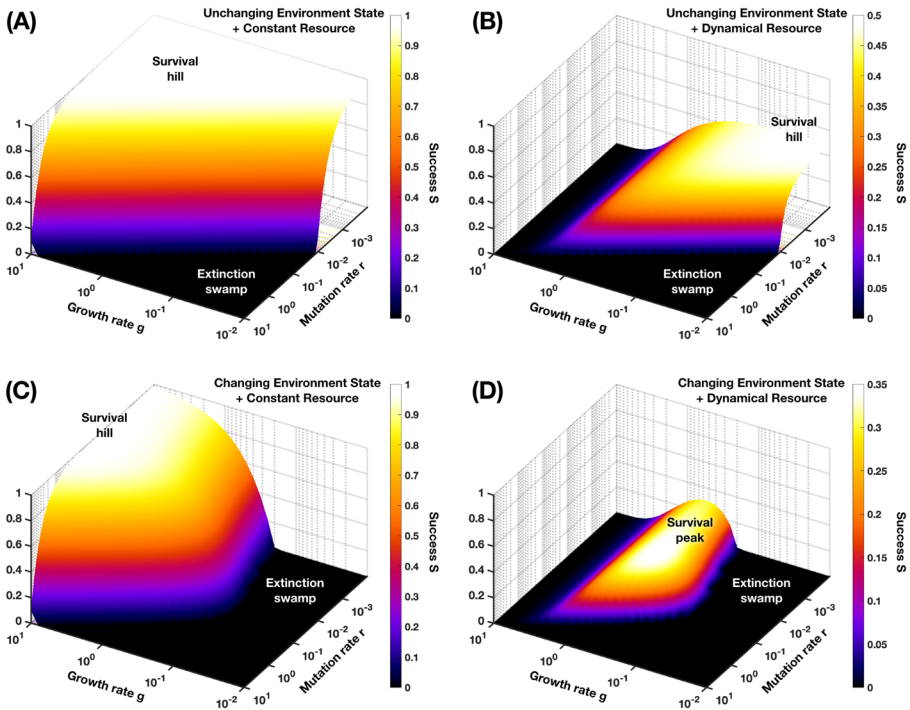
Fig. 4 The shape of surface surface S as a function of growth rate g and mutation rate r both in log-scale when $\Delta/2\pi = 10^{-1}$ and: (**A**) The environment state is unchanging $\Omega = 0$ and the resource is constant $\alpha = 0$, $\beta = 0$. (**B**) The environment state is unchanging $\Omega = 0$ and the resource is dynamical $\alpha = 1$, $\beta = 1$. (**C**) The environment state is time-changing $\Omega = 10^{-2}$ and the resource is constant $\alpha = 0$, $\beta = 0$. (**D**) The environment state is cyclically-changing at the rate $\Omega = 10^{-2}$ and the resource is exploitable $\alpha = 1$, $\beta = 1$. On a side note, the terminology "extinction swamp" in these figures is inspired by "swampland" in string theory landscape [21]

$$
N_{st} = \Delta \frac{N_{st}}{2\pi} \frac{1 - \frac{\Omega}{\Delta r \Xi}\left(1 - \exp\left(-\frac{\Delta r \Xi}{\Omega}\right)\right)}{\Xi}
$$
$$
\Rightarrow \quad \frac{2\pi}{\Delta} = \frac{1 - \frac{\Omega}{\Delta r \Xi}\left(1 - \exp\left(-\frac{\Delta r \Xi}{\Omega}\right)\right)}{\Xi} \ .
\tag{27}
$$

In general, to proceed further we need to do a numerical evaluation to solve for Ξ. Define $f(\gamma)$ to be the solution for x satisfying the following equation:

$$
\gamma = \frac{1 - \frac{1}{x}(1 - e^{-x})}{x} \ ,
\tag{28}
$$

note that for $\gamma \ll 1$ then $f(\gamma) \approx 1/\gamma - 1 - \gamma$, for $\gamma \gg 1$ then $f(\gamma) \approx -\ln(\gamma)$. The solution for Ξ is given by:

$$
\Xi = \frac{\Omega}{\Delta r} f\left(\frac{2\pi}{\Delta} \frac{\Omega}{\Delta r}\right) \ .
\tag{29}
$$

With Ξ, from Eq. (25) we can obtain the stationary number population N_{st} and then the success value S:

$$S = \frac{N_{st}}{N_{R_c}^c} = 1 - \frac{r}{g}(1 - \Xi) .$$

(30)

Figure 4(C) describes the success surface for an environment with time-changing environment state and constant resource, which correspond to Eq. (30). Here growth helps success because of fixed resources as in Fig. 4B, but too low a mutation rate removes the ability to adapt to a changing environment.

2.4 Success in a changing environment state and exploitable resource landscape

Finally, we consider the most realistic scenario, where we have both resource exploitation and externally imposed changes in the environment.

Figure 4D describes the success surface for an environment with time-changing environment state and dynamical resource, which is qualitatively different from the previous three conditions: it has a well-defined single peak in the (g, r)-plane. This success peak can be understood both mathematically and intuitively.

Mathematically, while in general the position of the success peak cannot be found analytically, in the special case of slow-changing environment $\Omega \to 0$ we can approximate the position (g, r) for maximum success. From Eq. (28) and Eq. (29), we obtain the approximation:

$$\Xi \approx \frac{\Delta}{2\pi} - \frac{\Omega}{\Delta r} - \frac{2\pi}{\Delta} \frac{\Omega^2}{\Delta^2 r^2} .$$

(31)

Plugging this in Eq. (30) gives:

$$S \approx 1 - \frac{\Omega}{\Delta g} - \frac{2\pi}{\Delta} \frac{\Omega^2}{\Delta^2 gr} - \frac{r}{g}\left(1 - \frac{\Delta}{2\pi}\right) .$$

(32)

Including the resource dynamics, this becomes:

$$S \approx \frac{1}{\left(1 - \frac{\Omega}{\Delta g} - \frac{2\pi}{\Delta}\frac{\Omega^2}{\Delta^2 gr} - \frac{r}{g}\left(1 - \frac{\Delta}{2\pi}\right)\right)^{-1} + \alpha\beta e^g} .$$

(33)

Note that for un-physical values $S < 0$ and $S > 1/\alpha\beta e^g$ (corresponds to negative resource $R < 0$), the stationary solution corresponds to extinction of the population $N_{st} = 0$. For unchanging environment $\Omega = 0$, Eq. (32) and Eq. (33) become Eq. (20) and Eq. (21). We define:

$$F = \frac{2\pi}{\Delta} \frac{\Omega^2}{\Delta^2 gr} + \frac{r}{g}\left(1 - \frac{\Delta}{2\pi}\right) ,$$

(34)

so that Eq. (33) can be written as:

$$S \approx \frac{1}{\left(1 - \frac{\Omega}{\Delta g} - F\right)^{-1} + \alpha\beta e^g} .$$

(35)

For a fixed value of growth-rate g, the maximum value of S is where we have the function $F(r)$ to be minimum, which followed from the inequality of arithmetic and geometric means (also known as the AM-GM inequality) [22]:

$$F(r) \geq 2\sqrt{\frac{2\pi}{\Delta}\frac{\Omega^2}{\Delta^2 gr} \times \frac{r}{g}\left(1 - \frac{\Delta}{2\pi}\right)} = 2\sqrt{\frac{2\pi}{\Delta} - 1}\frac{\Omega}{\Delta g} . \tag{36}$$

The equal-sign is found at $r = r_*$ that satisfies:

$$\frac{2\pi}{\Delta}\frac{\Omega^2}{\Delta^2 gr_*} = \frac{r_*}{g}\left(1 - \frac{\Delta}{2\pi}\right) \Rightarrow r_* = \frac{1}{\sqrt{\frac{\Delta}{2\pi}\left(1 - \frac{\Delta}{2\pi}\right)}}\frac{\Omega}{\Delta} . \tag{37}$$

For this value of the mutation rate, we plug the minimum value $F(r_*)$ into Eq. (35) to obtain the success S as a function of g:

$$S \approx \frac{1}{\left(1 - \left(1 + 2\sqrt{\frac{2\pi}{\Delta} - 1}\right)\frac{\Omega}{\Delta g}\right)^{-1} + \alpha\beta e^g} . \tag{38}$$

For small growth rate $g \ll 1$ then $e^g \approx 1 + g$, we can further approximate:

$$S \approx \frac{1}{\left(1 - \left(1 + 2\sqrt{\frac{2\pi}{\Delta} - 1}\right)\frac{\Omega}{\Delta g}\right)^{-1} + \alpha\beta(1 + g)} . \tag{39}$$

The extrema of S can be found by solving for $\partial_g S = 0$, which in general gives two solutions but in the limit $\Omega \to 0$ it only has a single positive solution:

$$g = g_* = \sqrt{\left(1 + 2\sqrt{\frac{2\pi}{\Delta} - 1}\right)\frac{\Omega}{\Delta\alpha\beta}\left(1 + \sqrt{\left(1 + 2\sqrt{\frac{2\pi}{\Delta} - 1}\right)\frac{\Omega\alpha\beta}{\Delta}}\right)} . \tag{40}$$

In summary, at the limit $\Omega \to 0$, the peak position of the success landscape is given by:

$$\max(S) \approx \frac{1}{\left(1 + \sqrt{\left(1 + 2\sqrt{\frac{2\pi}{\Delta} - 1}\right)\frac{\Omega\alpha\beta}{\Delta}}\right)^2 + \alpha\beta} \approx \frac{1}{1 + \alpha\beta} , \tag{41}$$

which is located around:

$$(g_*, r_*) \approx \left(\sqrt{\frac{\Omega}{\Delta\alpha\beta}\left(1 + 2\sqrt{\frac{2\pi}{\Delta} - 1}\right)}, \frac{\Omega}{\Delta}\frac{1}{\sqrt{\frac{\Delta}{2\pi}\left(1 - \frac{\Delta}{2\pi}\right)}}\right) . \tag{42}$$

The faster the changing rate Ω and the narrower the fit region Δ on genetic space, the faster the growth rate and the mutation rate has to be for the population to survive.

Intuitively, the emergence of a success peak can be understood due to the confluence of resource exploitation (which is never a good thing) and the two-edged sword of mutations which both allows for adaptation to changing externally imposed but also threatens the integrity of a fit genome through risky changes.

3 Conclusions

So what have we learned from the success landscape of the simple models we have considered in this paper? We can see how the change of season and the dynamics of resource shape the success surface as a function of growth and mutation rates.

If there is no time-changing environment state and no resource dynamics, then a high growth rate and low mutation rate can ensure the survival of the population. Of course, on the surface of Earth as well as within the human body, this scenario is not realistic. However, if we include resource dynamics while keeping the environment state unchanging, then moderate growth rate with a low enough mutation rate can help the population to be successful. Moreover, if we include both time-changing environment states and resource consumption, then the population also dies out if the mutation rate is too low. Combining both influences from time-changing resources and resource back-reaction from interactions with the population, then there is a single peak in the whole success landscape for optimal survival strategy which is a combination of growth rates, mutation rates, and resource consumption.

The latter scenario is arguably the only realistic out of the four within landscapes that matters to modern animals and to humans, i.e., in niches on the surface of Earth or within the human body where the access to resources are ceaselessly fluctuating. The finding of a single peak in the success landscape of a species can contribute to our understanding of species-species interactions as well as of clade diversifications and extinctions.

Perhaps the most interesting part of this exercise is the strongly asymmetric shape of the success peak in Fig. 4D. That is, a fixed mutation rate of $r_* \sim 5 \times 10^{-2}$ and a changing growth rate there is a slow climb to maximum success as the growth rate *decreases* due to resource exploitation, but once the peak is past there is a very precipitous drop in success with small relative decreases in growth. On the other hand, for a fixed growth rate of $g_* \sim 3 \times 10^{-1}$ success does not change much as mutation rates are increased from low values, in fact one moves almost along a ridge line, but once the peak is passed relative increases in mutation lead to rapid extinction.

Although this is a toy model, we feel that there is enough of reality connected to it to suggest that for a complex disease such as cancer where uncontrolled cell growth, high mutation rates, easily exploited and exhausted resources and rapid externally driven changes in the due to clinical interventions such as chemotherapy our toy model might be of some utility in providing guidance to lead a cancer cell population via chemotherapy along the success landscape on the steepest gradient into an extinction swamp. It won't be easy. Our results suggest for example that, in administering a drug that say inhibits growth, coming from low drug levels up paradoxically the tumor might grow in size rather than shrink, only to abruptly die with increasing dose beyond the maximum in size. The asymmetry of the success peak tells the oncologist that finding the quickest approach to shrinking a tumor is not so simple or intuitive.

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