Forthcoming in *The British Journal for the Philosophy of Science*. https://doi.org/10.1093/bjps/axz048

# Chances and propensities in evo-devo

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**Abstract**

While the notion of chance has been central in discussions over the probabilistic nature of natural selection and genetic drift, its role in the production of variants on which populational sampling takes place has received much less philosophical attention. This paper discusses the concept of chance in evolution in the light of contemporary work in evo-devo. We distinguish different levels at which randomness and chance can be defined in this context, and argue that recent research on variability and evolvability demands a causal understanding of variational probabilities under which development acquires a creative, rather than a constraining role in evolution. We then provide a propensity interpretation of variational probabilities that solves a conceptual confusion between causal properties, variational probabilities and extant variation present in the literature, and explore some metaphysical consequences that follow from our interpretation, specifically with regards to the nature of developmental types.

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## 1. Introduction

Chance in evolution has been a major focus of attention in evolutionary biology, both at the level of the generation of variation—how chancy is the production of new variants—and at the level of its perpetuation—how chancy is the diffusion and disappearance of those variants along evolutionary time.[1] Philosophers of biology have been classically concerned with the latter sense, the notion of chance being central in discussions over the probabilistic nature of natural selection and the stochasticity of genetic drift. In this frame, evolutionary changes are regarded as the result of probabilistic sampling processes in populations resulting in random or non-random outcomes. In a common analogy, the sample space of alleles or genotypes in a population is represented by colored balls in an urn, the colours corresponding to fitness values. A hand picking balls on the basis of their color represents natural selection, whereas a blind hand illustrates random drift (Millstein [2003]). The role of chance in the production of variants on which discriminate or indiscriminate sampling takes place—that is, how balls are introduced into the urn—has received much less philosophical attention. The reason seems to lie in the apparent consensus on the validity of the Modern Synthesis (MS) understanding of chance in this context as restricted to mutations, the ultimate source of heritable variation. According to this restricted notion, mutations are chancy insofar as their production is independent of their fitness values (Huneman [2017]; Lenski and Mittler [1993]; Merlin [2010]). In the urn analogy, the probabilities of balls of each color being in the urn before the sampling are causally independent of their probabilities of being picked on the basis of their color. Philosophers and historians of biology agree that this notion of chance was established against the hypothesis of 'mutational Lamarckism', according to which the environment can induce mutations directed towards producing fitter phenotypes in that particular environment (Razeto-Barry and Vecchi [2016], p. 2).

However, this restricted definition does not exhaust the different meanings of the concept of chance which were crucial in articulating the MS view on the production of variation. Insofar as chance was generally invoked as opposed to the directionality of natural selection (Eble [1999]; Millstein [2011]), it not only served to dismiss mutational Lamarckism. It was also instrumental in confronting other alternative explanatory strategies where the production of variants had a creative role. The classic debate between mutationists and selectionists that pervaded the early days of the MS illustrates this point. In a recent paper, Beatty ([2016]) has forcefully argued that the main target of mutationists was the creative role of natural selection, as based on the assumption that variation was not a driver, but just a precondition of evolution. Such an assumption demanded that mutations were not only undirected with respect to selection—a statement that mutationists never questioned—, but also with regard to the phenotypic variants they affected. For selection to be creative, mutations needed to be copiously available, have a continuous effect on phenotypic traits, and be capable of affecting them with almost equal probability. Trait variation, in other words, should be abundant, gradual and non-directional. In contrast, mutationists conceived of natural selection as a filter or a 'sieve' (de Vries [1905]) that merely discarded or preserved variations (see Stoltzfus and Cable [2014]). From their perspective, only if new phenotypic variants, as introduced by new mutations, occurred—only if new types of balls were added into the urn from time to time, or if some of them were more likely to be added than others—then selection could align with the range of variation in some of these new

[1] There are other meanings of chance in evolutionary theory that do not fit into this division of the debate, such as chance as ignorance of causes (see Millstein [2011]), but we constrain ourselves to objective meanings (see section 2).

directions. In this view, the production of variation appeared, together with the selection of variation, as a causal directing factor of evolution. In contrast, the MS view of chance stood against the idea that variation is a major source of novelty in evolution, guaranteeing that selection, permanently acting upon copious and unbiased variation, is the only causal factor explaining "anything that is not a random outcome of evolution" (Wagner [2013], p. 2006).

Beatty ([2016]) concludes that the major lesson to be drawn from this controversy is that our understanding of evolution as consisting of two conceptually and temporally distinct processes—namely, those involved in the production and in the sampling of variation—should be radically abandoned. The reason, he argues, is that selectionists were right in their claim that in sampling variation, natural selection creates it as well. The analogy of the urn indeed falls short in accounting for this creative role of selection. In picking realised phenotypes, natural selection not only multiplies the balls of a certain colour, but it also increases the probability of new variants arising in the same color range. Given that selection influences both the generation and the fixation of variation, the very project of analysing variational probabilities as a distinct problem from the probabilities of sampling standing variation might be objected to be ill-founded.

However, new research agendas in evolutionary biology agree that the mechanisms involved in producing variation generate non-random probabilities which are independent of populational sampling. In this context, variation is invoked again as causally determinant of, rather than as a precondition for, evolutionary change (Stoltzfus [2006]). In particular, since the early 1980s, authors working on the synthesis between development and evolution have recurrently confronted what they perceive as a received notion of random variation:

> [. . .] in evolution, selection may decide the winner of a given game but development non-randomly defines the players. (Alberch [1980], p. 665)

> While the mutation may be random with respect to whether it improves or reduces the fit to the environment, it is not random with respect to which traits it affects. (Pavlicev and Wagner [2012], p. 234)

> [. . .] a "developmental bias" acting on the distribution of phenotypes subject to natural selection [. . .] suggest that random genetic mutation will rarely mean random variation in phenotypes. (Bateson and Laland [2013], p. 714)

This paper focuses on the concept of chance in the light of new work in evolutionary developmental biology, or evo-devo. Evo-devo is a heterogeneous discipline (Love [2015]), and much research in it is addressed to answer specific questions about actual changes in developmental mechanisms which have causally undergirded phenotypic changes along evolution. For instance, how did the modifications in the gene regulatory networks shared by the extremities of fishes and land vertebrates underlie the fin-to-limb transition? Additionally, a major epistemic goal in evo-devo concerns how the properties of development relate to the probabilities of phenotypic variants arising, rather than being fixed in a population.[2] For example: how does development influence the probability that fore

[2] Just like evo-devo is not only concerned with the probabilities of traits arising, the MS, and particularly population genetics, is not only interested in the probability of their fixation. Our contrast only applies to their differing research agendas insofar as they concern the distribution of traits.

and hind limbs vary independently in some tetrapods? And how does this affect the likelihood of favourable changes arising in this lineage? The study of variational probabilities as resulting from developmental tendencies is instantiated in the notions of 'variability' and 'evolvability'—themes that arguably constitute the main novel contribution of evo-devo to evolutionary theory (Hendrikse *et al*. [2007]). This paper examines how variational probabilities are represented in evo-devo studies of variability and evolvability and their creative role in evolution. We argue that the chancy character of variation in this context, rather than being random with respect to selection, is better understood as objectively probabilistic, that is, as showing probabilities that are generated by the causal structure of a chance setup.

The structure of the paper is as follows. In section 2, we distinguish the different levels at which randomness and chance in variation can be defined, and assess them from a philosophy of probability perspective. Sections 3 and 4 discuss how variational probabilities are conceptualised in evo-devo studies of variability and evolvability, respectively, and show how these studies challenge some of the received assumptions on the role of chance in the production of variation in evolution. The last section argues that a propensity interpretation can help in clarifying the relation between the different ways in which variability and evolvability are defined in the literature, where causal properties, probabilities and frequencies are often confused.

## 2. Chance and Randomness in the Production of Variation

As outlined in the introduction, the MS view of chance included an engagement with a selectionist, thus externalist view of evolution that neglected the causal role of internal—genetic and developmental—mechanisms in evolutionary change. Both the generative processes of variation and their resulting phenotypic outcomes were considered random in virtue of not being aligned with the direction of natural selection (Eble [1999]; Millstein [2011]). Although characterising a pattern of variation as random in this sense does not reject the possibility that some other pattern may be present (Eble [1999]), the exclusive focus on the adaptive direction of variation seems to have obscured the recognition of other relevant evolutionary patterns. Since variation is the sample space of evolution, we believe that a precise definition of what is considered a random pattern in such space and what are the processes that generate it will help in clarifying the senses of chance involved in current claims on the evolutionary role of the mechanisms producing variation.

In the philosophy of probability, randomness applies to outcomes and chanciness to the processes that produce them (Eagle [2019]). Random trials are procedures with a defined set of possible outcomes, namely the sample space—e.g. the numbers one through six for dice rolls—. Each outcome—e.g. landing on six—, or set of outcomes—e.g. landing on an even face—, is called an event, and each event has a probability measure—e.g. the probability one sixth of landing on six—. Taken together, the sample space, the set of events and the probability measure constitute a probability space. A set or a series of outcomes is random if it does not present any order or pattern. For instance, the series of a die landing 1, 6, 5, 3, 1 is a random series. According to objective views of probability, a process involved in a random trial is chancy if it is causally responsible for probabilities that represent real features of the world rather than our epistemic limitations. Thus, the process of rolling a die is chancy insofar as its objective properties—for instance, the mass distribution of the die or the initial conditions of the roll—are causally responsible for the probability

distribution of the outcomes it produces—in this case, of landing on the six faces with a probability of one sixth for each of them—. Importantly, this notion of chance also applies to nonrandom phenomena. For instance, the irregular mass distribution of a loaded die is causally responsible for the probability of landing on six being higher than the probability of landing on one. In this case, the series of landing events will be nonrandom in the previous sense, but the rolls are chancy insofar as their objective properties define a probability space.

We now consider what are the probabilistic patterns of variation described in internalist approaches to evolution, where internal mechanisms of organisms involved in the production of variation are claimed to chanell evolutionary change. As the theoretical biologist Andreas Wagner ([2012]) has recently made explicit, the sample space of variation in evolution can be defined with respect to the effects of mutations on three different aspects of a living system. While the most widely discussed notion of randomness in evolutionary biology regards the effects of mutations on fitness, these effects can also be defined at the genotypic and at the phenotypic level. In the following, we will define different sample spaces with respect to the effects of mutations at these three levels—genotypic, phenotypic and adaptive—, and will consider the kind of processes involved in these random trials, namely in the reproductive events where mutations take place. We will argue that the generative role attributed to these processes entails a causal, productive notion of chance that contrasts with the views of variational probabilities as non causally responsible for evolutionary outcomes, neither imprinting directionality—against mutationism—, nor causing adaptation—against mutational Lamarckism—. In contrast, we defend that these trials are causal probabilistic processes, that is, processes whose causal structures are responsible for the probabilities they generate (Abrams [2017]; Strevens [2010]).

### 2.1. Mutational randomness

Molecular genetics has recently shown that the effects of mutations on the genome are not random in the classical expectation of equally probable (Wagner [2012]). Different kinds of mutations—point mutations, inversions—have different probability distributions, and even nucleotide changes are not equally likely nor have independent probabilities. Based on this new empirical evidence, the so-called ‘neomutationism’, or the theory of mutation-driven evolution (Nei [2013]) has brought back the debate on the explanatory role of variation in evolution (Stoltzfus [2006]; Wagner [2013]). In contrast to classical mutationism, neomutationism considers the probabilities not only of point mutations, but also of all kinds of genomic change—genome duplication, fusions, lateral gene transfers...—as well as the molecular causes underlying such probabilities (Nei [2013], p. 197). At this level, different kinds of mutational outcomes define the sample space, while their associated probabilities gain accuracy with scientific practice. In turn, molecular processes can be interpreted as taking part in the random trials that bring about these outcomes.

### 2.2. Morphological randomness

Some authors have tended to assume that developmental biases entail the same conceptual challenge to the chanciness of variation as mutational biases. For example, Lenormand and coauthors consider that saying that development biases variation is ‘just another way to say that mutations are not occurring in other possible directions’ ([2016], p. 198). Both mutational and developmental biases certainly entail that the internal mechanisms generating variation, rather than external, selective

forces, are important directing causes of evolution. However, the probabilities invoked in evo-devo do not concern the distribution of mutations, but rather the distribution of the resulting phenotypes.[3] What evo-devo confronts is precisely the assumption according to which the alleged properties of variation at the genetic level can be extrapolated to the morphological level. That is, even if mutations were random in the sense of being equally likely to arise in the genome, the phenotypic variants resulting from these mutations would not: 'mutational randomness' does not entail 'morphological randomness'.

The distinction between mutational and morphological randomness would be irrelevant for the present discussion if genotypic variation mapped directly onto phenotypic variation, as it is implicitly assumed in the classical models of population genetics (Hallgrímsson and Hall [2005]). Insofar as these models do not include phenotypic traits—that is, they map genotype to fitness directly—, they necessarily exclude development from the explanation of evolutionary dynamics. Importantly, the 'morphological randomness' assumption underlying such models played not only an instrumental role but rather a representational one, where randomness implicitly refers to real features of the phenomenon under study (see Millstein [2006]). Thus, at least in Fisher's canonical case, heuristic simplification was not the only reason for excluding development from the population genetics models of adaptive dynamics (Hansen [2006]). On the one hand, the complexity of development was taken like statistical noise not only for the sake of simplicity, but in virtue of its assumed capacity to average over all possible allele combinations in an ideal, large population. On the other hand, organismal complexity was considered to imply that advantageous mutations are always possible and that they will arise and become fixed given a large enough population.[4] Therefore, classical population genetics assumes that, at a population level, development does not bias the effects of genes on phenotypic traits. As a consequence, the mapping between genes and phenotypic variants can be treated as a simple, linear one, and evolution can be defined as a change in gene frequencies.

In contrast, the claim that development should be included in the explanatory structure of evolutionary theory came from the empirical evidence on the 'nonrandom and highly structured' patterns of phenotypic variation (Wagner [2012], p. 96). The early advocates of evo-devo highlighted that morphological variants were not random in the sense of isotropically distributed in all directions of the phenotypic space (Alberch [1982]). From an evo-devo perspective, then, the sample space of variation needs to be defined at the phenotypic level that results from development. In turn, mutations have phenotypic effects insofar as they affect the developmental processes that generate them. For example, evo-devo models of the evolution of mammalian teeth show that, depending on the developmental parameters they affect, different mutations can generate similar tooth morphologies,

[3] Specific kinds of mutational outcomes have phenotypic probabilities associated as well. For example, there seems to be a correlation between gene duplications and organismal complexity. Given that the size of the genome has increased from unicellular to multicellular organisms, the higher probability of gene duplications in the bigger genomes of multicellulars might have influenced the evolution of complexity (Nei [2013], p. 93). Nonetheless, the association of mutational to phenotypic probabilities does not need to include the causal developmental structure connecting the two.

[4] We do not mean that the founders of the MS endorsed the naif assumption that the actual frequencies of variation are isotropically distributed in each generation. The assumption on isotropic variation applies to how a given trait, as established by past evolutionary processes, *can* possibly vary.

or the other way round: similar mutations can lead to different tooth shapes (Salazar-Ciudad and Jernvall [2002]).

While in the 1980s the role of development in evolution was mainly perceived as a constraint or a limitation to natural selection, since the mid-1990s more positive terms, such as variability and evolvability, have been introduced in the evo-devo literature in order to capture the creativity of development (Brigandt [2015a]). From this perspective, developmental systems do not constraint selection, but rather create the morphological variants that can arise through mutations (Amundson [1994]). Non-realizable morphologies simply do not belong to the sample space defined by the possible outcomes of developmental processes. Therefore, highlighting the order and discreteness of the morphospace is not a way of relativizing the importance of natural selection in evolution, but rather a claim on how selection itself works. The reason is not only that selection acts on phenotypic traits, but also that each selected organism contains, in addition to its realized phenotype, a generative mechanism capable of creating new, structured variation. Thus, whereas developmental biases can be seen as the weak, non-controversial claim that variation is limited by what is developmentally possible, a stronger claim considers them as productive causes of evolutionary outcomes (Salazar-Ciudad [2006]; Stoltzfus [2006]). We believe that the implications of this stronger claim are better understood under a causal interpretation of the variational probabilities at work in evo-devo. Consequently, developmental systems can be seen as probabilistic systems or chance setups, exhibiting particular setup conditions that give rise to a probability distribution of phenotypes as possible outcomes.

### 2.3. Adaptive randomness

As outlined in the introduction, the received view of chance, insofar as it concerns the production of variation, accounts for the effects of mutations on fitness:

> Mutations are evolutionary chancy iff 'there is no specific causal connection between the probability of a mutation being beneficial in a given environment and the probability of it occurring in this environment' (Merlin [2010], p. 6)[5]

Recent discussions on directed mutator mechanisms, which seem to get activated under certain environmental conditions have come to question the scope of this notion (see Razeto-Barry and Vecci [2016] for a review). For instance, thermal stress might increase the rate of mutations in bacteria *E. Coli*, increasing as well the probability of fitter, thermotolerant variants to arise in a population (Jablonka and Lamb [2005]).[6] However, developmental approaches to evolution do not concern this restricted view, but rather the more general formulation of 'evolutionary chance', according to which variation is chancy in the sense of causally 'independent of the generally adaptive direction of natural

[5] This definition reformulates Simpson's probabilistic version of chance in *The Major Features of Evolution*, an exemplary instantiation of the MS view (Merlin [2010]). Note that causal connections do not connect probabilities themselves, but rather the causal factors responsible for these probabilities.

[6] Against this argument, advocates of the MS have replied that the notion of chance as independent probability still holds: just like tossing a coin more times increases the number of head results, mutator mechanisms increase the number of mutations independently of their associated fitness values. Other authors have argued that some induced mutations might increase the relative frequency of adaptive variants in a population, and that deciding on their chanciness is an empirical question (Razeto-Barry and Vecchi 2016).

selection' (Millstein [2011], p. 435; see also Eble [1999]), Under such a view, causal factors as distinct as drift, mutations, or development count as chancy, and produce outcomes that are random with respect to adaptation. Nevertheless, since the mid-1990s, evo-devo research on evolvability has shown that the ability to generate fitter phenotypic variants can be causally influenced by developmental variational tendencies. Defined as an ability that increases the probability of adaptive evolution, evolvability touches the very core of this general 'evolutionary chance' concept. At this level, the sample space of variation is a space of the adaptiveness of phenotypic variants generated through development, and with non-random associated probabilities.

In this section, we have argued that the variational probabilities found in evolutionary biology are conceptually independent of sampling probabilistic processes at the population level, and can be generated in different ways: the probabilities of genotypic variation stressed by neomutationists are causally explained by mutational mechanisms, whereas the probabilities at work in evo-devo are dependent on the structure of developmental systems. We have seen that the patterns of variation at the phenotypic level are not random, neither morphologically nor adaptationally, and we have suggested that development plays the role of a chance setup for variation. In the next two sections, we introduce in more detail how the probabilities of generating phenotypic variation, as well as the probabilities of evolving, are conceptualised in evo-devo models of variability and evolvability, respectively.

## 3. Variability and Phenotypic Probabilities

A recurrent distinction in evo-devo is that between variation and variability (Hallgrímsson and Hall [2005]). Variation refers to the extant variants of traits in a population, and can therefore be 'measured as a series of static observations within a sample' (Willmore *et al*. [2007], p. 99). Variability concerns 'the way a phenotypic trait changes in response to environmental and genetic influences' (Wagner and Altenberg [1996], p. 969),[7] and, as a consequence, includes not only the realised variation, but also all possible outcomes (Willmore *et al*. [2007]). In evo-devo, phenotypic variability is associated with developmental variability, or 'the tendency of developmental systems to change' (Hallgrímsson *et al*. [2005], p. 526).

Developmental systems differ in the amount and the type of morphological variation they can deliver. For instance, some developmental systems can produce more gradual morphological variation compared to others generating more complex and diverse variation, while some of them can generate more modular variation than others. Different variabilities hence correspond to 'different types of developmental mechanisms giving rise to different types of morphological variation from genetic and environmental variation' (Salazar-Ciudad [2007], p. 398). In turn, each of the possible outcomes of the sample space of phenotypes has distinct associated probabilities. In this sense, variability, insofar it concerns 'what is more likely to be generated' (Alberch [1982], p. 314), can be defined in probabilistic terms as a probability distribution over sets of possible types of phenotypic variants. Finally, the term variability is also used to refer to the 'underlying variational tendencies' responsible for the generation of such patterns and their probability distributions (Wagner [2014], p. 19).

[7] For the purposes of this paper, we will focus on genetic influences, therefore excluding environmental influences on phenotypic plasticity or niche construction from the present discussion.

It is commonly held that these tendencies depend on the structure of the genotype-phenotype map (hereafter, GPM), while they are conceptually independent of population parameters such as allele frequencies and variances (Hansen [2006]). The GPM is the core tool used in evo-devo to represent the distinct tendencies—of organisms, developmental systems or genotypes—to produce distributions of phenotypic variants with different probabilities (see Pigliucci [2010]). The GPM is a function that maps molecular genetic variation onto phenotypic trait variation. It summarizes all the possible developmental processes connecting the genotypic space—i.e. all possible genotypes resulting from mutations in a genome or a region of it—and the phenotypic space—i.e. all possible associated phenotypic variations. GPMs capture both structural and dynamical properties of development. For instance, the effects of mutations in a given GPM can be structured in a modular way, meaning that they affect some phenotypic traits independently of others (see, e.g. Wagner *et al*. [2007]). But the mutational effects can also differ depending on the developmental stage at which they are expressed. Thus, mutations affecting early development have been claimed to be 'generatively entrenched', insofar as they should be more likely to have widespread downstream effects (Wimsatt [2001]). Moreover, GPMs can be defined at different levels of organisation, and at different taxonomic scales, in order to examine how variation is structured within a population, a species, a lineage or even a whole kingdom. For instance, the structure of the metazoan GPM can be described as a modular structure regardless of the extreme diversity of developmental processes it represents. The wider its range of application, the more abstract the structural relationships represented in a GPM.

The consensus on the applicability of GPMs to variational probabilities in evo-devo lies, we believe, in their representational role of development as a structuring cause of variation. Regardless the level of abstraction at which these maps work, they stand for developmental conditions that remain stable across the trials generating phenotypic results. They represent abstract properties of developmental chance setups as defined in the previous section. A typical way to illustrate the causal properties of chance setups is by alluding to gambling games, such as fortune wheels, dice rolling and coin tossings (see, for instance, Strevens [2010]). In this line, the analogy of the dice and the probabilities of landing different numbers intends to capture the causal nature of the probabilities at work in evo-devo (Lewens [2009]). Taking a well-established conceptual distinction, namely that between triggering and structuring causes (see Ramsey [2016]), the velocity and the angle in which the die is thrown are the triggering conditions of the roll, while the shape and weight of the die are the structuring conditions that determine the sample space and probability distribution of results. Similarly, mutations set up different initial conditions for the developmental process, but it is the properties of this process that structure the possible phenotypic effects of those mutations. Although development depends on genetic inputs, and in turn could be altered by certain mutations, its general, structural properties tend to remain stable. Such structuration is, we claim, what is represented in GPMs. Nonetheless, the dice analogy has serious limitations for capturing the properties of developmental chance setups. The main reason is that, in this case, the possible outcomes of random trials—the six faces where the die can land—preexist the rolling of the die and cannot change through the iteration of this process. As it will become apparent in the next section, this major disanalogy carries with it several derived limitations. In the following, we will use instead a well-known toy model of the GPM, the so-called RNA model, for illustrating the ways in which variational probabilities are conceptualised in evo-devo.

### 3.1. The RNA model as a model for evo-devo

The RNA model is a very simple GPM in which the RNA nucleotide sequence represents the genotype and the RNA secondary structure or shape is taken as the phenotype (Schuster [2001]; Stadler *et al*. [2001]; Fontana [2002]). The mapping function is given by the way sequences fold into shapes. The RNA model is an ideal analogy for evo-devo (Fontana [2002]), and is particularly useful to illustrate the way variational probabilities are conceptualised in this field. Firstly, this model allows to separate the probabilities of being generated from the probabilities of being selected, since it is logically prior to and independent of natural selection. Secondly, while most probabilities in evo-devo are qualitatively characterized due to the complex developmental interactions that give rise to complex phenotypes, in this model variational probabilities can be quantified, insofar as all possible genotypes, as well as their corresponding phenotypes, are known. Thirdly, the folding process by means of which a sequence reaches its structure is analogous to a developmental process, while the algorithmic rules that assign a given shape to a set of sequences correspond to the mapping relation. As in complex evo-devo GPMs, the actual physical processes are abstracted away in these algorithmic rules. Finally, in the RNA model variational probabilities do not depend on the probabilities of mutations arising. A genotypic change corresponds to a movement from one point of the genotypic space to another, and this movement can be modelled as random in the statistical sense of equiprobable. However, as Wagner ([2012]) points out, this 'simplifying assumption' still leads 'to the conclusion that phenotypic change is nonrandom' (p. 112, n. 6; see also Stadler *et al*. [2001]).

[Insert Figure 1 about here]

In the RNA model, the genotypic space, or the space of all possible sequences, is represented by a network, where each node corresponds to a sequence, and each edge connects the sequences which are separated by a single point mutation (see Figure 1). Neutral networks are those subsets of sequences that fold into the same shape. A single point mutation in certain nodes of the network will be neutral with respect to the phenotype, thus illustrating the lack of a one-to-one correspondence between genotypes and phenotypes. In this model, the variability of a phenotype *j* is defined as the probability that any point mutation inside its neutral network ($S_j$) gives rise to a change in the RNA secondary structure ($S_k$). This probability is given by the following equation (Schuster [2001]):

$$\square\ (S_k\,;\, S_j) = \square_{kj} \,/\, |\, B_j\,|$$

Where $\square_{kj}$ is the number of point mutations leading from phenotype *j* to phenotype *k*, and $B_j$ is the set of all possible point mutations in the neutral network of phenotype *j*.[8] Now, a given GPM will have specific variational probabilities depending on how neutral networks are distributed in the genotypic space. Through this model, we can quantify the variability of a phenotype as a probability function over the phenotypes it can give rise to upon mutation. This property depends on how constrained—or accessible—a phenotypic change is by the structure of the GPM, obtained as a result of the way generative processes—folding, in this case—connects sequences to shapes. The probability distribution of phenotypic changes is not explained by genetic movements in the network

[8] Note that from this model, it will be *prima facie* possible to derive the variability of an entire GPM, as well as the variability of each sequence. The former will be a function of both the number of possible phenotypes for a given GPM and their closeness. The latter could be quantified through the number of non-neutral neighbors for a given sequence (Fontana [2002]).

but by the structure and distribution of neutral networks in the genotypic space, that is, by the structure of the GPM. Due to this distribution, heritable phenotypic variation can only be generated in certain phenotypic directions. The study of variability shows that the structure of GPMs, in representing developmental relations, accounts for the patterns of phenotypic variation across generations, and their associated probabilities.

GPMs structures allow the establishment of a probability measure over a sample space of phenotypic changes. In the RNA model, both genotypic and phenotypic closeness—that is, mutational distances between sequences as well as between resultant phenotypes—are represented for a given trait, making it possible to measure phenotypic change events under mutation. The GPM determines how individuals can explore the phenotypic space across generations, navigating from one set of phenotypic outcomes to another. Individual sequences 'move' throughout the genotypic space, every mutation changing the accessibility to the shapes of the phenotypic space. In this sense, developmental setups are not only chance setups for repeated trials of indefinite iteration, each trial corresponding to a reproductive event. They are also history-dependent chance setups, where the outcome of a trial may change the space of initial conditions for the next one.[9]

However, in accounting for long-term evolution, it is essential that the probability space itself can change. While developmental robustness will make this highly improbable, some mutations can affect the very structure of the GPM, hence altering the probability distribution of the resulting phenotypes. Unlike typical chance setups, the probability distributions generated by development do not remain the same across trials in the long evolutionary term. The reason is that, in chance setups such as dice rolling, triggering causes—the velocity and the angle in which the die is thrown—are not causally connected with structuring causes—the shape and weight of the die—. As a consequence, the possibility that some triggerings of the throw can affect the structure of the die is not represented in these analogies. The RNA model has indeed the same limitation as an analogy for variational probabilities in evo-devo, given that the biochemical rules that determine RNA folding do not change. In contrast, the structure of more complex GPMs is causally influenced by the setup—physical, genetic, and epigenetic—conditions of the developmental process, and can therefore evolve. For instance, as we saw above, the modular architecture of the GPM explains that tetrapod limbs have a higher probability of evolving independently of other tetrapod traits. However, in some groups—birds, bats and pterodactyls—the ancestral developmental correlation between fore and hindlimbs is broken. As a consequence, these traits have evolved independently, and have a higher probability of doing so in the future (Wagner *et al*. [2007]). Accordingly, the developmental tendencies of limbs to vary in such groups have themselves evolved, and the extant GPM of these groups differs from the ancestral one.

## 4. Evolvability and the Probability of Evolving

Given the architectural complexity of organisms, the idea that random mutations can provide with adaptive phenotypic variants frequently enough to make evolution itself possible is not straightforward. Evolvability has recently become a central concern in evolutionary biology. While some philosophers of biology have intended to develop a unifying characterization of this concept

[9] Variational probabilities, therefore, violate the condition of independent probability (Eagle [2019]).

(Brown [2014]), definitions of evolvability in different disciplinary contexts are not easily reducible (Nuño de la Rosa [2017], Pigliucci [2008]). Here we focus on evolvability the way it is understood in evo-devo, as illustrated by the following highly cited definitions of the term:

> the ability of random variations to sometimes produce improvement (Wagner and Altenberg [1996], p. 967)

> the capacity to generate heritable, selectable phenotypic variation (Kirschner and Gerhart [1998], p. 8420)

> the capacity of developmental systems to evolve (Hendrikse *et al*. [2007], p. 394)

On the basis of these definitions, one can infer the main components of developmental approaches to evolvability. On the one hand, just like variability, evolvability is a variational property that cannot be reduced to the properties of extant variation in a population. In this regard, measures of evolvability at the population level—e.g. mean-scaled additive genetic variances, or mutational rates—are regarded as particular quantifications, rather than definitions, of the ability of populations to respond to selection (Hansen [2006], p. 129). On the other hand, while evolvability depends on variability, the ability to vary is not a sufficient condition for a system to be evolvable. Evolvability is defined as the capacity to vary in an adaptive way, and therefore has two aligned components, namely variability, as dependent on the GPM, and fitness (Watson *et al*. [2014]), as dependent on the so-called phenotype-fitness map (see Figure 1).[10] In evo-devo, this ability is attributed to developmental properties (Kirschner and Gerhart [1998]) and, more generally, to the structure of the GPM and its associated variational patterns (Pavlicev and Wagner [2012]).[11] Although the ability of populations to evolve does depend on populational parameters such as population size, and on the actual selection regime, evo-devo approaches to evolvability are restrained to understanding how adaptive evolution causally depends on the structure of development. For instance, the tendency of developmental systems to react in a coordinated fashion to environmental and genetic perturbations has been claimed to facilitate adaptive variation (Gerhart and Kirschner [2007]). Finally, evolvability is regarded as being responsible for predictable probabilistic outcomes. In this regard, and similarly to variability, evolvability is sometimes defined as the probability to evolve rather than as an ability:

> the probability that random mutation will improve the phenotype. (Pavlicev and Wagner [2012], p. 232)

> the likelihood of parents being able to produce offspring fitter than themselves. (Altenberg [1995], p. 43)

[10] It is important to note that in associating gene variants to fitness values, classical population genetics treats both maps as black-boxes. While there has been a lot of criticism to the neglect of the first map, evo-devo theory has tended to ignore the second. It is in this context that some authors define evolvability as the ability to generate heritable phenotypic variation, therefore identifying it with variability (see, for instance, Schlichting and Murren [2004]).

[11] Development is also invoked sometimes in evo-devo as structuring fitness effects through internal selection: '[developmental processes] provide internal, non-random evolutionary variation [...] Because of the internal requirement that modified ontogenies be functional, only a subset of all theoretically possible phenotypes will be generated' (Raff [1996], p. 325). Similarly, Bonner [2013] argues that randomness plays a minor role in complex organisms with longer developments that filter out deleterious mutations.

As outlined in section 2, evolvability does not challenge the restricted definition of chance as 'evolutionary chance mutation' (Merlin [2010]), according to which the causes of specific mutations are independent of their fitness effects in particular environments. However, it does challenge a general notion of adaptive chance, as formulated by Millstein: 'evolutionary chance is primarily characterized by the causes that it prohibits entirely, namely, causes that proceed primarily in an adaptive direction' ([2011], p. 436). Evolvability research shows that, under some conditions, there is a causal connection between the probability to vary and the probability to adapt, or, more precisely, between the probability of a mutation resulting in an adaptive phenotypic variation and the probability of any other mutation resulting in an adaptive variation as well given the same type of selective environment. Here the causal connection between variation and fitness is not established between specific mutations and the local optima of the environment, but between the variational properties of developmental systems and the general structure of the fitness landscape. In this regard, evolvability models represent chance setups that distance themselves in two crucial ways from those involved in the classical models of evolutionary genetics.

On the one hand, unlike traditional optimisation models, which address a solution or output directly, evolvability models can be described as variational models of good outputs, namely the parameters of a developmental system that generate fit phenotypes (Watson *et al*. [2016]). In these models, fitness values are not attributed to the distinct phenotypic outcomes a GPM can deliver, but to the structure of the GPM itself. For instance, modular GPMs are claimed to be more evolvable in virtue of how they structure variational possibilities. In the case of metazoans, variational modularity is considered to facilitate their evolution by allowing selection to act on different traits independently, hence preserving the functional coherence of the organism (Wagner and Altenberg [1996]).

On the other hand, classical population genetics models the evolutionary environment as a local environment operationalized by the fitness values assigned to genetic variants. In contrast, evolvability models work with a generalised notion of the selective environment, defined by the structural regularities shared by a set of local environments that are invariant over time (Watson *et al.* [2016]): 'environments in nature do not vary randomly, but rather seem to have common rules or regularities' (Parter *et al*. [2008], p. 2). Accordingly, selection seems to favour phenotypic variation distributions that are structurally similar to the structure of the selective environment.[12] For instance, when the environment varies in a modular way, switching between several goals, modular developmental systems have a higher probability of generating adaptive variation and therefore tend to be selected (Parter *et al*. [2008]; Pavlicev *et al.* [2011]). In modelling biological systems and environment this way, evolvability models do not attempt to make probabilistic predictions of short-term evolution in populations, but rather long-term probabilistic predictions across taxa. Thus the random trials, and consequently the chance setups, involved in generating the sample space of evolvability include general variational tendencies as well as a selective pattern, which conjointly determine what types of variation, rather than what phenotypic outcomes, favour adaptive changes.

A further question concerns whether evolvability itself can evolve. While the fact that phenotypes vary in their ability to respond to natural selection is widely accepted, the evolution of evolvability is

[12] It is important to emphasize that these models only work when the future environment entails characteristics of the past one and will fail if fluctuations bring about completely different environments.

generally distrusted as entailing a teleological approach to evolution: natural selection cannot produce adaptations for an environment it has not yet encountered (Sniegowski and Murphy [2006]). However, theoretical models have recently shown that gene regulatory networks sequentially exposed to different selective environments can 'learn' their general structure. This facilitates their evolution in new and previously unseen environments—proven they have the same underlying regularities—, varying in a way that makes it highly likely for the associated phenotypic variants to be selected in the next generations (Watson *et al*. [2016]). For instance, two phenotypic traits that are frequently selected together can become causally correlated through the evolution of gene-regulatory interactions that cause them to co-vary in future environments (Pavlicev *et al.* [2011]).

## 5. Variational Propensities in Evo-Devo

In the previous sections we showed how the variational properties involved in evo-devo models of variability and evolvability challenge the received notion of 'morphological randomness', as well as a general notion of 'evolutionary chance'. However, we have seen that these variational properties are invoked in different ways in the literature, sometimes as patterns of variation, others as abilities, and others as probabilities. Given the lack of consensus on how to understand these properties, in this section we propose a frame for interpreting them: that of propensities. Propensity interpretations understand probability as a physical disposition or tendency of a system to produce an outcome. We have argued that variational probabilities are grounded in the properties of developmental systems as chance setups. We now defend that these properties are better understood as propensities or probabilistic dispositions of developmental types. Moreover, distinguishing propensities, objective probabilities, and frequencies (see Suárez [2016]) allows us to introduce the role of generative mechanisms in the causal view of probability endorsed by the conceptualisation of variational properties at work in evo-devo.

Interpreting variational probabilities as propensities is a natural way to fit the analysis of chance in evo-devo with current philosophical discussions in evolutionary biology, where separating frequencies, probabilities, and propensities has played a key role in clarifying some of the conceptual puzzles entailed by the notion of fitness. According to the well-known propensity interpretation (Mills and Beatty [1979]), fitness does not refer to an organism's actual survival and reproductive success, but rather to its propensity, expressed in probabilistic terms, to survive and reproduce in a particular environment and population. This distinction enabled the additional recognition of the distinct roles that fitness plays in evolutionary explanations—as a propensity—and in their quantitative models—as a probability measure that can be compared with actual frequencies (Sober [2001]). We believe that the roles of variability and evolvability are similarly threefold and that a propensity interpretation of them can help in clarifying the relation between the different ways in which these terms are defined in the literature.[13]

[13] The ambiguous way of referring to variational properties in the biological literature is also reflected on the philosophical literature. For instance, Brown ([2014]) indistinctly refers to evolvability as an 'abstract disposition' and as an 'objective probability'.

### 5.1. Individuating variational propensities

Variational propensities can be defined as dispositions to generate specific patterns of phenotypic variation when genetic and environmental changes take place in reproduction. These propensities determine the probability of generating different types of variation—such as plastic, modular, or robust—as well as the probability of evolving in adaptive directions. Dispositional properties are defined as functions relating stimulus conditions and manifestations, and are instantiated by any causal mediator between the two (see Austin [2017]). We believe that the causal role attributed to variational properties in evo-devo is dispositional, and therefore independent of the particular mechanisms realizing it (see Austin and Nuño de la Rosa [2018]). Although specific developmental mechanisms can be certainly identified for particular variational events, multiple developmental processes can instantiate the propensity to vary in a certain way, or the propensity to evolve. Consequently, the general tendencies explaining patterns of variation are not reducible to any disjunction of those mechanisms. Moreover, these propensities can be triggered in a variety of ways, by different environmental or genetic perturbations. Variational propensities thus capture general, probabilistic tendencies that play an irreducible explanatory role in evolutionary theory.

When talking about dispositions, it is important to distinguish them from their 'manifestation' and their 'effect' (Molnar [2003]). The manifestation of a disposition is the end-state of the function that individuates the property—for instance, breaking in the case of fragility—, while the effect of a disposition is the resulting event to which it contributes when triggered, such as a particular way for a window to break when hit. Instead of manifesting in a single type of effects, propensities manifest themselves in the probability distribution of their possible effects. For example, a fair coin has a certain propensity to land heads up when it is tossed, a property that is causally rooted in the physical properties of the coin, such as its symmetric mass distribution. The manifestation of this propensity is the one half probability of the event 'landing heads up' given certain tossing conditions, whereas its effect—the actual events of landing on heads or tails—will differ in every particular toss. Propensities are therefore causal properties that explain, but are not identical to, probability distributions, which in turn are instantiated in frequencies of events. Some developmental dispositions can be individuated by the particular type of morphological outcomes they causally produce, always manifesting in the same type of event, such as the formation of the vertebrate eye or the tetrapod limb (Austin [2017]). However, variational propensities are individuated by a probability distribution of phenotypic changes in response to environmental and genetic influences. For instance, one might define the disposition of an RNA sequence to fold into a given shape. By contrast, the variability of the sequence manifests in the distribution of changes in shape that can take place through the iteration of folding processes upon mutation. Similarly, the variational modularity of tetrapod limbs is not concerned with the probability of this trait being produced in each ontogeny. Rather, it explains phenomena such as that, in tetrapods, limbs have a high probability of evolving independently of other traits, like the head or the tail.

### 5.2. Developmental types

While there is a general agreement in evo-devo that variational propensities and their associated probabilities depend on developmental properties, there is no consensus in the literature on the entities these propensities are predicated of. Some authors attribute them to individual organisms (Wagner

[2014]), others to genotypes (Fontana [2002]), others to developmental systems (Salazar-Ciudad [2007]), and yet others to GPMs (Wagner and Altenberg [1996]). As we have argued in the previous sections, variational propensities can only be derivatively attributed to genotypes. GPMs, in turn, represent the general causal structure of developmental chance setups, but abstract functions cannot bear propensities. Research on developmental plasticity has shown that organisms are certainly bearers of a capacity to vary with important evolutionary consequences. However, individual organisms do not vary in our defined sense of variability, nor do they evolve. The variational propensities of interest in evo-devo belong to developmental types instead. Variability models include the space of all possible genotypes resulting from mutational perturbations that act as an input in a given GPM, as well as all possible developmental rules connecting this space with the output, phenotypic space. A developmental type can then be defined as the causal, generative structure shared by a manifold of—actual and possible—developmental processes that map genotypic variation onto phenotypic variation in the same way. Variational propensities are then responsible for general or type level causation relations rather than actual or token level ones.

Millstein ([2003]) suggests that type level causation in evolutionary biology is identifiable with 'long-run' propensity interpretations, where propensities are 'associated with repeatable conditions' that produce frequencies similar to the probabilities 'in a long series of repetitions' (Gillies [2000], p. 822).[14] According to Millstein, the relevant conditions for evolutionary biology explanations are not those repeatable in long series of the same trial, but in ensembles of similar ones ([2003], p. 1324, n. 4). Although she concludes that the distinctive types in evolutionary biology are defined at a population level, developmental types do not define types of populations. The relevant causes for variational patterns are to be found in ensembles of developmental mechanisms that share a causal structure across populations, generating a distribution of phenotypic changes with distinct associated probabilities. Whenever the structure of a GPM remains stable, determining the causal relevant factors shared across populations or taxa, and throughout evolutionary time, evo-devo models can be said to represent a developmental type. Insofar as they include non-realized perturbations and developmental processes within a specific GPM logic, we believe that developmental types cannot be interpreted as mere abstractions from populations of individual ontogenies, contrarily to what authors such as Lewens ([2009], p. 263) have defended. The setup conditions of variational probabilities are repeatable in the sense of remaining stable through the historical series of reproductive events that connect the individual organisms constituting evolutionary lineages. Therefore, this stable structure seems to be more properly attributable to lineages rather than ensembles of individuals or populations.[15] In any case, the typological character of variational propensities seems to be at least indispensable for their explanatory role of probabilistic patterns.

[14] Long-run interpretations have been challenged on the basis of their dependence on sequences of repetitions, thus entailing the difficulties associated with frequency accounts (Suárez [2014]). However, we believe that the repeatability of the developmental and environmental setup conditions is an indispensable requirement in evolutionary explanations of variational probabilities, at least when it comes to how these probabilities are conceived and modelled in practice.

[15] Sterelny ([2011]) has also identified evolvability as a property of lineages, but reduces the causal determinants of evolvability to the 'interactions between individual developmental mechanisms, populations and environments' (p. 96). In this sense, he considers evolvability explanations as 'lineage explanations' (Calcott [2009]). Brown ([2014]) has argued instead that evolvability explanations are of a different kind, insofar as they invoke dispositions rather than gradual changes in actual, developmental mechanisms. We agree

While variability models abstract selection away, the repeatable conditions required for evolvability as a causal probabilistic process also include a general characterisation of the adaptive environment: given that environments tend to change in certain ways, some lineages will have a better chance to generate fitter traits than others. For instance, modular GPMs will tend to manifest into modular variation independently of the environmental conditions but they will only be more evolvable under a modular selective pattern. In analysing evolvability as a general disposition, philosophers have tended to agree that factors external to developmental systems, such as population size, geographic range or climate conditions, can influence evolvability, and therefore should be included in its causal, dispositional basis (Love [2003]). However, we have seen that in evo-devo not all the environmental factors that influence the ability of a population to evolve are included in the definition of this capacity. Evolvability has been shown to occur if and only if the environmental patterns of spatio-temporal variation are stable. Selective factors do not only 'differ depending on the probability of being experienced repeatedly by organisms' (Abrams [2014], p. 127), but also on the probability of varying with a certain pattern. In developmental explanations of the probability of evolving, these structural features of the selective environment belong to the chance setup accounting for such probability, rather than being a general condition for the manifestation of the propensity, as in variability.

Moreover, in evolution, the frequencies of variational patterns need not approximate, in the long term, the variational probabilities associated to a given GPM. Because of the deep historical dependence of variational propensities, some pathways are explored while others are not, the former not needing to be the most probable ones from a developmental perspective.[16] Since different phenotypic results will be more or less favoured by selection or drift, and since every outcome in evolution determines the initial conditions of the following trial, the areas of the probability spaces explored by lineages may not be representative of the possibilities modelled in a given GPM. Furthermore, variational probabilities can themselves evolve: a change in the structure of a developmental type involves a change in the repeatable conditions, hence in the propensities that are being modelled. In turn, this second-order evolutionary dynamics has its own rules of change, some developmental types being more likely to evolve than others.

Insofar as variational propensities are predicated of developmental types, we claim that the conception of variational probability at work in evo-devo is compatible with their existence in deterministic processes.[17] Stochasticity is a major source of developmental variation, both at the level of the inputs of development—environmental factors, mutations, and recombination—and at the level of developmental processes themselves—developmental noise. However, the probabilistic properties that concern us here are not necessarily indeterministic in nature. Instead, we refer to those properties that remain stable across taxa and throughout generations, allowing for the existence of stable patterns of variation. Variational probabilities depend on the ability of developmental systems to generally react to mutational or environmental perturbations (Brigandt [2015b]), regardless of the fact that such perturbations might or might not be the result of indeterministic processes. Variability and

with Brown in this regard but not with her attribution of the categorical basis of evolvability to the internal features of populations.

[16] This historical dependence of evolutionary pathways has been generally referred to in the literature as the 'contingency' sense of chance (Beatty [1995]).

[17] See Millstein ([2003]) for an analogous argument on the probabilities at work in microevolutionary theory.

evolvability are not irreducible indeterministic propensities, but they refer to a higher level dispositional feature of developmental systems, defining a probabilistic dynamics at the typological level. In this sense, we defend that variational propensities have an explanatory role in evo-devo, insofar as the generalizations afforded by them are indispensable in accounting for the nonrandom distribution of heritable variation. They are responsible for probabilistic patterns in virtue of the structure of the causal interactions they represent, and not in virtue of a fundamentally indeterministic nature.

## 6. Conclusion

The evolutionary role of chance in the production of variation has tended to be neglected due to the focus on the effects of mutations on fitness. This restricted view has obscured other meanings of chance endorsed by the MS against alternative explanatory strategies in evolutionary biology. We have argued that evo-devo research on variability and evolvability demands a different conceptualisation of chance, where the probabilities of varying and evolving are causally dependent on the variational propensities of developmental types. Insofar as these propensities have a creative, rather than a constraining role, in explaining evolutionary patterns, we believe that the philosophical reflection on the probabilistic nature of evolution would benefit from incorporating them. How variational probabilities relate to the probabilities involved in populational dynamics is a further philosophical path that remains to be explored.

## Acknowledgements

This work was funded by the Spanish Ministry of Economy, Industry and Competitiveness: LNdR's by two Juan de la Cierva fellowships (FJCI-2014-22685 and IJCI-2017-34092) and a postdoctoral fellowship at the Complutense University of Madrid, and CV' by a predoctoral contract (BES-2015-072779) at the Complutense University of Madrid. Research towards this paper was conducted within the framework of two projects funded by the Spanish Government (FFI2013-47849-P and FFI2014-57064-P). We thank the audience at the conference 'On the nature of variation: random, biased and directional' held in Lisbon in October 2017, as well as the participants at the reading groups coordinated by María Cerezo at the University of Murcia, by Grant Ramsey at KU Leuven, and by Mauricio Suárez at Complutense University of Madrid for their very helpful comments. Mihaela Pavlicev, Philippe Huneman, Miguel Brun-Usan, Juan Campos, and three anonymous reviewers made many insightful comments on early drafts of this manuscript that have greatly contributed to its improvement. LNR and CV are currently hosted by the Centre for Advanced Study at the Norwegian Academy of Science and Letters.

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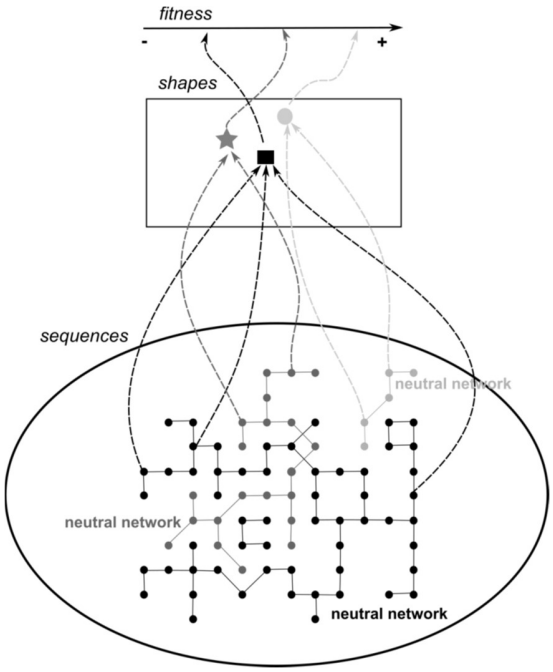


**Figure 1.** The RNA model. The bottom networks represent a genotypic space, where each point corresponds to an RNA sequence differing from their neighbors by a single point mutation. Each shade of gray corresponds to a distinct phenotype. There are thus three neutral networks—black, dark grey and light grey networks—in the genotypic space, that is, three sets of sequences that fold into a specific phenotype or RNA shape, as represented by the star, square and circle shapes. The mid-level corresponds to the phenotypic space, where the three different phenotypes are represented. A fitness value is assigned to each of them, illustrated in the top level. The sequences-shapes relation corresponds to a genotype-phenotype map, while the shapes-fitness values relation is a phenotype-fitness map. Figure modified from (Stadler *et al*. [2001]).

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