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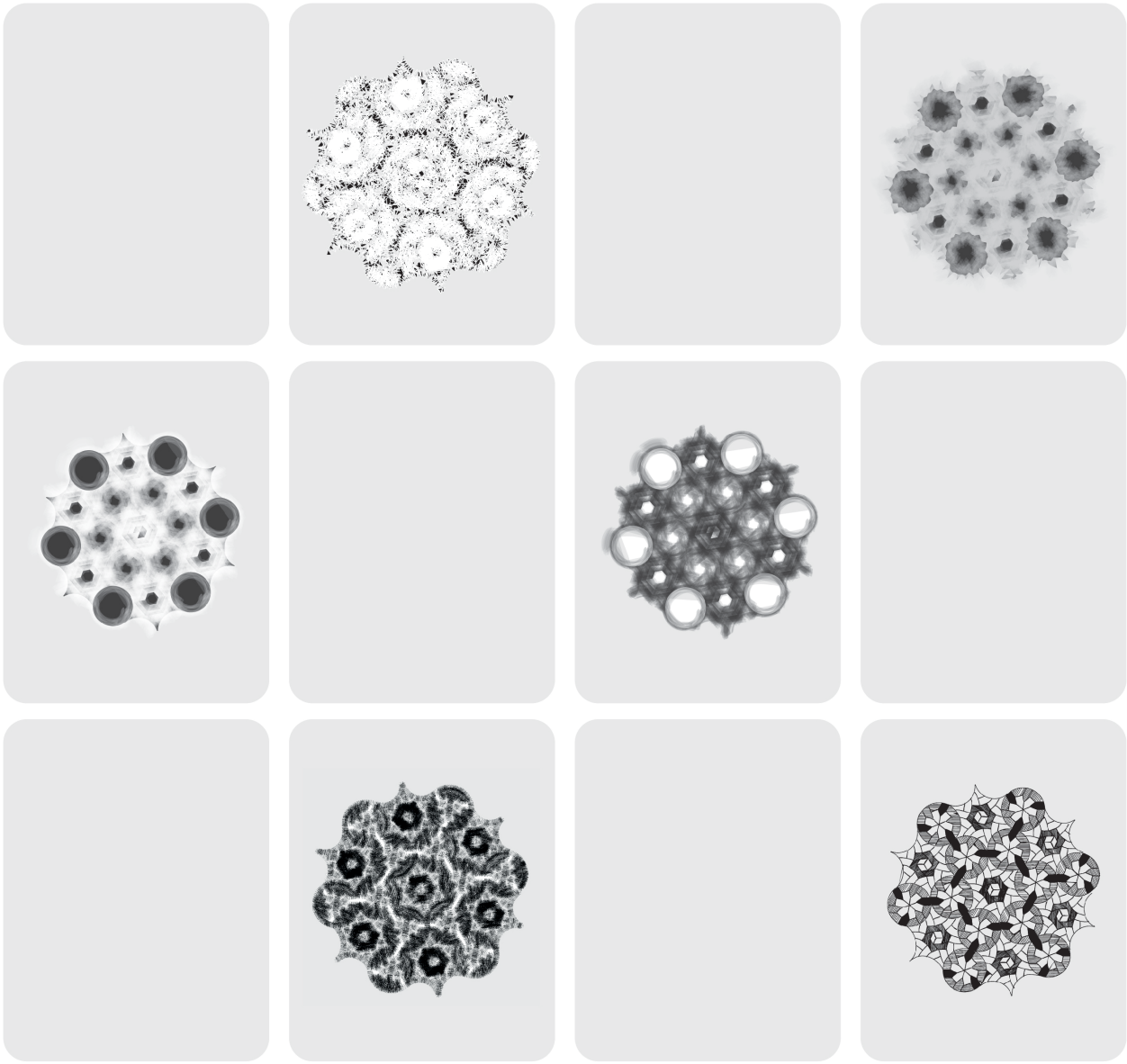

On the nature of variation: Random, biased and directional

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Giorgio AIROLDI
Universidad Nacional de Educación a Distancia, Madrid, Spain

Evolution without selection: how shrinking the kingdom of fitness can reconcile adaptationism and pluralism

In this paper, I claim that the rejection by adaptationism of non-adaptationist explications of phenotypic traits depends less upon some fundamental assumptions of the former than on their claimed scope of application. I analyse four such assumptions and show that the only inalienable one for the adaptationist view rests on the idea that there is no evolution without selection. This might not be incompatible with pluralism, if applied to just a sub-set of evolutionary phenomena. To define such sub-set, I suggest a theoretical framework for pluralism, where adaptationist accounts can coexist with non-adaptationist ones.

Empirical adaptationism relies on the following general assumptions (Godfrey-Smith 2001, Orzack & Forber 2017): the source of evolutionary variation is random and unconstrained; the action of natural selection is ubiquitous, i.e. it acts on all phenotypic traits; the order of living beings is shaped by natural selection only; natural selection acts continuously and progressively on long time-scales.

Some of these assumptions are more fundamental than others, but all are interconnected and giving up one without affecting the others is an exercise of variable complexity.

The assumption about ubiquity, for example, can be loosen thanks to the idea about natural selection timing: if a trait does

not currently show any apparent adaptive rationale, sooner or later it will. No trait is free of becoming target of competition, either actual or potential (Mayr 1983).

Assumption about unconstrained randomness of variation is also flexible regarding timing. Adaptationism can admit the existence of constraints on variations in the short-term, but these are eliminated by mutations in the long-term (Parker & Maynard Smith 1990).

The assumption about unconstrained randomness of variation and the belief that order only comes from natural selection, however, are closely linked: it is difficult to turn down one while keeping the other. If variation is not random/unconstrained, organisms are also shaped by processes other than natural selection: therefore, we could detect their action by inspection of the organism. Given that the variety and complexity of leaving beings spring 'from the war of nature, from famine and death', admitting biased/constrained variation undermines one of the Darwinian core ideas.

Yet, the incompatibility between non-random/constrained variation and adaptationism is not rooted in the assumption about the role of natural selection, but in the claim about the scope of its application. Adaptationism focuses on the last stage of the flow leading from variation to selection, but pretend to rule on the whole path, by postulating that whatever happens before the selection stage is irrelevant on the long run and cannot leave any enduring markings on the organism: natural selection, provided enough time is granted, wipes all previous marking out and puts its final seal on the phenotype. Fitness optimization is the only driver for any evolutionary phenomenon (Parker & Maynard-Smith 1990): phenotypic evolution is just selection.

I propose to restrict the extension of the adaptationism kingdom (for example to a limited set of morphological changes, Wilkins &

Godfrey Smith 2009), and to add another driver (e.g. robustness) for architectural phenotypic changes linked to non-adaptationist processes, undetectable through fitness. The proposed approach would remove adaptationism incompatibility with pluralistic proposals and would allow to integrate into a more encompassing model the increasing evidence that non-adaptationist processes contribute to shape phenotypes (e.g. Barve & Wagner 2013, West-Eberhard 2005) with the classical neo-Darwinian view.

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Lorenzo BARAVALLE
Universidade Federal do ABC, Santo André, São Paulo, Brazil

The cultural selection of chance

Cultural evolution models traditionally assume that cultural innovation is introduced in a society at some constant rate (cf. Cavalli-Sforza & Feldman 1981). This is obviously an unrealistic idealisation; nonetheless, there is no agreement about how it could be refined. Enquist and his collaborators (Enquist *et al.* 2008) have recently suggested that, due to the cumulative nature of culture, innovation rate tends to grow exponentially over the history of a society. By contrast, Mesoudi (2011) has pointed out that a large accumulation of cultural (scientific, technological) knowledge may produce a significant deceleration of innovation rate. In my opinion, the choice of a more realistic model of cultural innovation is indissolubly interconnected with considerations concerning the epistemology of creativity.

This is because, I shall argue, different strategies of creative thinking may lead to different — more or less efficient — outcomes, in terms of innovation, depending on the stage of cultural knowledge accumulation. Taking as reference the history of science (and, especially, of mathematics), Mesoudi's model assumes that, in order to be optimally efficient — i.e., to lead to innovation —, creativity always requires to be *guided* by relevant previous knowledge. That is to say, in order to be able to generate potentially innovative cultural items, a precondition is that individuals must be adequately *instructed* by acquiring all the available information about the cultural domain on which they are supposed to innovate.

As a consequence, when — due to cultural accumulation — relevant previous knowledge becomes too extensive to be appropriately learnt during individuals' lifetimes, little time is left for creativity and innovation rate drops (Mesoudi 2011). In this

presentation, I would like to challenge this conclusion by showing that in such states of cultural overload, a different kind of creativity, less directed or even random (that is, decoupled from innovation criteria; cf. Campbell 1960, Simonton 2004), can be culturally rewarded. This situation — epitomised by scientific paradigm shifts — frequently produces readjustments in cultural knowledge, allowing the exponential growth predicted by Enquist and his collaborators.

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Enquist, M., Ghirlanda, S., Jarrick, A. & Wachtmeister, C. –A. (2008). Why does Human Culture Increase Exponentially? *Theoretical Population Biology*, 74, 46-55.

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Eva BOON (Keynote address)
Technische Universiteit Eindhoven, The Netherlands

In which sense is Lateral Gene Transfer random, and why does it matter?

It is an empirical question whether the variation that underlies population change by natural selection is generated in a random fashion. However, it is not an empirical question how to decide

what counts as relevant variation, and how ‘random’ should be defined. Here, I consider how these issues are connected in a case study on microbial communities.

Within microbial communities, levels of organisation can be described by various patterns of variation that may be more or less relevant to evolutionary change on that level. A singular mechanism that makes the boundary between levels fuzzy is Lateral Gene Transfer (LGT). LGT is the movement of genetic material between genomes other than the 'vertical' transmission of DNA from parent to offspring. LGT can severely complicate microbial identification and classification based on genome information. Most importantly, this mechanism can have significant effects on the evolutionary trajectory of a microbial lineage, allowing for the loss or gain of biological functions on short timescales.

In what sense can LGT be considered random? In population genetics, 'random' is a relative judgment with respect to a particular expectation (null model) in a particular context, such as environment (selection) and demographic parameters (migration, drift). It makes sense to ask to what extent LGT limits or promotes randomness thus defined. If we further consider functional and developmental constraints on different levels of organisation within a microbial community, it seems that LGT can promote randomness on one level, and limit it on another.

We are left with a dynamic picture of the link between LGT and randomness in microbial evolution. I conclude with some reflections on how this picture affects assessments of function in microbial communities.

Pietro CORSI (Keynote address)
University of Oxford, UK and EHESS Paris, France

The inheritance of acquired characteristics: Darwin vs Lamarck, or Darwin and Lamarck?

More quoted than read, more misrepresented than understood, Jean-Baptiste Lamarck remains a fascinating, controversial figure in the history of evolutionary biology. For some the true founder of evolution, for others a mind prone to unrestrained flights of imagination, views and doctrines have been attributed to Lamarck that bear no resemblance to his actual writings. Lamarck is still seen as the man talking of giraffes stretching their necks, in spite of the fact that the example occurs only four times in his corpus (check, if you like, at http://www.lamarck.cnrs.fr). He is supposed to have argued for an inner drive pushing life to gain higher levels of organisation, from monad to man, as Charles Lyell put it, and for having asserted that it is the organism's "will" that causes change and new forms of adaptation.

Darwin insisted on Lamarck's foolishness in calling upon "will" to explain adaptation, in spite of Lamarck repeatedly pointing out that 9 on 10 animals (let alone plants) do not have a nervous system, so they cannot "will" anything at all. The French naturalist is also credited for the ill-famed theory of the inheritance of acquired characteristics.

A view, it will be argued, that Darwin endorsed with greater determination than Lamarck. True, Darwin's acquired characters had to be submitted to the complex process he and we call "natural selection". Yet, Darwin elaborated the principle of acquired characteristics in much finer detail than Lamarck ever did: the French naturalist held a very restrictive view of its action. Moreover, it was not a "character" that was transmitted to the progeny, but a slight modification of organic fluid dynamics that

in the course of very long periods of time contributed to alter the organic structure as a whole.
My purpose is not to vindicate Lamarck against Darwin: for the historian, the real issue is to understand the past for what it was, not according to our scientific, ideological or political prejudices. ”Darwinism” and “Lamarckism” have historically meant different things to different communities, and it is perhaps time to concentrate on actual research than on labels serving the sole purpose of drawing a priori criteria of credibility.

James DiFRISCO
Konrad Lorenz Institute for Evolution and Cognition Research, Austria

Variation across levels of organization: insights from evo-devo

A key assumption in evolutionary biology in the 20th century has been that genetic variation neatly maps onto phenotypic variation. This assumption has several enabling roles, but perhaps the most important one is that it encourages the central idealization strategy of evolutionary genetics, which is to collapse phenotypic variation onto underlying genetic variation in order to describe and explain evolutionary dynamics purely in terms of the latter (Dobzhansky 1937; see Lewontin 2001).
Against this neat mapping assumption, recent advances in biology have shown that molecular and morphological evolution are de-coupled to a significant degree (Müller 2003; Sarkar 2014). Particularly in eukaryotes, due to small population sizes, genomic evolution appears to be driven largely by non-adaptive processes such as mutation, drift, and gene and genome duplication (Lynch 2007), whereas the same does not seem to hold for phenotypic evolution (Pigliucci 2009; Sarkar 2014). Similar patterns have

been observed in the context of evolutionary developmental biology (evo-devo). In the widespread phenomenon of "developmental system drift" or "phenogenetic drift," homologous characters come to be produced by different developmental processes and gene regulatory networks (True and Haag 2001; Weiss and Fullerton 2000).

The decoupling of molecular and morphological evolution forces us to revise our conception of the genotype-phenotype (GP) map in ways that may have profound implications for biological theory. In this talk, I propose to examine some of the theoretical consequences of fully taking into account this more complex picture of the GP map.

- **Phenotypic evolution**. If selection acts on phenotypes, then we can only reliably ascribe fitness directly to genes when the GP map is linear and deterministic. Whenever it is not (probably most of the time), we cannot abstract from higher levels of organization and still capture the causes of evolutionary change (particularly selective dynamics).
- **Characters**. "Decoupling phenomena" (particularly developmental system drift) threaten to undermine our ability to generalize about GP maps across different taxa (True and Haag 2001). In particular, these phenomena conflict with accounts of homology in which characters are individuated by their developmental-genetic causes (such as Wagner 2014). This is because traits that should belong to the same type will often have developmental-genetic causes that have drifted apart in evolution. A "level-specific" account of homology or character kinds is needed.
- **Variation**. Most generally, we cannot adequately understand the nature of variation and its evolutionary significance without taking into account (1) multiple developmental levels (i.e., genes, gene networks, developmental processes, phenotypic characters) as well as, critically, (2) the

mechanisms by which variations at different levels are causally connected.

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Leonore FLEMING (Keynote address)
Utica College, USA

Nothing in biology makes sense except in the light of variation

Charles Darwin struggled with understanding the role of variation in evolution. His challenge with it is best seen in his formulation of the Principle of Divergence around 1857. Although he was working on a theory to oppose Paley's Natural Theology, it is clear that Darwin was still subtlety influenced by Paley's notion of Perfect Adaptedness, which in turn skewed his interpretation of variation in nature. In 1857, Darwin's understanding of variation was that it is not random, but rather it is directed, helping organisms adapt or get back into perfect harmony with an environment that has changed. This idea of "Limited Perfect Adaptedness" caused Darwin many problems and I argue it is the main reason that most of his work on the Principle of Divergence did not get published in the Origin. As I will show in this talk, Darwin's misunderstanding that variation is directed led to a number of problematic conclusions, many of which we still need to be wary of today. While much of this talk will be historical, this is in order to provide a foundation for discussing how variation and randomness can be understood in evolutionary theory today. To discuss variation as directed, and not fall prey to the problems Darwin encountered, I argue that we must recognize that biological entities and evolutionary systems are hierarchical, that evolutionary change occurs at these different levels independently, and thus, randomness is relative to a hierarchical level of interest (and similarly, so is bias, direction, and notions of adaptation).

In this talk I will demonstrate how directed events at one level can be random at another level, and how random events at one level can be predictable at another level. Additionally, when looking at processes or systems over time, there are degrees of contingency, which makes discussing something like the major transitions in evolution difficult, as different transitions have different likelihoods of reoccurring. Whether the focal level is proteins, cells, organisms or colonies, the proper role for variation is a primary one, as evolutionary systems only require two things—variation and heredity. And while it might be tempting to talk about variation as clearly fitting into categories of random, biased, or directional, or making claims such as "If variation is not random, then it is either biased or directional," it is important to remember that evolutionary systems are hierarchical and dynamic, built on the underlying tendency of variation accumulation, a tendency which is present at every level of hierarchy.

Philippe HUNEMAN (Keynote address)
IHPST, CNRS, Université Paris 1 Sorbonne, France

Distinguishing types of variation and assessing challenges to the Modern Synthesis

It is pervasively claimed that the framework of evolutionary theory, the Modern Synthesis (MS), has to be deeply revised, changed, "extended" or "expanded". Empirical and conceptual reasons are supposedly converging to support such a move. Supporters of a new Synthesis may disagree on many things but they generally think that the MS, as a scientific theory through which explanations for biological phylogeny, adaptation and diversity should be sought, gave too much importance to natural selection or that its focus on genes, exemplified by the textbook

definition of evolution as a change in genotypic frequencies, was exaggerate. In this talk I ask what kinds of empirical facts regarding variation would force us to strongly re-conceptualize evolutionary theory. I will argue that, even though the explanatory role of selection can be constrained by the structure of variation, and that such constraint compels us to reshape the explanatory factors in evolutionary biology, very few kinds of variations are likely to force dramatic theoretical changes to the core claims of MS regarding natural selection and genetics.

Gerd MÜLLER (Keynote address)
Universität Wien, Austria

The morphogenetic basis of discontinuous variation

Morphogenesis is an essential feature of embryonic development and contributes to the generation of phenotypic variation on which natural selection can act in evolution. This variation is traditionally thought to be small, incremental, and continuous, conforming with the gradualist prerequisites the Modern Synthesis theory has inherited from Darwinism. Whereas the evolution of organismal shapes and proportions is often in line with the notion of gradual change based on additive genetic variation, the origin of individualized structural elements or the loss of such elements, as based on cell and tissue dynamics, may not be continuous. In the case of digit variation in vertebrate limbs, for instance, discontinuous effects can be observed as a consequence of experimental, mutational, pathological, or evolutionary modifications to the limb developmental system. A model for discontinuous digit variation will be presented. The results indicate that phenotypic variation is neither necessarily gradual nor random, but is channeled by morphogenetic properties that provide sources of phenotypic bias and novelty.

Laura NUÑO DE LA ROSA[1] & Cristina VILLEGAS[2]
[1]Euskal Herriko Unibertsitatea/Universidad del País Vasco, San Sebastian, Spain
[2] Universidad Complutense de Madrid, Spain

Possible forms and possible adaptations, or how evolvability challenges random variation

Whereas the received view of evolution was grounded on the theoretical pillars of molecular randomness and historical contingency (Monod 1971), the theoretical and empirical advances undergone by evolutionary biology in the last few decades have challenged the randomness of evolutionary change from a phenomenological, as well as an explanatory perspective. The investigation of the tempo and mode of evolution has entailed an increasing interest in the directionality of evolutionary change and the logics of morphospace.
From a causal perspective, evo-devo has brought to evolutionary biology many dispositional terms that highlight the 'inherency' of evolution, or the tendency of organismal systems to change along certain routes (Newman and Müller 2006). However, it has been recently argued that these new developments do not really compromise the concept of chance innate to the Modern Synthesis (MS), insofar as the randomness of variation is not formulated in absolute, but relative (evolutionary) terms. In this context, variation is random *with regards to* the adaptive value it has for the organism. In other words, there is no causal connection between the probability of a mutation being beneficial in a particular environment and the probability of it occurring in this environment (Lenski and Mittler 1993, Merlin 2010). In contrast, in this paper we argue that the introduction of developmental dispositions into the causal structure of evolutionary biology does challenge the idea of random variation

underlying the inherited view of evolution. In order to do so, we analyze how the dialectics between the actual and the possible underlies many theoretical tensions between the population and developmental approaches to evolution.

In this context, we distinguish two notions of the possible associated to different epistemological goals in evo-devo: the morphologically possible (variability) and the functionally possible (evolvability), and argue that both research programs clash with the notion of chance of the MS. Firstly, we argue that if change is defined with regards to form (vs adaptation), random variation loses its explanatory force and needs to be replaced by a developmentally grounded notion of variability. If variation is defined at the phenotypic level, the dispositional properties of developmental systems constrain the possible outcomes associated to genotypic variation. In this context, variation is not chancy, for the target of variability is not the genetic material but its relation to phenotypic outcomes (the Genotype-Phenotype map).

Secondly, we argue that the evo-devo approach to evolvability, in articulating the relationship between variability and adaptation, does not only render inoperative the synthetic concept of random variation, but entails a serious challenge to the very notion of *adaptive* chance. In this regard, our main line of argument is that, whereas population genetics deals with fine-grained micro-environments whose structure cannot be predicted in the long term, evolvability research investigates how developmental systems generate variation that correlate to certain general and predictable traits of the environment.

What the evo-devo approach adds to the MS view concerns the possibilities in this generation, and has explanatory power insofar as it introduces dispositional properties that are not reducible to statistical, population-based correlations. This, we claim, is the

real challenge that the evo-devo research program represents for the MS consensus view about the randomness of variation.

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Pablo RAZETO-BARRY[1] and Davide VECCHI[2]
[1] Instituto de Filosofía y Ciencias de la Complejidad, Chile
[2] Universidade de Lisboa, Portugal

Genomic change randomness: a net-fitness-effect account

The received view that genomic change is 'random' is supported by the canonical interpretation of natural selection theory provided by the Modern Evolutionary Synthesis. However, the Modern Synthesis enshrined natural selection as the director of adaptive evolution not by providing evidence that it did, or could, account for observed adaptations (Leigh, 1999), but rather by eliminating competing explanations (Mayr, 1993). One of the eliminated competitors was Lamarckism, a hypothesis according to which the environment can induce organic changes directed towards producing phenotypes that increase the fitness of the organism in that particular environment.

Contrary to the Lamarckian hypothesis, the Modern Synthesis' view claims that genomic change is 'random' (Lenski & Mittler, 1993; Merlin, 2010). However, current evidence in favour of the existence of legitimate cases of mutational Lamarckism (Jablonka & Lamb, 2005; Koonin & Wolf, 2009) has revitalized interest in seeking clarification of the meaning of the term 'random' in this evolutionary context (Millstein, 1997; Brisson, 2003; Sarkar, 2005). In a previous publication (Razeto-Barry and Vecchi 2017) we proposed a new, formal and precise definition of randomness based on the probabilistic concept of conditional independence. We defended a characterization of mutational randomness in terms of the concept of net fitness effect, i.e., the comparative weight of the fitness effects of beneficial and deleterious mutations independently of their relative proportions. In defining mutational Lamarckism, what matters, we argued, is only that the fitness effect of the beneficial mutations produced by the mutational mechanism overpowers the fitness change produced by the deleterious effect of the other induced mutations, independently of their number.

The concept of net fitness effect allowed us to show that many definitions of mutational randomness are deficient. Those suggesting comparing the absolute number of beneficial mutations with that of non-beneficial ones (including neutral ones) are deficient because, by definition, neutral mutations do not affect net fitness effect. We also argued that comparing relative number of beneficial mutations (to a specific part of the genome) to deleterious ones is unsatisfactory: what suffices is to ascertain whether the net fitness effect of the induction is positive. Thus, the genomic specificity of the mutational process is not a necessary condition for the existence of mutational Lamarckism (Koonin and Wolf 2009).

In this talk we would like to extend the context of our analysis. It is well known that a variety of mechanisms of genomic regulation

and change exist, varying from hypermutation to stress-induced mutagenesis to CRISPR-cas to gene duplication etc. All these processes result in a wide range of potentially different net fitness effects: while hypermutation is a basic evolutionary response with probably no common net fitness effect gain, CRISPR-cas has a clear positive net fitness effect. Thus, there seems to exist a continuum between very random (producing a vast majority of non-beneficial genomic changes) and very directional (producing a vast majority of beneficial genomic changes, e.g., CRISPR-cas) processes of genomic change that cannot be captured through absolutistic concepts of randomness and directionality. In our opinion, the concept of net fitness effect might be used to capture this gradualness. We have argued that cases in which the net fitness effect is positive might be considered Lamarckian, but an additional question remains open: how should processes of genomic change that lead to a relative increase, though still negative, of the net fitness effect be considered? Our question is whether cases in which the probability of deleterious genomic changes increases at a lower rate than that of beneficial ones, that is, cases with a relatively higher negative net fitness effect, might be considered directional changes at all.

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Sahotra SARKAR (Keynote address)
University of Texas at Austin, USA and Presidency University, Kolkata, India

Blind variation and evolutionary explanation

Ever since Weismann's work enshrined the neo-Darwinian interpretation of evolution, it has been a matter of faith that natural selection acts on random variation. There are two problems with this doctrine: (1) There has never been a successful explication of what randomness means (and many commentators have resorted to a return to Darwin's metaphor of blindness). (2) None of the experimental work that is supposed to establish the randomness of variation even addresses the problem. What we are left with is a much weaker claim that the processes that generate variation act independently of the processes that result in selection. Given a genotype-phenotype

distinction, this weaker view leaves open the possibility that many phenotypic features are the result of the processes that generate variation and the processes that connect the phenotype with the genotype with no role for the processes of selection. Elaborating such a view is one of the goals of developmental evolution.

Arlin STOLTZFUS (Keynote address)
Institute for Bioscience and Biotechnology Research, NIST, USA

A new kind of variational cause, and some implications

How do the variational inputs to evolution affect the output? Using Sober's (1985) distinction of source and consequence laws, what are the mutational and developmental source laws that determine the spectrum of variational inputs, and what are the population-genetic consequences?

For instance, given a B-fold bias in the chance that X appears rather than Y, what is the impact on evolution? The answer depends on conditions. In mutation-limited models, a B-fold bias in the mutational introduction of new alleles may have a B-fold effect. At the opposite extreme are models in which all relevant alleles are present initially, and evolution is just a matter of shifting frequencies: there is no introduction process, and mutations among alleles can be ignored given the smallness of mutation rates.

Interestingly, the theoretical demonstration that a bias in the introduction of variants can impose a bias on evolution occurred only in 2001. This principle plays no role in the Modern Synthesis (MS) and is conspicuous by its absence in (for instance) the seminal "developmental constraints" paper by Maynard Smith, et al. (1985). Instead, MS writings invoke an argument from Fisher and Haldane, to the effect that variation-induced

tendencies (orthogenesis) are impossible because mutation rates are too small. Nevertheless, recent work has established mutation-biased evolution. Understanding this new kind of causation sheds a new light on the MS, the "forces" theory, and the "random mutation" doctrine.

The original MS of Fisher, Mayr, Dobzhansky, et al. took precisely the position that evolution is "shifting gene frequencies" in a "gene pool" without new mutations, the condition where mutation becomes unimportant (classical theory often lacks terms for mutation entirely, e.g., Edwards, 1977). By contrast, origin-fixation models that relate the rate of evolution directly to the rate of mutational origination were introduced in 1969 to address patterns in molecular evolution. They are now a major branch of theory with many applications.

The "forces" theory, likewise, only works by defining evolution as process in the topological interior of an allele-frequency space. There, the common currency of causation is to change a frequency from f to f + delta, which mutation, selection and drift can do. If we allow shifts from 0 to 1/N, simple "forces" reasoning breaks down, because only mutation can jump the system off of an axis into the interior. Scientists frequently reason incorrectly with "mutation pressure" (mass-action force) when they should be considering the origination process (point process). The "forces" debate in philosophy has yet to recognize this issue.

Finally, there are implications for "random mutation". Scientists confident that there are no consequence laws for mutational tendencies would naturally believe that nothing important is to be gained from studying mutation, e.g., as argued in Ch. 1 of Fisher (1930). The literature provides some evidence to support interpreting "mutation is random" along these lines, as "mutation is irrelevant". The way to upset the doctrine, then, is to show that tendencies of variation are consequential.

David SUÁREZ PASCAL
Universidad Nacional Autónoma de México (UNAM), México

A function-based analysis of randomness in evolutionary change

According to Stephen Jay Gould (2002), two central tenets of Neo-Darwinism have been that biological variation is essentially random (isotropic) and also that natural selection is the main directing force in evolution. Hence, this pattern of variation seems to be an assumption that is required if one is to assert that the only, or the main, process responsible for evolutionary creativity is selection—at least many evolutionary biologists think this way. However, against Gould, such requirement is not only too strong but also unrealistic: even hard core adaptationists will agree that variation between consecutive or close generations is highly constrained—although they will surely also assert that the cumulative action of natural selection through many generations is able to overcome such limits (see Ayala, 1999; Neander, 1995).
Gould's construal of the Neo-Darwinist stance on variation is wrong for two reasons. First, contemporary proposals in evolutionary biology which aim to account for the effects of structural or developmental constraints over the range of variation available to organisms certainly contradict the assumption that variation is isotropic, but they do not necessarily oppose the current and past Neo-Darwinists' assertion that natural selection is the main creative force in evolution. On the other hand, approaches which look into the contribution of genetic and phenotypic plasticity to adaptation certainly can challenge the exclusivity—and also the centrality—of natural selection in driving evolution.

Structural constraints and developmental plasticity impact in two distinct ways upon one of the central tenets of Neo-Darwinism—that natural selection is responsible for the directing, or the creative, part of evolution. This is due to the fact that there is not one, but two different concepts of randomness that have been used in relationship with evolution. One of them is causal and it is employed in the context of Physics or Probability, while the other one is functional, closer to the notion of accident, and more commonly employed in relation to the human sciences. This last meaning, although it is foreign to many natural sciences, has a central place in biological thinking.

The most well-known concept of randomness (see Carnap, 1945; Salmon, 1984; Von Mises, 1957), the one which physicists and statisticians commonly employ, refers to the existence of a phenomenon's cause or causes, to our awareness of such causes or even to our ability to predict a system's future states based on our knowledge of current conditions. To the contrary, the second concept of randomness, which frequently enters into discussions regarding the meaning or the significance of some result, involves weighting the value or usefulness of such result in a certain domain. The distinction between adaptations and exaptations, as defined by Gould and Elisabeth Vrba, hinges on precisely this functional concept of randomness.

In this work, a proposal is made regarding the analysis of the second concept of randomness based on a concept of function as a valuable effect. Then, this analysis is employed to show the place that both notions of randomness have in evolutionary thinking and particularly in discussions about evolutionary creativity.

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Predrag ŠUSTAR and Zdenka BRZOVIĆ
Sveučilište u Rijeci/University of Rijeka, Croatia

Gene duplication between mechanism and random process

In this paper, we focus on gene duplication, an important source of genomic innovation and variation that occurs when a gene (or even a whole genome) is duplicated and results in a pair of identical genes within a single cell. That can lead to divergence in the function of the genes, since the new copy is free from selective pressure and can acquire a new function. For that reason, it is considered the main source of functional diversity of the genotype (Conant & Wolfe, 2008). Most interestingly, gene duplication can arise due to malfunctioning of different mechanisms (Hurles, 2004; Beams & Roth, 2015).
We address the following questions: (Q1) What is the best way to characterize the process of occurrence of genomic variation and novelty through gene duplication? and (Q2) Is phenotypic variation non-adaptive in the same sense as the vast majority of genomic variation is taken to be? More precisely, what is the

relation between variation occurring at the genotypic level and corresponding modifications at the phenotypic level and what is the role of selection therein?

(Q1) examines the issue, furthermore, of whether we can consider such processes as random, given that they seem to result from errors in the regulatory mechanisms of DNA replication and repair. That is, they arise as a result of unequal crossing-over, replication slippage, retrotransposition, aneuploidy and whole genome duplication. Here we distinguish two notions of randomness: randomness as non-directionality or non-adaptiveness, and randomness as pure chance (Wagner, 2012), and focus mainly on the first notion. It is interesting to examine how events such as gene duplication, standardly considered as non-adaptive, can still be considered as results or byproducts of selection acting on the mechanisms of replication and recombination. More specifically, we can hypothesize that some of the errors in the mechanisms in question were not selected against and wiped out by purifying selection, because they might bring about some beneficial consequences for the containing living system. Naturally, this does not mean that every such error will produce a beneficial effect. Here it is useful to distinguish between two ways of understanding selection, the so-called positive Darwinian selection and negative or purifying selection.

With regards to (Q2), we argue against the standard presupposition that genomic variation is often a product of non-adaptive processes, while phenotypic variation is a product of adaptive ones. We use the example of neo-functionalization via gene duplication to explore the complexity of the relationship between functional novelty at the genotypic and a corresponding outcome at the phenotypic level. As a case study, we consider the evolution of trichromacy in human color vision. We use this rather unproblematic case as an instantiation of the verticalization or alignment of genotypic and phenotypic levels

(Sustar & Brzovic, 2014). In this case, the introduction of a rather small molecular change at the genotypic level has clear phenotypic consequences and it can be concluded with relative certainty that natural selection acted to preserve the trait in question (Hunt, 1998; Surridge, 2003; Melin, 2013). Nevertheless, even though we can infer the role of selection relatively unproblematically, the number of alternative hypotheses to be considered demonstrates that such an inference is far from being straightforward. The relation between those two levels is complex and one should be wary of overly simple, adaptationist stories. In order to infer that natural selection is responsible for the fixation of a phenotypic trait and provide plausible explanations, we need to combine distinct kinds of biological data: information on phylogeny, structural information, information on physiology and ecological conditions.

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Julian Z. XUE
McGill University, Canada

From mutation rates to eukaryotic organization: how variation drives evolution even in regimes of strong selection

Mutation rate is an evolutionary important trait. Kimura and others computed optimal mutation rates and, in a classic case of adaptationism, assumed that natural selection can move natural mutation rates to these optimal values. This led to adaptationist theories of how mutation rates change (Kimura 1960, Gillespie 1981). Now, multiple lines of theory have shown us that this likely is not true even when natural selection is strong (Painter 1975, Sniegowski *et al* 2000, Andre & Godelle 2006, Taddei *et al* 1997). Instead, the forces driving the evolution of mutation rates likely stem from the mechanisms underlying the variation of mutation rates, that is, the mutation of mutation rates (Johnson 1999, Gerrish *et al* 2007).
The core reason for this is that any particular mutation rate can be associated with a wide range of different fitnesses. Two strains with the same mutation rate can actually be very different strains, with very different phenotypes. Thus, it is impossible to sketch a fitness curve for mutation rates, since for any mutation rate, a wide range of different phenotypes (and fitnesses) are possible. Once we realize this, we can generalize the mechanism underpinning the evolution of mutation rates to other traits. Many other traits share this property, so creatures with the same intelligence (however measured), the same complexity (however measured), or the same developmental plan (however

defined), can in fact be very different creatures, with very different fitnesses. I will present how, for any such trait, even in regimes of strong natural selection, adaptationism provides a false perspective and its evolution will be driven by the nature of its variation (Xue *et al* 2016).

I will show a concrete model of such a process, the evolution of eukaryotes from prokaryotes. I argue that prokaryotic vs. eukaryotic organization is a trait that, like mutation rate, can be associated with a vast range of fitnesses. Once the first proto-eukaryotic organism came about by an Archea engulfing a prokaryote without digesting it, the nature of variation will lock the eukaryotic organization into place, because the genomes of the mitochondria and the nucleus are much more likely to mix than to stay separated. The reason is a simple entropic one, like how two solutions will mix. However, this is not simple mutation pressure. Because there are so many more different ways to mix than not to mix, the fittest phenotype is likelier to be among the set of organisms that mixes, than among the set that does not.

I will show that this framework might mean that, for many interesting traits (mutation rate, intelligence, complexity, developmental plan, hierarchy of organization), we can understand their evolutionary trajectory by having a close understanding of the nature of variation rather than needing to understand how natural selection was generated from the environment.

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