Ecology dictates evolution?

de Vos, Marjon G. J.; Schoustra, Sijmen E.; de Visser, J. Arjan G. M.

Published in:
EPL

DOI:
10.1209/0295-5075/122/58002

Publication date:
2018

LETTER

Ecology dictates evolution? About the importance of genetic and ecological constraints in adaptation

To cite this article: Marjon G. J. de Vos *et al* 2018 *EPL* **122** 58002

epl A Letters Journal Exploring the Frontiers of Physics

June 2018

EPL, **122** (2018) 58002 www.epljournal.org
doi: 10.1209/0295-5075/122/58002

Focus Article

Ecology dictates evolution? About the importance of genetic and ecological constraints in adaptation[(a)]

Marjon G. J. de Vos[1,2(b)], Sijmen E. Schoustra[1,3] and J. Arjan G. M. de Visser[1]

[1] *Wageningen University, Laboratory of Genetics - Droevendaalsesteeg 1, 6708 PB, Wageningen, The Netherlands*
[2] *University of Groningen, GELIFES - Nijenborgh 7, 9747 AG Groningen, The Netherlands*
[3] *University of Zambia, Department of Food Science and Nutrition - Great East Road Campus, Lusaka, Zambia*

received 30 May 2018; accepted in final form 28 June 2018
published online 17 July 2018

PACS 87.23.-n – Ecology and evolution
PACS 87.23.Kg – Dynamics of evolution
PACS 87.18.Vf – Systems biology

Abstract – The topography of the adaptive landscape is a major determinant of the course of evolution. In this review we use the adaptive landscape metaphor to highlight the effect of ecology on evolution. We describe how ecological interactions modulate the shape of the adaptive landscape, and how this affects adaptive constraints. We focus on microbial communities as model systems.

Introduction. – Biological adaptation is driven by natural selection upon heritable variation in populations. This variation is ultimately generated by novel mutations and the rate at which this happens depends on a combination of internal mechanisms (*e.g.*, DNA repair and fidelity mechanisms) and influences of the external environment (*e.g.*, mutagenic compounds). On longer time scales, the capacity of organisms to evolve depends on multiple factors. Natural selection and genetic drift determine which variants will contribute to evolution, which is in turn mediated by the effective size of the population, and hence under the influence of both genotype and environment. The population's supply of mutations can be too small for natural selection to act on, either since the population is too small or the mutation rate is too low. What level of adaptation can be achieved, depends on how well multiple mutations combine to produce new functions. Fitness is a function of the genetic make-up and the prevailing environmental condition and can be depicted as a fitness or adaptive landscape [1]. The tempo and mode of evolution thus depend on an ensemble of factors, among which the topography of the adaptive landscape. To put it simply: the adaptive landscape presents the possible adaptive solutions, while population dynamic parameters, such as population size and mutation rate, determine which of these solutions may be realized. If we can estimate the shape of the adaptive landscape, *e.g.*, whether it is rugged with many peaks and valleys or relatively smooth, then we can in theory predict the dynamics and repeatability of evolution under various environment-dependent scenarios. For example, we can expect that populations faced with a relatively smooth landscape rapidly evolve towards the optimum, whereas fitness valleys will likely constrain the speed and affect the direction of evolution, and evolving populations may end up on different (suboptimal) peaks. In this review, we focus on the factors that shape the adaptive landscape and determine the ability of populations to travel across the landscape, and the consequences for evolvability.

This manuscript is divided into sections, in which we build up the number of components playing a role in the effect of ecology on evolution. We first merely describe the genetic components involved, and incrementally add the effect of the abiotic and biotic environments and their consequences for adaptation, investigated experimentally in a variety of organisms, mostly microbes.

What shapes the adaptive landscape?. –

Interaction between genotypes shapes the topography of the adaptive landscape: $G \times G$. The fitness effect

[(a)] Contribution to the Focus Issue *Evolutionary Modeling and Experimental Evolution* edited by José Cuesta, Joachim Krug and Susanna Manrubia.

[(b)] E-mail: m.g.j.de.vos@rug.nl

of a mutation can be influenced by the genetic background. This concept is called epistasis or genotype-by-genotype interaction, G × G [1–4]. For instance, a mutation that is beneficial in one genetic background can be neutral or deleterious in another background. By mapping the genotype-phenotype-fitness map, epistatic interactions can be visualized. Bear in mind that this map is in nature highly dimensional, depicting it in 2D or 3D cannot capture all details. When the landscape is smooth, there is at least one mutational trajectory accessible by natural selection that leads to the optimum from any point in the landscape. However, when there is reciprocal sign epistasis, which occurs when mutations are only beneficial if they occur jointly, the landscape is rugged consisting of fitness peaks and valleys. In this case evolution may be constrained, because an evolving population may "get stuck" on a sub-optimal adaptive peak [5]. A general finding is that the selective benefit of mutations depends inversely on the fitness of the genetic background, giving rise to the so-called diminishing-returns epistasis [6,7]. Another consequence of the topography of the adaptive landscape is the number of beneficial mutations available to a genotype, which affects the direct response to selection [8].

The adaptive landscape was initially merely a metaphor for describing the possibilities or potential trajectories of evolution [1]. But an increasing number of studies has experimentally mapped small parts of the genotype-fitness map of different organisms, often microbes [9–14]. These empirical adaptive landscapes give us a small-scale glimpse of nature's limitations and opportunities to adaptation.

The shape of the landscape depends on the environment. Environment-dependent epistasis: G × G × E. The physicochemical environment often alters the effect of mutations. For instance, by assessing the fitness effects of all point mutations in the gene encoding Hsp90, a chaperone in yeast, in four environments, it was shown that many mutations have environment-dependent fitness effects, indicating the importance of genotype-by-environment (G × E) effects [15]. Some of the mutations caused a considerable fitness increase relative to the wild type in one environment, but these beneficial mutations typically showed trade-offs, *i.e.*, fitness losses in other environments. Another study that focused on environment-dependent fitness effects, constructed the genotype space of five mutations in the genome of *Escherichia coli*, and measured the phenotype of these genotypes in 1920 environments [16]. The fitness effects of the mutations significantly changed in 203 environments. Moreover, by focusing on the adaptive landscapes involving all interactions among these five mutations in the three, most distinct-effect environments, they observed significant changes in the topography of the adaptive landscape. The global adaptive peak was represented by another genotype in different environments, hence epistatic interactions were also different in the different

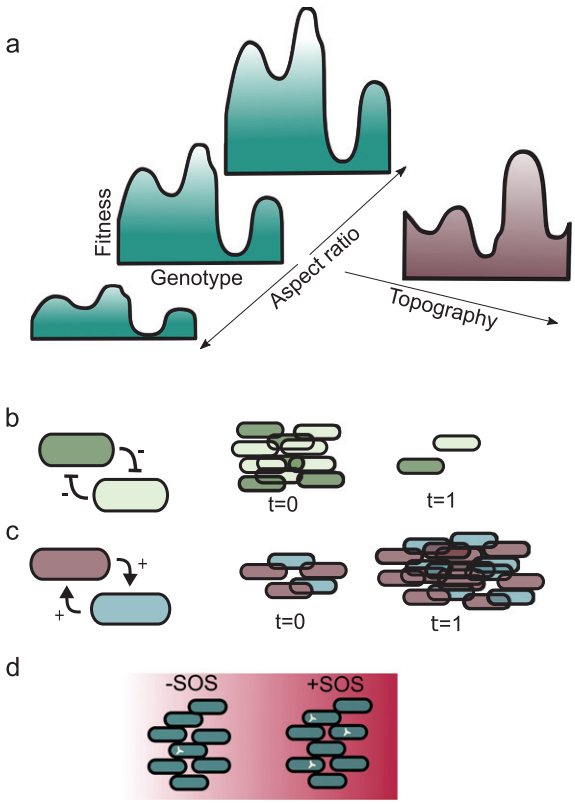

Fig. 1: (Colour online) The effect of ecological interactions on adaptation. (a) Ecological interactions can affect the aspect ratio and topography of the adaptive landscape. (b) Strong interference competition can lead to decreased population sizes. (c) Positive interactions can lead to increased population sizes, as well as negative frequency-dependent fitness interactions. (d) Abiotic and biotic environmental factors may induce a stress response causing an increase in the mutation rate in a member of the community.

environments, *i.e.*, there were genotype-by-genotype-by-environment interactions, G × G × E [16]. The change in epistatic interactions in different environments seems to be a general phenomenon, in which either the magnitude or sign of epistatic effect can affect the aspect ratio or topography (fig. 1(a)). In a reconstruction of evolved, functionally inverted, *lac* repressor mutants [17], epistatic patterns also differed substantially between the two environments in which the transcription factor evolved [18].

Environment-dependent epistasis affects the ability of an evolving population to adaptively keep up with a changing environment. In a gradually changing laboratory environment, the rate of this environmental change, and hence the environmental modulation of epistasis, determined whether an evolving population of *E. coli* could keep up with the environmental change or went extinct [19]. Gorter *et al.* compared adaptation of yeast to gradually *vs.* abruptly increasing concentrations of three heavy metals and found distinct types of G×E interactions for essential and non-essential metals [20]. A population evolving to a non-essential metal (*i.e.*, cadmium) that is

toxic at all concentrations, did not show a difference in the fitness rank order of mutations at low and high metal concentrations. Mutations such as these could thus potentially lead to environmental adaptation at each metal concentration. However, for compounds that are essential in low doses but toxic in high doses (*i.e.*, zinc and nickel), the fitness rank order of the mutations changed for different concentrations, and different mutations were selected under abrupt and gradual change [20].

Environmental changes can also help to overcome genetic constraints that limit evolution. The adaptive landscapes of six mutations that determine the binding and unbinding of the *lac* transcription factor to the DNA are multi-peaked in two environments, in the presence and absence of inducer [21]. There are thus no monotonically increasing trajectories from one transcription factor-DNA binding pair to another transcription factor-DNA binding pair in each single environment. Due to trade-offs between genotypes in the two environments, the adaptive landscapes in both environments are partially anti-correlated. By alternating between the two environments, many trajectories are opened up, such that mutational trajectories with only functionally increasing steps became accessible to positive selection. Adaptive constraints due to genetic interactions could hence be overcome in fluctuating environments.

In computationally generated rugged adaptive landscapes there is a low probability of finding a selectively accessible path [22]. However, in the presence of cross-environmental trade-offs, the probability of finding selectively accessible paths increased in fluctuating environments until virtually all random *in silico* generated landscapes contained selectively accessible paths at a level of 50% trade-offs between adaptive landscapes in two environments [21].

Not only the extent of trade-offs in the different environments matters, but also the locations of the anti-correlations in the topography of the landscapes are important. The mean first-passage time, which is proportional to the number of beneficial substitutions necessary to cross the landscape in fluctuating environments, can be calculated for different fractions of time spent in either one or the other environment. This will give a prediction on the dwelling time and environmental fluctuation rate which will lead to a maximum adaption rate [21].

Whether environmental change will speed up or slow down adaptation thus critically depends on the timing and the duration of the environmental change in combination with the topography of the adaptive landscapes. Trade-offs in different environments, due to antagonistic pleiotropy, and environmental change have long been thought to impede, rather than facilitate adaptation. With this idea in mind, drug cycling strategies are being explored that limit adaptation, where resistance to drug A is expected to lead to collateral sensitivity of drug B [23]. Indeed, in such scenarios antagonistic pleiotropy sometimes constrains adaptation [24,25]. However, the success of slowing down resistance evolution crucially depends on the genetic background of the assessed strains [26,27], as well as the duration of the environmental cycles.

Biotic and abiotic interactions affect the environment: $G \times G \times E \times B$. Not only does the environment affect the phenotype and fitness of a population, evolving populations may also alter the environmental condition and size of the population. Environment-dependent biotic-genotype-by-genotype interactions (G × G × E × B) can thus affect the population structure, the population size and the genetic composition of the population, as well as the course of evolution. An extreme example is ecological suicide, observed in soil bacteria in the laboratory [28]. Bacteria modified the environmental *p*H to such a degree that it led to a rapid extinction of the whole population once it reached a high population density (fig. 1(b)). Not all eco-evolutionary feedback has such a severe impact. Positive frequency-dependent fitness interactions, where a trait becomes more beneficial when common, can affect the fraction of different genotypes in a population. This is exemplified in the cooperative formation of fruiting bodies of *Myxococcus xanthus* in starvation conditions [29]. Negative frequency-dependent fitness interactions, where the fitness of genotypes in a population is higher when rare, are particularly relevant, as they may cause the stable coexistence of community members (fig. 1(c)). This is for example the case in bacteria sensitive to β-lactam antibiotics. They cannot survive in the presence of beta-lactam antibiotics however, when they are together with resistant cells producing β-lactamase, an enzyme that degrades β-lactam antibiotics, they may be protected and be maintained in the population. This is particularly the case when sensitive cells grow faster in the absence of antibiotic. In this manner, the selective force caused by antibiotics is effectively reduced, and a more diverse population structure consisting of resistant and sensitive genotypes is maintained [30].

Populations often live in complex communities with multiple species, in which the members may have intricate metabolic interactions which drive nutrient cycling [31] and affect community stability. For instance, genome reduction by gene loss in free-living species may render micro-organisms dependent on co-occurring microbes which produce metabolic compounds that compensate for the lost gene. Such Black Queen dynamics may lead to the coexistence of microbes through metabolic dependences [32]. A recent study used genomic information in combination with game theory to understand such metabolic interactions *in silico*. Based on cross-feeding caused by amino acid leakage they determined the stability of communities based on Nash equilibria, in which a pair of genotypes exists stably if none of the two members can benefit by changing its interaction strategy [33]. Epistatic interactions, based on the architecture of the metabolic pathways important for coexistence in the donor, were found to constrain the interactions

between genotypes, due to dependences on specific biochemical pathways present in the other member required for cross-feeding. For example, a mutant strain lacking the biosynthesis pathways for the amino acid glutamate is not able to synthesize and leak arginine, and will therefore not allow another strain to cross-feed on this compound.

Metabolic interactions can also shape the topography of the adaptive landscape of an evolving bacterial population. A recent study, measuring clones from the long-term Lenski evolution experiment with *E. coli*, found that even though short-range evolutionary trajectories were hardly affected, mutations with a relatively large environment-changing effect could reshape distant areas of the adaptive landscape [34]. Current changes in microbial interactions may thus affect evolving populations in the future, even when they have little effect right now. This leads to non-transitive fitness interactions, where a later evolved genotype may be less fit than the ancestor in the original environment. In this case evolved genotypes are only more fit when competing with their immediate predecessors due to changes in the selective environment [35,36].

Multi-species microbial interactions can also modulate the selective pressure applied by chemical compounds in the environment, with possible effects on subsequent evolution. For example, different bacterial species cultured from patients diagnosed with polymicrobial urinary tract infections affect the tolerance to antibiotics of a focal species, *e.g.*, by affecting the population size that can be sustained for a given concentration of antibiotics [37]. This may, in turn, affect the probability of resistance mutations to occur and subsequently spread in the population [38].

Ecological interactions with direct effect on the genotype. Ecological interactions can directly affect the generation of novel genotypes in the population if they alter the rate or pattern of mutation or recombination. Stressful environments, for instance due to β-lactam antibiotics [39] or starvation conditions, are known to increase the mutation rate [40–42] (fig. 1(d)). Such increases of the supply of mutations may affect the rate of adaptation [43,44] and can potentially help crossing fitness valleys in the landscape by increasing the probability of appearance of beneficial double mutants [45].

Mutation rates can also vary with population density, since it was recently found that individuals in smaller populations have higher mutation rates [46]. The mutation supply affected by stress-induced mutagenesis on the one hand, and by population density effects on the other hand, was recently assessed in *E. coli* populations in a gradient of cell densities [47]. Such ecological factors may thus modulate the mutation rate in evolving populations.

Even though an elevated mutation rate will increase the number of beneficial mutations in the population, it will not necessarily speed up adaptation to the environment. In a recent study [48], the mutation rate was moderately increased by SOS-induced mutagenesis. SOS-induced mutagenesis is part of the bacterial stress response triggered by DNA damage, which was in this case induced by the antibiotic ciprofloxacin. However, since the increased mutation rate was offset by an increase of the competitive ability of the microorganisms within the population, the selective strength at the population level was effectively decreased.

The SOS-response not only increases the frequency of point mutations, it also affects the recombination rate of integrons [49] and promotes horizontal gene transfer via plasmids [50], both of which generate genetic variation which may speed up adaptation, allowing the population to "jump" to other regions of the adaptive landscape.

However, not all combinations of plasmids and genomic backgrounds are beneficial. This obviously depends on the environment in which an organism lives, as the expression of superfluous traits may be costly [51], but also on the interaction between the incoming DNA and the genomic background. In a recent study [52], it was found that few factors determined the benefit of antibiotic resistance encoding DNA in the genetic backbone of *E. coli*: the phylogenetic origin, as well as the dependence of a resistance mechanism on host physiology. Such epistatic interactions have also been found in a worldwide occurring pathogenic strain of *E. coli*. Core genome substitutions in regulatory regions were found to be associated with the acquisition and maintenance of different accessory genome elements [53]. This suggests that physiological constraints play a major role in the evolution of drug resistance, also via horizontal gene transfer.

Multi-copy plasmids may buffer constraints by providing functional redundancy. Multiple copies of plasmids harboring the TEM-1 β-lactamase gene in one cell were found to promote the coexistence of ancestral and novel traits for multiple generations during an evolution experiment, allowing bacteria to escape evolutionary constraints imposed by antagonistic pleiotropy [54]. Such partial penetrance of the genotype to the phenotype was also observed in *Bacillus subtilis* spore formation [55]. In this case, the stochastic expression of the phenotype due to gene dosage effects could potentially aid crossing adaptive valleys. The presence of multiple plasmid copies in bacterial lineages has also been shown to be underlain by positive epistasis, which may further promote multi-plasmid retention [56]. Indeed, many bacterial species in natural environments carry more than one type of plasmid [57,58].

Discussion and outlook. – In summary, evolutionary constraints occur in many flavors, and may stem from the genetic make-up in combination with the abiotic and biotic environment. In both cases, these constraints affect the topography of the adaptive landscape such that adaptive trajectories are effectively blocked by low-fitness intermediate genotypes. The epistatic interactions underlying such constraints are often environment-dependent. Since biotic interactions alter the environment, they have the ability to modulate the topography of the adaptive landscape, as well as the spatial structure of the population,

the size and the genetic composition of the population. Additionally the environment can have a direct effect on a population by affecting the mutation or recombination rate, or the rate of horizontal gene transfer. It is to be determined how informative a topography mapped for one environment will be for evolution in other environments. For instance, are main features, such as the "ruggedness" of the adaptive landscape, primarily properties of the genotype network, and are they thus conserved across environments? Or are they mostly environment-dependent, such that the topography is very different across environments? In the latter scenario, the topography of the adaptive landscape in one environment bears little information for other environments. An analysis correlating different landscapes in different environments, in combination with an assessment of the dwelling time in the respective environments, may be helpful to assess adaptive constraints in these environments. It may also inform drug cycling treatments or adaptation protocols for biotechnological purposes.

The informative role of adaptive landscapes in spatially structured environments remains to be determined. Wright [1] realized the importance of spatially structured environments when he introduced the concept of adaptive landscapes. In his shifting balance theory, environmental spatial structure allows populations to become subdivided into semi-isolated demes. Demes would move from peak to peak on a rugged landscape more easily by a diminished force of selection and an increased role of genetic drift. Such a relatively large role for stochasticity is indeed confirmed in yeast adapting on a surface [59], and by an increased diversity in the population in structurally evolved *E. coli* by limiting competition [60]. A more prominent role of stochasticity may thus diminish the relative impact of constraints from the adaptive landscape. Chance events in small or structured populations [61] may allow them to explore further, distinct peaks on the adaptive landscape compared to non-structured populations which relatively quickly converge to a close-by peak. Spatially structured environments thus allow for different community dynamics than well-mixed environments. Theoretical studies that use the adaptive landscape metaphor for adapting populations often assume such large, well-mixed populations, and a strong influence of selection combined with a low mutation rate (the so-called SSWM regime) [62]. Under such a regime, the adaptive dynamics are dictated by the selective benefit of the individual mutations involved. The speed at which adaptation can proceed is thus predictable to some degree, as it is proportional to the product of the fixation probabilities of the individual mutations [63]. As populations evolving in a spatially structured environment may be less likely to follow such simplified dynamics, it is an open question how useful the adaptive landscape framework is for assessing the repeatability of adaptation under such circumstances.

In this manuscript, we have discussed studies on the effect of ecology on adaptation, using the adaptive landscape metaphor as a guide. Experiments with microbes are most ideally suited to answer questions related to this topic, due to their relative ease of handling in the laboratory, the possibilities of genetic engineering, their tractable populations and relatively cheap next-generation sequencing strategies. For instance, adaptive landscapes can be constructed and mapped in environments with and without other community members. These recent methodological and conceptual developments are apt to yield novel insights in the relative roles of genotype and ecology in determining the course of evolution in diverse settings.

* * *

MGJdV was supported by Netherlands Organization for Scientific Research (NWO) Earth and Life Sciences (ALW) VENI Project 863.14.015, JAGMdV by Research Grant RGP0010/2015 from Human Frontier in Science Program and CRC1310 Predictability in Evolution from DFG, and SES by the NWO-WOTRO Grand Challenges Programme.

REFERENCES

[1] Wright S., in *Proceedings of the Sixth International Congress of Genetics*, Vol. **1** (Brooklyn Botanic Garden, Brooklyn, New York) 1932, p. 356.
[2] Kauffman S. and Levin S., *J. Theor. Biol.*, **128** (1987) 11.
[3] Arnold S. J., Pfrender M. E. and Jones A. G., *Genetica*, **112** (2001) 9.
[4] Poelwijk F. J., Kiviet D. J., Weinreich D. M. and Tans S. J., *Nature*, **445** (2007) 383.
[5] Poelwijk F. J., Tanase-Nicola S., Kiviet D. J. and Tans S. J., *J. Theor. Biol.*, **272** (2011) 141.
[6] Schoustra S. E., Hwang S., Krug J. and De Visser J. A. G. M., *Proc. R. Soc. B. Biol. Sci.*, **283** (2016) 1376.
[7] Chou H. H., Chiu H. C., Delaney N. F., Segre D. and Marx C. J., *Science*, **332** (2011) 1190.
[8] Burch C. L. and Chao L., *Nature*, **406** (2000) 406.
[9] Lunzer M., Miller S. P., Felsheim R. and Dean A. M., *Science*, **310** (2005) 499.
[10] Weinreich D. M., Delaney N. F., Depristo M. A. and Hartl D. L., *Science*, **312** (2006) 111.
[11] Lozovsky E. R., Chookajorn T., Brown K. M., Imwong M., Shaw P. J., Kamchonwongpaisan S., Neafsey D. E., Weinreich D. M. and Hartl D., *Proc. Natl. Acad. Sci. U.S.A.*, **106** (2009) 12025.
[12] Schoustra S. E., Bataillon T., Gifford D. R. and Kassen R., *PLoS Biol.*, **7** (2009) e1000250.
[13] De Visser J. A. and Krug J., *Nat. Rev. Genet.*, **15** (2014) 480.
[14] Aguilar-Rodríguez J., Payne J. L. and Wagner A., *Nat. Ecol. Evol.*, **1** (2017) 45.
[15] Hietpas R. T., Bank C., Jensen J. D. and Bolon D. N. A., *Evolution*, **67** (2013) 3512.
[16] Flynn K. M., Cooper T. F., Moore F. B. and Cooper V. S., *PLoS Genet.*, **9** (2013) e1003426.
[17] Poelwijk F. J., de Vos M. G. J. and Tans S. J., *Cell*, **146** (2011) 462.

[18] de Vos M. G. J., Poelwijk F., Battich N., Ndika J. and Tans S., *PLoS Genet.*, **9** (2013) e1003580.

[19] Lindsey H. A., Gallie J., Taylor S. and Kerr B., *Nature*, **494** (2013) 463.

[20] Gorter F. A., Aarts M. G. M., Zwaan B. J. and De Visser J. A. G. M., *Genetics*, **208** (2018) 307.

[21] de Vos M. G. J., Dawid A., Sunderlikova V. and Tans S. J., *Proc. Natl. Acad. Sci. U.S.A.*, **112** (2015) 14906.

[22] Franke J., Klozer A., de Visser J. A. and Krug J., *PLoS Comput. Biol.*, **7** (2011) e1002134.

[23] Bech-Hansen N. T., Till J. E. and Ling V. J., *Cell Physiol.*, **88** (1976) 23.

[24] Imamovic L. and Sommer M. O. A., *Sci. Transl. Med.*, **5** (2013) 204ra132.

[25] Schenk M. F., Witte S., Salverda M. L., Koopmanschap B., Krug J. and de Visser J. A. G. M., *Evol. Appl.*, **8** (2015) 248.

[26] Jiao Y. J., Baym M., Veres A. and Kishony R., *bioRxiv* (2016) 082107.

[27] Barbosa C., Trebosc V., Kemmer C., Rosenstiel P., Beardmore R., Schulenburg H. and Jansen G., *Mol. Biol. Evol.*, **34** (2017) 2229.

[28] Ratzke C., Denk J. and Gore J., *Nat. Ecol. Evol.*, **2** (2018) 867.

[29] Rendueles O., Amherd M. and Velicer G. J., *Curr. Biol.*, **25** (2015) 1673.

[30] Dugatkin L. A., Perlin M., Lucas J. S. and Atlas R., *Proc. R. Soc. B. Biol. Sci.*, **272** (2005) 79.

[31] Embree M., Liu J. K., Al-Bassam M. M. and Zengler K., *Proc. Natl. Acad. Sci. U.S.A.*, **112** (2015) 15450.

[32] Morris J., Papoulis S. E. and Lenski R. E., *Evolution*, **68** (2014) 2960.

[33] Zomorrodi A. R. and Segrè D., *Nat. Commun.*, **8** (2017) 1563.

[34] Bajić D., Vila J. C. C., Blount Z. and Sanchez D. A., *bioRxiv* (2018) 293407.

[35] Le Gac M. and Doebeli M., *Mol. Ecol.*, **19** (2010) 2430.

[36] Paquin C. E. and Adams J., *Nature*, **306** (1983) 368.

[37] de Vos M. G. J., Zagorski M., McNally A. and Bollenbach T., *Proc. Natl. Acad. Sci. U.S.A.*, **114** (2017) 10666.

[38] Levin-Reisman I., Ronin I., Gefen O., Braniss I., Shoresh N. and Balaban N. Q., *Science*, **355** (2017) 826.

[39] Gutierrez A., Laureti L., Crussard S., Abida H., Rodríguez-Rojas A., Blázquez J., Baharoglu Z., Mazel D., Darfeille F., Vogel J. and Matic I., *Nat. Commun.*, **4** (2013) 1610.

[40] Chu H. Y., Sprouffske K. and Wagner A., *J. Evol. Biol.*, **30** (2017) 1692.

[41] McKenzie G. J., Harris R. S., Lee P. L. and Rosenberg S. M., *Proc. Natl. Acad. Sci. U.S.A.*, **97** (2000) 6646.

[42] Hastings P. J., Slack A., Petrosino J. F. and Rosenberg S. M., *PLoS Biol.*, **2** (2004) e399.

[43] de Visser J. A. G. M., Zeyl C. W., Gerrish P. J., Blanchard J. L. and Lenski R. E., *Science*, **283** (1999) 404.

[44] Wielgoss S., Barrick J. E., Tenaillon O., Wiser M. J., Dittmar W. J., Cruveiller S., Chane-Woon-Ming B., Medigue C., Lenski R. E. and Schneider D., *Proc. Natl. Acad. Sci. U.S.A.*, **110** (2012) 222.

[45] Ram Y. and Hadany L., *Proc. R. Soc. B. Biol. Sci.*, **281** (2014) 1025.

[46] Krašovec R., Richards H., Gifford D. R., Hatcher C., Faulkner K. J., Belavkin R. V., Channon A., Aston E., McBain A. J. and Knight C. G., *PLoS Biol.*, **15** (2017) e2002731.

[47] Krasovec R., Richards H., Gifford D. R., Belavkin R. V., Channon A. and Aston E., *bioRxiv* (2018) 256305.

[48] Torres-Barceló C., Kojadinovic M., Moxon R. and MacLean R. C., *Proc. R. Soc. B. Biol. Sci.*, **282** (2015) 20150885.

[49] Guerin É., Cambray G., Sanchez-Alberola N., Campoy S., Erill I., Da Re S. Gonzalez-Zorn B., Barbé J., Ploy M. C. and Mazel D., *Science*, **324** (2009) 1034.

[50] Beaber J. W., Hochhut B. and Waldor M. K., *Nature*, **427** (2004) 72.

[51] Price M. N., Wetmore K. M., Deutschbauer A. M. and Arkin A. P., *PLoS ONE*, **11** (2016) e0164314.

[52] Porse A., Schou T., Munck C., Ellebaan M. and Sommer M. O. A., *Nat. Commun.*, **9** (2018) 522.

[53] McNally A., Oren Y., Kelly D., Pascoe B., Dunn S., Sreecharan T., Vehkala M., Välimäki N., Prentice M. B., Ashour A., Avram O., Pupko T., Dobrindt U., Literak I., Guenther S., Schaufler K., Wieler L. H., Zhiyong Z., Sheppard S. K., McInerney J. O. and Corander J., *PLoS Genet.*, **12** (2016) e1006280.

[54] Rodriguez-Beltran J., Hernandez-Beltran J. C. R., DelaFuente J., Escudero J. A., Fuentes-Hernandez A., MacLean R. C., Pena-Miller R. and San Millan A., *Nat. Ecol. Evol.*, **2** (2018) 873.

[55] Eldar A., Chary V., Xenopoulos P., Fontes M. E., Loson O. C., Dworkin J., Piggot P. J. and Elowitz M. B., *Nature*, **460** (2009) 510.

[56] San Millan A., Heilbron K. and MacLean R. C., *ISME J.*, **8** (2014) 601.

[57] Ramirez M. S., Traglia G. M., Lin D. L., Tran T. and Tolmasky M. E., *Microbiol. Spectrum*, **2** (2014) 1.

[58] Song X., Sun J., Mikalsen T., Roberts A. P. and Sundsfjord A., *PLoS ONE*, **8** (2013) e62248.

[59] Hallatschek O., Hersen P., Ramanathan S. and Nelson D. R., *Proc. Natl. Acad. Sci. U.S.A.*, **104** (2007) 19926.

[60] Habets M. G., Rozen D. E., Hoekstra R. F. and de Visser J. A. G. M., *Ecol. Lett.*, **9** (2006) 1041.

[61] Nahum J. R., Godfrey-Smith P., Harding B. N., Marcus J. H., Carlson-Stevermer J. and Kerr B., *Proc. Natl. Acad. Sci. U.S.A.*, **112** (2015) 7530.

[62] Orr H. A., *Nat. Rev. Genet.*, **6** (2005) 119.

[63] Szendro I. G., Franke J., de Visser J. A. G. M. and Krug J., *Proc. Natl. Acad. Sci. U.S.A.*, **110** (2013) 571.