



Higher level constructive neutral evolution

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Abstract

Constructive Neutral Evolution (CNE) theory provides selectively neutral explanations of the origin and maintenance of biological complexity. This essay provides an analysis of CNE as an explanatory strategy defined by a tripartite set of conditions, and shows how this applies to cases of the evolution of complexity at higher-levels of the biological hierarchy. CNE was initially deployed to help explain a variety of complex molecular structures and processes, including spliceosomal splicing, trypanosomal pan-editing, scrambled genes in ciliates, duplicate gene retention and fungal ATP synthetase structure. CNE has also been generalized to apply to phenomena at the cellular level, including protein-protein interaction network modularity, obligate microbial symbioses, eukaryogenesis and microbial unculturability. This essay further extends CNE to cases of complexity at levels of organization higher than the molecular and cellular. These are (1) multicellular phenotypic complexity, (2) multicellular ecological complexity and, (3) some cases of cultural complexity.

Keywords Constructive neutral evolution · Neutral evolution · Evolution of complexity · Obligate symbiosis · Cultural complexity

Introduction to CNE

Some complexity of evolving systems results from processes of Evolution by Natural Selection (ENS) resulting in increases in fitness and producing adaptations. However, some evolving systems come to be more complex without thereby resulting in increases in fitness or producing adaptations. Sometimes evolutionary processes are *constructive* (resulting in increased complexity) while nonetheless being *neutral*

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(resulting in no net benefit). One theory about how this can occur is Constructive Neutral Evolution (CNE) (Stoltzfus 1999; Gray et al. 2010; Brunet and Doolittle 2018; Wideman et al. 2019; Brunet et al. 2021; for similar, see also Starr et al. 2017/18, Shah et al. 2015; Brandon and McShea 2020; McShea and Brandon 2010; Schank and Wimsatt 1986). Disentangling CNE and ENS is theoretically interesting and empirically challenging. Many authors have shown the broad range of molecular and cellular cases of biological complexity to which CNE is applicable (see Muñoz-Gómez et al. 2021); this essay examines some cases that sit higher in the biological organizational hierarchy: cases from multicellular, ecological and cultural complexity.

This section describes CNE then attempts to pre-empt some common misconceptions. Arlin Stoltzfus (1999) coined the term CNE to explain, *inter alia*, the origin of an all-things-considered obscure process in an obscure organism: RNA editing in trypanosomes.¹ Trypanosomes are a group of unicellular algae that express their genes in a complex way (Benne 1989). Ordinarily gene expression has the following overall structure: a stretch of DNA is *transcribed* into a piece of mRNA by an enzyme, which is either a pre-mRNA that is cut into smaller pieces and *spliced* back together into a mature mRNA by a series of proteins and other guide RNAs, or left as is, then the resulting mRNA is *translated* into protein by the ribosome. This is the so-called Central Dogma of molecular biology: DNA is transcribed into pre-mRNA, which is spliced into mRNA, which is translated into protein. In *Trypanosoma* there is an extra step: a large portion of the mRNA is *edited*² by a complex of proteins that change some nucleotides of the sequence before translation.³ If this editing step did not occur then translation would not produce functional protein. Trypanosomal RNA editing is “discordant to the rules of the Central Dogma” (Benne 1989 p.136). Explaining how RNA editing evolved has far-reaching implications for our understanding of the evolution of molecular complexity.

Here are the fundamentals of the evolutionary explanation for RNA editing. A straightforward explanation by ENS is possible, but not well supported. That explanation goes as follows: the genes of the trypanosome acquired mutations that made them produce non-functional protein, subsequently an editing system evolved to correct these mutations at the mRNA stage and this restored or corrected function that was previously lost. This explanation involves hypothesizing a state prior to the evolution of the editor where the trypanosome has a (possibly very significant) loss of function mutation (see Fig. 2 in Brunet and Doolittle 2018). It is unclear why this loss of function mutation would not be corrected by a reversion more easily than by the evolution of a complex editing apparatus. In short, the explanation by ENS for a

¹ Patrick Covello working as a postdoc with Michael Gray and in consultation with Ford Doolittle, published the first instance of an evolutionary explanation using CNE, though without using the term ‘CNE’, in Covello and Gray (1993). Subsequently, Arlin Stoltzfus generalized the sort of evolutionary explanation given in Covello and Gray (1993), and coined the term ‘CNE’ in Stoltzfus (1999).

² Ordering of transcription, editing and splicing is unclear. Some editing processes occur co-transcriptionally (see Hsiao et al. 2018).

³ Editing is *prima facies* similar to splicing, where parts of the mRNA are cut out and the remaining parts are rejoined (spliced) back together. However, editing characteristically involves the insertion of RNA residues. Interestingly, both of these processes have been explained as cases of CNE (more below).

function restoring mutation correcting a mutational problem requires us to assume an unlikely (selectively disadvantaged) intermediate state. This makes the ENS explanation an unlikely fit.

A different explanation of RNA editing is possible and more likely, *ceteris paribus*. It differs importantly in the temporal *order* in which the editing system and the loss of function mutations occur. In the explanation by ENS the loss of function mutation occurs first and is corrected or (post-)suppressed by the editing system which evolves second. It is possible however to provide an explanation where the editing system appeared first, while the edit-requiring mutations appear second. If the editing system was already in place, then any other mutation that it can correct may then occur without loss of fitness.⁴ In this case, the mutation is no longer a loss of function mutation, since the consequences of the mutation are “neutralized” or (pre-)suppressed by the editor. However, once a significant number of editing sites emerge, the preexisting editing system becomes essential. The loss of the editor would result in the expression of non-functional proteins, which could be deleterious or lethal. This explanation does not involve an intermediate state where there are non-edited mutations leading to loss of function, so no significant reductions in fitness along the evolutionary trajectory. For that reason it is more likely than the explanation above using ENS alone. This latter sort of explanation for the origin of RNA editing is one of the prototypical cases of CNE.

If we abstract away from the molecular details of editing and describe this as a general sort of evolutionary process, then there are a remarkable number of examples of CNE. For the purposes of this essay, any system S containing some entities or classes A and B (traits, components, processes or organisms) is evolving by CNE just in case the following general conditions hold.

- (1) **Presuppression:** There is a pre-existing entity A that has the capacity to presuppress (edit, neutralize, reverse) subsequently occurring mutations in B. Entity A presuppresses B-mutations.
- (2) **Construction:** There is an accumulation of mutations in B that are (near) neutral for S due to the presence of A. Entity A suppresses a series of B-mutations.
- (3) **Dependence:** After sufficiently many B mutants emerge the loss of A becomes deleterious (in extreme cases loss of A is lethal), since loss of A would lead to the failure to suppress accumulated B-mutations.

I will indicate these conditions for CNE, in examples, with (1), (2) and (3) throughout the text.⁵ Muñoz-Gómez et al. (2021) provide a comprehensive list of molecular and cell-level phenomena that have been explained in part by CNE.

⁴ It is also important to note that the initial emergence of the editor may have been adaptive. Perhaps it indeed evolved to correct some specific non-lethal mutation. However, that does not imply that the entire process of accumulating editing sites was adaptive.

⁵ Versions of this generalization appear elsewhere (Stoltzfus 1999; Brunet and Doolittle 2018; Muñoz-Gómez et al. 2021; Brunet et al. 2021). (1)–(3) are approximately what are termed (a) pre-suppression, (b) ratcheting and (c) locking-in, in Brunet and Doolittle (2018) and Stoltzfus (1999) described CNE as, “(i) the presence of excess capacity in biological systems, (ii) biases in the production of variants, and (iii) a compounding of selective constraints due to epistatic interactions with neutrally evolving sites.” It should

[T]he ribosome, the replisome, the proliferation of transposons in eukaryotic genomes, the interdependence between endosymbiotic organelles and their host cells, the metabolic division of labor in insect nutritional symbionts, mitochondrial respiratory complexes, light-harvesting antennae in algae, protein folding and import machinery, the cytoskeleton and its associated motors, gene-regulatory network architecture, and trans-splicing in diverse eukaryotes (e.g., roundworms, kinetoplastids, and dinoflagellates) ... CNE has recently been extended to higher levels of biological organization, including the topology and degree of modularity in protein–protein interaction networks, the complexification of the eukaryotic cells, and the division of labor in microbial communities...—Muñoz-Gómez et al. (2021) Sect. 3, see their Table 1.

The purpose of this paper is to extend CNE again to higher levels of organization. This time, to ([Neutral evolution of multicellular complexity](#)) the physiology and anatomy of multicellular organisms, ([Neutral evolution of multicellular ecological complexity](#)) communities and groups of macrobes and, most contentiously, ([Neutral evolution of cultural-level complexity](#)) to artefacts and human cultural level phenomena. The remainder of this section addresses common misconceptions about CNE, before turning to new potential cases in the following sections.

Common misconceptions about CNE

First, it would be a misunderstanding to see CNE in conflict with the *initial* adaptive effects of the presuppressing entity. The presuppressor may have been a fully-fledged adaptation while nonetheless the subsequent construction of complexity and emergence of dependence is a neutral (or even mildly deleterious) process. It is important to note this early, since a common sort of objection to CNE evolutionary narratives (see Speijer 2006 and response in Gray et al. 2010) is to point to a plausible ENS account of the origin of the presuppressing entity. This should not refute CNE. The editosome may have evolved by ENS for the function of editing, and indeed that would explain why it is an effective editor. Nonetheless, the occurrence of hundreds of edit-requiring sites thereafter was effectively neutralized, making subsequent evolution of editing sites potentially an episode of CNE, not ordinary ENS. CNE and ENS are not in general contradictory narratives about the long-term evolution of a trait; actual evolutionary episodes may oscillate between CNE and ENS.

The initial coinage of CNE (Stoltzfus 1999) focused on the “constructive” – meaning relative complexity increasing – aspects of the process. Complexity is notoriously difficult to define directly (though for an account relevant to neutral evolution see McShea and Venit 2000; McShea 2021). Comparisons of complexity are easier. Here is a working definition of comparative complexity: *A is more complex than B if A contains a larger collection of processes, parts and/or interactions than B.* CNE does often result in the net increase in complexity. However, CNE can lead to net-negative

also be clear that the choice of the word “presuppression” (l) over “excess capacity” (i) is immaterial, indeed Stoltzfus (1999 p.178) noted that, depending on the case, the words “buffering,” “tolerance,” or “unrealized potential” might feel more appropriate.

complexity changes.⁶ In light of this, it is better to focus on the portion of complex dependencies that is increased, since CNE always leads to increases in the complexity of dependencies between entities. In the examples considered here, the important change generated by CNE is an increase in the proportion of those processes, parts and interactions which are interdependent.

Moreover, since CNE applies to the evolution of entities that may already be variously adapted, there is a corresponding variety of types of dependence between entities that can be generated. In some cases, CNE can even produce *essential traits*: those that a system is so powerfully dependent on that their loss or reduction would lead to death or strongly negative fitness impacts. Depending on the preexisting dependencies in a system, the constructive aspect of CNE can lead to different dependence relationships later on. I describe these in brief.

CNE can lead to *conditional dependence*: given a pair of entities A and B the loss of A *alone* results in fitness reduction, but the loss of *both A and B* recovers near-normal fitness. This can happen famously in cases of toxin-anti-toxin pairs, where A is the “anti-toxin” without which B, the “toxin” negatively impacts fitness. CNE can also lead to *unconditional dependence*: the loss of some entity A has negative fitness effects, yet there is no entity B that might be lost to rescue fitness. This can happen when the presuppressive effect of A is “distributive” over a very wide range of other entities, so that no single entity B is presuppressed (the broad range of editing sites in trypanosomes is an example). This can also happen when the mutations that are presuppressed by A (e.g. leading to misfolding, plaque formation etc.) appear in some already essential B, so that loss of B is lethal for other reasons (e.g. loss of metabolic potential). Finally, CNE can lead to *change of dependence*: the fitness consequences of mutation in some B prior to evolution by CNE are transferred over to an entity A. In extreme cases, CNE can transfer essentiality. This can happen when, supposing B is essential for some effect F, the emergence of some A that presuppresses reductions in F can result in total loss or non-functionalization of B. In these cases, the presuppressor effectively *deessentializes* B. We will see one example of this in amino-acid biosynthesis and another in energy acquisition in aphotosynthetic plants in [Neutral evolution of multicellular ecological complexity](#). Of course, ENS can also lead to each of these sorts of dependencies, yet what is interesting about CNE is that it explains dependency without evoking positive selection.

Third, we should be careful to distinguish CNE from other theories used to explain the neutral origin and maintenance of biological complexity. Notably, the Zero Force Evolutionary Law (ZFEL), due to Brandon and McShea (2020), McShea and Brandon (2010) and McShea et al. (2019), and to the more recent work on contingency and entrenchment by Shah et al. (2015) and Starr et al. (2017; 2018). Moreover the notion of presuppression is similar to Gould and Vrba’s (1982) notion of a “pre-adaptation”, although the latter comes with the requirement of being fitness enhancing (see *ibid.* pg.11). For some connection between these views see Brunet et al. (2021,

⁶ Although assessing relative complexity is a perennial difficulty, there are plausible cases of CNE where an entire synthetic apparatus has been lost, damaged, or pseudogenized after the introduction of a comparatively simple presuppressor (see case of heterotrophic plants in Sect. 3). In these cases net complexity at the organism level is reduced, but the proportion of essential complexity is increased.

Sect. 4). Since the present connection deals with CNE in the context of macrobes, the relationship between CNE and the theory of generative entrenchment (GE) due to Wimsatt and colleagues (Shank and Wimsatt 1986) merits attention. Though their consequences for organisms are similar, GE is a special case of CNE. Mostly obviously, this is because CNE applies to cases that are not developmental systems.

To characterize the relationship between GE and CNE in the case of organisms it helps to have a model of developmental dependencies. At each stage of development s there is a set of expressed traits $T(s)$. Let us say a trait B depends on a trait A if the loss or reduction of function of A causes a loss or reduction of function of B . Supposing A and B are both traits in $T(s)$, then either A depends on B , B depends on A , both are codependent, or neither one depends on the other. However, across developmental stages, given temporal asymmetry, the possible sorts of dependencies are reduced (Shank and Wimsatt 1987 p.42; see Rasmussen 1987). Supposing A is a trait of $T(s_1)$ and B a trait of $T(s_2)$, where s_2 is a later stage than s_1 (i.e., $s_1 < s_2$), then either B depends on A or it does not— A may not depend on a trait occurring only at a later stage of development. With this sketch of development we can characterize generative entrenchment. The following definition is given in Shank and Wimsatt (1986, p.38): “[features are] ‘*generatively entrenched*’ in proportion to the number of ‘downstream’ features which depend upon them”. Take $D(A)$ to be the size of the set of downstream traits B such that B depends on A . Then A_2 is more generatively entrenched than A_1 iff $D(A_1) < D(A_2)$. GE is then the claim that traits tend to become more generatively entrenched over time. This provides a powerful developmental constraint on evolutionary trajectories.

Wimsatt and colleagues have provided an impressive list of consequences and corollaries of GE, so it is natural to wonder whether CNE is among them. However, notice that this sketch of development is sufficient to show that GE follows from conditions (1)-(3) for CNE. CNE is occurring in a developmental system whenever there is some A satisfying (1)-(3) relative to any B occurring at the same or later stage as A . For (1), consider any presuppressing trait A . In (2), a presuppressing trait A is expected to accumulate dependencies with other traits B (which must be at the same or a later stage). After the point of satisfying (3), if A_1 is an ancestral version of A prior to construction and A_2 is a version of the trait after construction, then A_2 has gained some dependencies. At that point $D(A_1) < D(A_2)$, that is, that A has become generatively entrenched.

The remainder of this essay deals with cases of complex dependencies formed at higher levels of biological organization. CNE has already been extended to apply to multimeric macromolecular complexes and, higher still, to ecological interactions among microbes; the following section extends it further to macrobes (2.1-2), then to macrobe ecologies (3.0) and to social or cultural-level complexity (4.0).

Neutral Evolution of Multicellular Complexity

The evolution of complex organs is for good reason considered a paradigm of evolution by positive natural selection leading to complex adaptations. However, there is growing appreciation of the fact that non-adaptive processes can also shape complex-

ity at the organism level—e.g., Gould and Vrba's (1982) ad/ex/pre-aptation distinction—and moreover that many of the same explanatory strategies used in cases of genes and genomic complexity can apply at the level of organs and organismal complexity (Gregory 2008). The origin of CNE as a neutral explanation for molecular complexity might mislead us into thinking that it is only useful as a theory of complexity at that level. However, the conditions 1–3 for CNE are general, and likewise apply when the presuppressing entity is, e.g., a tissue or organ. This section shows how we can see CNE at the organism level as a natural progression from consideration of CNE at the level of microbial communities. I argue for this extension of CNE in principle, describe how CNE can be applied at the organism level, then examine some cases of organismal complexity that may have evolved by CNE.

To motivate CNE at higher levels, consider first that CNE may apply to *collections* of molecular interactions. CNE can apply when many different molecules contribute to the trait A, such as how multiple proteins contribute to the capacity for a cell to edit RNA or to chaperone the proteome. In these cases it is not specific molecules, but a host of them that contribute to the presuppressive capacity of the system and the presuppressed mutations do not occur in one single gene product but across the proteome. This is how that might work in the case of the chaperone system—a chaperone is a protein that “assists” in the folding of other proteins during their maturation. If a protein is self-folding, requires no chaperoning, then the additional complexity of the chaperone system will at first contribute nothing to it (or may even be mildly deleterious). However, once chaperone dependent folding-assistance is available, proteins are free to mutate in ways that can be presuppressed by the chaperone. After this occurs, loss of the chaperone is deleterious whatever its initial fitness effect. The same reasoning can be applied to the entire collection of proteins requiring folding assistance and the entire barrage of chaperones. That is, CNE can explain some portion of the complexity of the entire proteome. This section argues that it can likewise apply to the entire physiology of multi-cellular organisms.

In a way, we already know that CNE likely plays a role in the physiology of microbes: plants have RNA editing systems (Takenaka et al. 2013) and these likely contribute to the essentialization of genomic complexity by CNE and affect overall physiology. Similarly, Novick (forthcoming in the Cambridge *Elements*) raises the interesting possibility that CNE might have a role to play in the structural evolution of animal life generally, due to the impact of CNE type processes on morphological regulatory *hox* genes. However, to show that CNE is genuinely organism-level, this section considers entities that are macroscopic parts of organisms such as tissues and organs.

One canonical form of molecular CNE is the process of subfunctionalization of duplicate genes (Stoltzfus 1999). Sometimes gene duplication results in *neofunctionalization*: an adaptive divergence where each duplicate evolves, by ENS, new features that contribute positively to fitness in different ways. However, *subfunctionalization* obtains when each gene takes on a portion of the function of the original, such that both are required for a task formerly done by a single gene. Importantly, this might occur if the duplicates take on a subset of the set of functions performed by the original. It might also occur in terms of dosage, quantity, or activity levels. For example, the duplicates may each take on the role of producing a fraction of

the quantity of protein produced by the original, so that neither duplicate performs a different function and both must contribute to performing the same function. In such cases, each duplicate acts as a presuppressor of the reductions in function of the other. Since requiring two genes is more complex than requiring only one, and since after subfunctionalization neither gene can be lost without loss of fitness, this process generates the complex dependence that is the hallmark of CNE.

Indeed, genes are not the only things that duplicate and diverge in a way allowing for subfunctionalization and thus CNE. Brunet and Doolittle (2018) argued that a similar process can occur between groups of similarly functional cells in microbial populations (demes), so that one group will lose a functional capacity that is compensated for in another. When this is overall neutral⁷, it is a case of CNE at the community level. Macrobes are, in both a physiological and evolutionary sense, sorts of well-constituted microbial communities; macrobial demes are tissues and organs. This suggests a direct analogy: macrobes too may evolve by duplication and subfunctionalization when tissues or organs take on a subset of the roles present in some ancestral homologous structure.

When discussing the evolution of complex organs, Gregory (2008 p.362-4) makes a similar analogy. His list of types of exaptation, for example, include the case “Two organs (or genes) perform the same function and then one becomes more specialized for the original function while the other takes on a different role” (p.362 my emphasis). Gregory (2008 p.363) also indirectly raises the possibility of subfunctionalization after duplication, or “furcation”, of organs themselves. For example, a mutation in a developmental gene might lead to the duplication of a tissue layer, each member of which might immediately take on a subset of the functions of the original, without this distribution of labour resulting in any fitness increase. Subfunctionalization can also take place long after organs (or tissues) have adaptively diverged, that is, subfunctionalization can occur after neofunctionalization.

Consider the liver as a possible example. Specifically, consider why the liver has so many functions. The liver has an impressive variety of functions (see Kmiec 2001). Some combination of these are also essential since total liver failure is lethal. Of course, many organs are polyfunctional and their loss is lethal, but this is particularly interesting and merits explanation in the case of the liver because it is not clear that an organism *requires* a specialized organ to perform these functions. Livers are peculiar to chordates, where they may have ultimately originated from a modified yolk-sac in a chordate ancestor (Subbotin 2017). All non-chordates go without a liver, for example echinoderms such as starfish and sea cucumbers, which are close chordate relatives. Even assuming that each function the liver performs is or was an adaptation, we still require an explanation for the location of that function, for why that function is performed specifically by the liver, especially since many liver functions are carried out, to some extent, by other cells outside the liver (e.g. gluconeogenesis and amino-acid synthesis). Of course, an explanation by ENS is possible and may explain the localization of many such functions; perhaps specialization of the liver for synthetic capacities is overall more metabolically efficient and thus localiza-

⁷ As opposed to being an example of selectively driven gene loss, as in the BQH (Morris et al. 2012).

tion of functions to the liver is an adaptation. Nonetheless a CNE explanation is also available and may explain the localization of some functions.

On a CNE explanation for the localization of functions in the liver, (1) the presence of a liver (or its precursor) *presuppressed* the reduction of functions in other organs or tissues. In case of microbial communities, for a function to be compensated for by another community member, another group of cells, that function must be “leaky”: the benefits of performing the function are also shared locally by other cells. The canonical example for Morris et al. (2012) is the metabolic breakdown of peroxide: when one community member can degrade peroxide, the others benefit without themselves possessing the capacity. In the case of the liver, the connection of the liver to a filtered blood supply effectively allows its metabolic activities to have effects throughout the body, since it is connected “locally” via the circulatory system. Due to random mutation of tissue and organ specific metabolic expression profiles, (2) given non-liver tissues or organs will eventually lose or reduce their capacity to perform some of the functions that the liver presuppresses. This is the *construction* of a complex physiology. Finally, (3) once other organs or tissues have lost or reduced their functional capacities, the whole organism now has a *dependence* on the liver to perform these functions. Importantly, whether this narrative is correct may vary by particular hepatic function, and there may have been extensive secondary adaptation in liver cells. However, the CNE narrative shows that it is not necessary to assume that localization to the liver was initially an adaptation.

In addition to explaining the distribution of functions in organs, CNE can also play a role in explaining the persistence of organs despite their apparent loss of function. A number of organic structures of macrobes have been proposed to be non-adaptive, vestigial, or otherwise degenerated. In humans, the usual example is the appendix, but other examples include the palmaris longus muscle (a muscle visible in the wrist, when present), waxy secretions of the ear (Komai 1968), vibrissal capsular muscles of the upper lip (the muscles attached to the base of whiskers in other animals) (Tamatsu et al. 2007), as well as various structures associated with the human tailbone and occasional emergence of a vestigial tail (Dao and Netsky 1984). The human hymen, insofar as this is a recognizable human organ at all, is another often suggested example of a vestigial trait.⁸ In dinosaurs the diminished forelimbs of the Tyrannosaurs are the perennial example—so striking that Gould and Lewontin made it the topic of their infamous quip about the adaptationist programme: “male tyrannosaurs may have used their diminutive front legs to titillate female partners, but this will not explain *why* they got so small” (Gould and Lewontin 1979, p.1)—and a host of potential vestigial dinosaur traits are reviewed in Senter (2010). For examples from flowering plants see Wilson (1982), who treats the particularly interesting case of internal floral vascular structures which are retained in development despite the loss or vestigial reduction of the morphological features they originally supplied.

These sorts of traits were, presumably, created by selection. They have their *origin* in ENS, however, they are not likely to be now *maintained* by positive selection (see Linqvist et al. 2020) so come to degrade over evolutionary time. For some of

⁸ I owe this example to discussion with Eftihia Mihelakis. The vestigial nature of the human hymen remains contested.

these traits the populations containing them are small and their coefficient of selection weakly negative, so selection may have been too powerless to eliminate them, yet. What CNE adds to this assessment of non-functionality of anatomical features is another explanation of why relics and vestiges might persist, despite *prima facie* uselessness or even physiological costliness. That explanation proceeds by assuming that the relic, or some feature of the relic, continues to have some presuppressive effect or complex organism-level dependency, so that *loss* or *further reduction* of the relic would be deleterious. In terms of the conditions (1)-(3) for CNE given above, this involves (1) assuming that the ancestral organism S had a trait $A_{\text{pre-vestige}}$ with an organism-level presuppressive effect (e.g., compensating for changes in surrounding tissue characteristics, or detoxifying a biochemical product of another organ), then (2) changes (loss, mutation) of another organism-level $B_{\text{dependent}}$ accumulate, and (3) eventually these changes result in a dependency of S on $A_{\text{pre-vestige}}$. If $A_{\text{pre-vestige}}$ also undergoes relaxed selection for whatever function it had, it must still remain in S in a vestigial state A_{vestigie} , potentially reduced, yet sufficient for it to serve its presuppressive role. Put another way, a given trait may be functionally vestigial while still being presuppressive of disfunction elsewhere in the organism. Indeed, this is a generalization of developmental allometry⁹ to include cases where one of a pair of allometrically coupled traits is under mere maintenance selection, instead of positive selection.

An interesting example comes from cetacean hip bones, which have recently been proposed to retain some functional role and perhaps be under positive sexual selection. Indeed, a given “relic” may not be entirely so, and may retain *some* adaptive significance for the organism containing it. Dines et al. (2014) propose such an hypothesis for the maintenance of cetacean hip bones, explaining persistence of the trait as a consequence of continued sexual selection for the role of hip bones in anchoring tissues important in testes and penis function. However, cetaceans may use their hip bones to support penis function, but that need not explain how they became anchored to important tissues. A dependency between hip bones and penis function may explain the maintenance or persistence of these bones by purifying selection alone (Linguist et al. 2020; Brunet et al. 2021), since their loss would have negative impacts on sexual function, though hip bones never need to have had any positive effect on penis function during their origin to be used in such a maintenance explanation. The only feature *required* for a maintenance explanation is that loss of hip bones would be deleterious. Indeed, in cetaceans, the hip bones remain attached to a particular muscle the damage of which, in human and rat at least, results in erectile disfunction (Dines et al. 2014 and references therein). In CNE terms, in this case, contingent (A) attachments of hip bones to testes and penis tissues may have initially been neutral (they might have been lost without loss of fitness), however, once reductions in (B) hip bones took place, they may have been essentialized.

⁹ I owe this connection to developmental allometry to conversation with Adrian Currie.

Neutral Evolution of Multicellular Ecological Complexity

The purpose of this section is twofold. Firstly, I argue that many cases of ecological complexity are appropriately and helpfully understood as cases of CNE. These are cases where one community member (the presuppressor) is “preadapted for”, “permits”, “allows” or “facilitates” a change in another member that leads to dependence. Second, that some cases of ecological complexity that are described as ENS favouring dependence are better understood as cases of CNE.

The formulation of conditions 1–3 for CNE to take place has thus far been applied so that the system *S* is some organism, while *A* and *B* are some of its parts. However, the conditions are general enough for organisms to satisfy it as entities *A* and *B*, so that the containing system *S* might in principle be a microbial community, group, symbiotic association, holobiont or ecosystem. There are cases in which a pre-existing presuppressive relationships between two organisms and a constructive mutational change within one of them leads that organism to become dependent on the presuppressor, sometimes to the point of being unable to return to solitary life. This sort of change leading to essential dependence between organisms, to obligate symbiosis, has been used in microbiology to explain rampant unculturability. The initially motivating example of this was taken from evolved metabolic interdependencies in microbial ecologies, specifically the (selection driven) dependencies resulting from loss of a gene in one organism that is presuppressed by the presence of an analogous gene in another community member (see the black queen hypothesis of Morris et al. 2012, and the derivatively named gray queen hypothesis in Brunet and Doolittle 2018). It is tempting to construe this as unique to microbial life with its comparatively fast pace of gene loss (Iranzo et al. 2019). Nonetheless, analogous processes can occur in ecological relationships among macrobes, ourselves included.

An illuminating and simple example comes from the loss of vitamin C synthesis. Vitamin C is an essential part of animal physiology. However, some bats, some birds, some fish, guinea pigs and humans have lost the ability to synthesize their own vitamin C. We must obtain this from our diet or else suffer from scurvy. Interestingly, some bat and bird lineages that have lost vitamin C synthesis have occasionally regained it, though seemingly without effect on diet or fitness. Neutrality of vitamin C loss can be explained, by CNE, as a dependence on pre-existing organisms that serve as C rich foodstuffs and thus presuppress loss of the C synthesis pathway.

[C]urrent evidence favors the hypothesis that the multiple gains and losses in the ability to synthesize vitamin C are random, as would be expected for a neutral trait...The neutrality of vitamin C loss is a function of the environment in which the species lives. Individuals from a species which have lost the ability to make their own vitamin C will not be selected against as long as their diet contains sufficient quantities of vitamin C.—Drouin et al. (2011) p.377.

A more complex and interesting example comes from the concerted loss of multiple biosynthetic pathways. Consider Payne and Loomis (2006) on the loss of amino acid biosynthesis pathways in heterotrophs,

When an organism becomes a consumer by eating other organisms, all of the amino acids are available in the diet and no longer need to be synthesized. Unless amino acid biosynthetic pathways serve other essential functions besides providing amino acids, they are unnecessary and dispensable. Genes in dispensable pathways accumulate deleterious mutations, lose the ability to encode functional enzymes, and are eventually deleted from the genome.—Payne and Loomis (2006).

Heterotrophy deessentializes amino acid biosynthesis, unless the pathway is bifunctional, playing some role in another essential process. Autotrophs presuppress mutations in synthesis pathways of heterotrophs. Whether or not the additional complexity of a heterotrophic lifestyle was initially an adaptation, once amino acid synthesis pathways are lost, the heterotroph *depends* on autotrophs—heterotrophy becomes essential—and a return from heterotrophy to autotrophy is unlikely. Here is the CNE narrative for the origin of heterotrophy: (1) an initially facultative heterotrophy in the presence of autotrophs presuppressed loss of function in synthesis pathways, (2) loss of function mutations emerged in synthesis pathways from random mutation, essentializing heterotrophy, and (3) loss of function in genes required for heterotrophy would negatively impact fitness, so heterotrophy is maintained by purifying selection. This is a case of CNE as described above, by taking the containing system S to be some collection of (initially facultative) heterotrophs (B) and autotrophs (A).

This process of amino acid pathway degradation differs by lineage. Humans, for example, are able to synthesize only eleven of the twenty amino acids, and only ten amino acid biosynthesis pathways are conserved across animal life. Heterotrophy has emerged multiple times, in both contemporary organisms and, potentially, at the origins of life in hydrothermal vents (Schönheit et al. 2016). Which pathways are conserved and which lost during CNE moreover depends on environmental and lifecycle constraints. Humans retain the phenylalanine synthesis pathway (in healthy organisms), while the parasite *Cryptosporidium* lacks the phenylalanine degradation pathway. Payne and Loomis (2006) hypothesize that this was facilitated by the fact that phenylalanine can be rapidly exchanged with its host. If loss of this pathway was facilitated (1) by the additional capacity to exchange phenylalanine with the host, brought on by the complexities of parasitic lifestyle (2), and if this loss indeed contributes to why *Cryptosporidium* cannot free-live (3), then this complex and essential relationship with the host (requiring the host rather than simply benefiting from one) is an instance of a parasite-host ecological relationship generated by CNE. Parasitism, as a special sort of heterotrophy, is perhaps particularly liable to result in presuppression of parasite functions.

Here is the general description: a symbiotic pair S consisting of partners A and B may interact facultatively up to and including a time when A comes to have a presuppressive effect on some trait of B. However, if B mutates in a way that is neutralized by its association with A, then the association is no longer facultative: isolated B has *lower* fitness compared to B in symbiotic association with A. There has been a great deal of work attempting to explain the origins of obligate symbioses via advantages or adaptations favouring symbiotic associations, either individually or as

groups.¹⁰ However, the CNE narrative does not require adaptive individual or group level explanations; it explains obligate associations by coordinated *loss* of function. I submit that many obligate symbioses may have emerged by CNE rather than ENS favouring association. I now turn to a class of examples from fungal-plant symbioses.

Consider the odd niche of the achlorophyllous flowers *Monotropa uniflora* and *Monotropa hypopitys*. *M. uniflora* is also known as the *ghost flower* due to its white translucence. This flower almost entirely lacks chlorophyll and consequentially cannot photosynthesize. Instead, it is physiologically connected to the hyphae of nearby fungi that are themselves physiologically connected to nearby trees. Photosynthetic products of the trees are ultimately funneled through the hyphal network and metabolized by the ghost flower. The relationship is often characterized as parasitic (Ogura-Tsujita et al. 2009), since the flower does draw energetic compounds from the fungus. However, it is best at this point to remain neutral about the adaptive significance of the fungus-flower relationship; it is not known whether the fungus derives any ulterior non-energetic benefit from the floral association and it is difficult to imagine the associated tree is negatively affected. Other explanations for the association are adaptive, from the flower's perspective, including that this association allowed the flower to colonize low-light environments (Bidartondo 2005).

Let us assume that the initial association between *M. uniflora* and the fungus (and tree) was facultative. This is reasonable both from a theoretical position and comparatively. The ancestor of the flower was a "free living" angiosperm, capable of photosynthesis (for phylogeny see Liu et al. 2020), and saltational leaps to obligate aphotosynthetic mycoheterotrophy are unlikely. Moreover, there are other facultative nearly aphotosynthetic organisms for comparison, such as the albino orchids and "phantom orchids" (Klinkenberg and Klinkenberg 1991). Similar achlorophyllous relationships also obtain in the liverwort *Cryptothallus mirabilis* (see Wickett and Goffinet 2008 for phylogeny). For example, Suetsugu et al. (2021 p.9) studied green and albino orchids *Cypripedium debile*, finding that the former facultatively associated with fungal hyphae, and moreover suggested that high degree of orchid dependence on fungal carbon "probably facilitate the emergence of albino mutants".

Here is a CNE narrative for the emergence of obligate from facultative association between achlorophyllous or albino partners in fungal symbioses. (1) The availability of carbon from the fungus A presuppressed reductions in autonomous photosynthetic capacity in the flower B. (2) Mutations subsequently emerged in the photosynthetic apparatus of the flower, for instance, by reductions in chloroplast genes (see Liu et al. 2020) or loss of the chloroplast genome (Molina et al. 2014).¹¹ Finally (3) once a significant mutation of photosynthetic capacity occurred in the flower, leading to its ghostly or albino appearance, the flower was dependent on the fungus; the fungus became an essential ecological partner for the flower. In the specific case of *M. uniflora*, Logacheva et al. (2016 p.4) report that "all genes encoding components of

¹⁰ Too much to give due credit, but see Lean (2018) for a conceptual framework for understanding symbioses as potentially evolving individuals.

¹¹ Pseudogenization of formerly essential genes without reductions of size are possible. Indeed, if relaxed selection on photosynthesis gene content drives pseudogenization, this may even occur by transposon proliferation, so may result in increased plastid genome size.

the photosynthetic apparatus [have been] lost or pseudogenized,” suggesting that the process of CNE has been carried to complete dependence of flower on fungus. At the end stage, the loss of photosynthesis in mycoheterotrophs is just like the loss of amino acid synthesis in heterotrophs: both are plausible instances of CNE leading to essentialization of ecological interactions following presuppression of would-be loss of function mutations in synthetic capacities.

I take these cases to show that a neutral explanation of cases of ecological dependence are readily available and some are well supported by the available evidence. Nonetheless, there is a tendency to interpret these symbioses as necessarily adaptive, and this often requires assumptions that are not well supported. Often the only difference between a CNE and ENS narrative is whether the (presuppressed, entity B) dependent member of the association is assumed to have initially derived some benefit from the *loss* of some capacity. For example, in a recent review of *mutualistic dependence*, Chomicki et al. (2020) describe a number of plausible evolutionary pathways that can lead to symbiotic dependence. One of those pathways is evolution via trait loss (ibid. p.414), which can “lock a species into an obligate relationship” and “relax selection” on maintenance for traits with functions reliably provided by symbiotic associations. In order to characterize this as a pathway to *mutualism*, Chomicki et al. (2020) claim that it was “presumably costly” to maintain the lost traits, so that their loss would have been an advantage. Indeed, many mutualistic dependence relationships may have evolved like this. However, when trait loss leads to an *obligate* dependence on an imperfectly reliable community member, it is difficult to maintain that the costliness of maintaining a trait (e.g. the energetic costs of expressing a gene) outweighs the costliness, lethality, of being isolated from that community member. In these cases, it is better to drop the assumption that trait loss was selected for and adopt the CNE explanatory strategy instead.

Neutral Evolution of Cultural-Level Complexity

In this final section I examine some cases of the emergence of essential complexity in human affairs with the aim of showing that CNE applies to some cases more familiar to humanists and social scientists. The purpose of this section is not to bolster any theory of cultural evolution. The explanatory utility of cultural adaptations is questionable, and cultural evolution is a topic that provokes reasonable scepticism from both evolutionists and cultural theorists alike (Chellappoo 2022; Lewens 2015; Godfrey-Smith 2012; Fracchia and Lewontin 2005; Wilkins and Bourrat 2001). It is enough for my purposes that there are historical processes that lead to complexity in human affairs and that these historical processes sometimes lead to complex dependency relationships without apparent advantage. This section aims to show that the three part explanatory strategy of CNE applies well to some of these cases of complexity; in particular, to networks of human interactions and to complex interactions between humans and technologies. Indeed, insofar as CNE does apply to cultural phenomena, their status as cultural *adaptations* is even more questionable.

Note that molecular-level CNE has often been characterized in terms of analogies to cultural level complexity. For example, when Gray et al. (2010) advanced a CNE interpretation of some genome level complexity.

[A]lthough complexity in biology is generally regarded as evidence of “fine tuning” or “sophistication,” large biological conglomerates might be better interpreted as the consequences of runaway bureaucracy—as biological parallels of nonsensically complex Rube Goldberg machines that are over-engineered to perform a single task.—Gray et al. (2010)

The biologists who initially developed CNE turned to seemingly unnecessary or detrimental complexity in cultural or technological entities—to runaway bureaucracies, over-engineering and Rube Goldberg machines—when looking for helpful analogies or metaphors to describe the complexity generated by CNE in molecular systems.¹² Trypanosomal RNA *editing* is already described in the metaphorical information language common to molecular biology, and this makes analogies with cultural information more or less direct. This in mind, I begin with the example of text editing technologies, such as spellcheck (‘autocorrect’ or ‘spell-check’). If trypanosome RNA editing had been discovered in a different technological era perhaps it would have been named ‘transcriptcheck’.

I take spellcheck assistance to be a case of cultural complexity meriting historical explanation. As with RNA editing, a system requiring error-correction is more complex than a system that does not require a correction step, *ceteris paribus*, so the process leading to this state was a constructive one. The difficult question is whether it was a neutral process. As with RNA editing there is an evident positive or adaptive narrative to be told about the wide and apparently essential use of spellcheck: it exists because it provides the advantage of correcting spelling errors. David Sparshot vividly exemplifies this in *The Fasinatng... Fascinating History of Autocorrect*, claiming that without spellcheck we could not “compose windy love letters from stadium bleachers, write novels on subway commutes, or dash off breakup texts while in line at the post office”, or indeed use the highly inaccurate touchscreens characteristic of smartphones.

Here is a dry reconstruction of the adaptive narrative explaining spellcheck. A problem exists in the population of spellers: spelling is difficult to do at the quality or rate demanded by modern economies. To resolve this problem a technology was developed to detect and correct spelling errors. Perhaps the first was Blair (1960), though see Mitton (2010). This made spelling easier and improved the quality of writing and the rate of production. Because this improvement was noticed by many, spellcheck technology was intentionally propagated to new contexts (e.g., word processing software, phones, voice-to-text correction), and was developed to a stage of greater effectiveness. Overall, quality of spelled work has improved. This narrative

¹² Gray et al. (2010) use the analogy to bureaucracies and borrow the Rube Goldberg analogy from San-car’s (2008) work on the eukaryotic molecular clock. Similarly, Schank and Wimsatt (1987) and Rasmusen (1987) both use artefacts, locking mechanisms and automobiles, to illustrate generative entrenchment.

has the advantage of being a success story of technological progress and the disadvantage of being probably false.

What is doubtful about the narrative is *when* the problem of spelling at a given quality and rate is dated with respect to the advent of spellcheck technology. The adaptive narrative positions this problem *prior* to the origin of spellcheck as a problem to be resolved, but it may also be a problem that emerged or worsened after the origin of spellcheck. Indeed, the types of common errors have changed since the introduction of word processing software, with spelling errors now less common in spellchecked work, and this is probably due in part to the introduction of spellcheck assistance (see Lunsford and Lunsford 2008 p.796). However, typists prior to spellcheck were competent. Plenty of typed documents were produced; spellcheck is not essential for the production of written works. Moreover, spellcheck may also have had a negative effect on our *unassisted* spelling abilities; some of those who learned to spell before spellcheck may have since learned to be poorer spellers, and some of the rest poorly learned to spell. There is anecdotal evidence that spellcheck introduced new types of errors, e.g., the “Cupertino”, an error of selecting the first suggested spelling without attention to context (Mitton 2010).¹³ There is also survey based evidence that spellcheck may have affected the types of errors made. Connors and Lunsford (1992 p.418) report that, “papers that were word processed without spell-checking contained far more misspellings per paper than did our original sample [of 3,000 handwritten or typewritten essays]...[there were] slightly more than twice as many misspellings”. In our pre-edited transcriptions, there are probably now more errors than there were before. Overall, if the quality of unassisted spelling has worsened in groups with access to spellcheck software—just as the number of edit-requiring sites have increased in organisms with an RNA editing system—then spellers are in part *dependent* on spellcheck software.

Here is a CNE explanation of this process of cultural change, analogous to the origin of RNA editing. Consider a system consisting of spellcheck software and the spellers that use it. (1) Spellcheck was created with the intention to resolve problems with spelling while typing, it is an intentional form of presuppression. Either it succeeded or it did not – there is plenty anecdotal evidence that it also introduced a series of uncommon errors. However, it did correct common mistakes and was installed on updated Windows systems (Mitton 2010). (2) At this point there is reduced impetus for spellers to manually correct errors that can be corrected by spellcheck and spellers tend to produce *more* mistakes in the initially written text. Moreover, contemporary spellcheck software also learns from newly observed mistakes. This process is *constructive* and feed-forward, so that increases in the number or types of errors spellcheck can correct tends to encourage an increase in the production of more such errors in pre-edited text. (3) At a later stage, perhaps once there is an “epistatic” change that makes accurate initial spelling more difficult (e.g. by having buttons

¹³ For comedic example consult the unattributed spellcheck poem, appearing in Thomas, S. P. (1999, p.439), beginning with the lines, “Eye halve a spelling chequer // It came with my pea sea // It plainly marques four my revue // Miss steaks eye kin knot sea...”. A similar variant of the beginning of the poem, also unattributed, appears in Mitton (2010).

smaller than fingertips), spellers become *dependent* on the technology, so that any loss of spellcheck capacity would have a negative effect on the system.

Importantly, a negative effect of loss of automation of spelling can occur even if there was no net benefit of the origin of the technology. Likewise there is nothing about this narrative that prevents there being certain benefits of the technology – to users or their corporate suppliers – on occasion. It does however suggest that the current state of complex dependence on the technology is not explained by benefits. On a CNE explanation, typographical benefits are not the cause of our dependence on spelling automation.

In Stoltzfus (1999), the initial cases of CNE were taken from editing, but also from subfunctionalization of duplicate genes.¹⁴ I conclude this section with two examples of the origin of cultural complexity that are analogous to subfunctionalization: (1) *roles* within institutions and (2) *networks* of information flow.

Here is the three step narrative explaining some of the complexity that exists within bureaucracies as a form of neutral subfunctionalization of roles.¹⁵ Initially, (1) a task X must be performed that is difficult for any given individual I1, so someone partitions the responsibility for completing X to two individuals I1 and I2. Since the task is divided between I1 and I2, neither individual is ever tasked with the entire completion of X. Both individuals presuppress the other's loss of ability or authority to complete X. As time passes, (2) either or both of I1 and I2 progressively lose the ability to complete X. Perhaps they forget how to do X. Eventually, (3) I1 and I2 lose the ability or authority to complete X alone, so can complete X only when/if co-operating. In this situation, I1 and/or I2 have been *subfunctionalized*. Moreover, supposing X is essential to the system of roles in which I1 and I2 work, then both have become *essentialized* by this process. Since the system containing I1-2 and X is more complex, and no benefit in doing X has obtained, this is directly analogous to molecular cases of CNE by duplication and subfunctionalization.

Although it is tempting to construe cases like the above as intentional consequences of human reason, in most cases it is only the initial use that is intended, rather than the complex form of dependence that is subsequently engendered. Although there is an initial *intention* for the subfunctionalization of a role to lead to ease or efficiency, there is nothing naturally ensuring that this happens—it might just as well complicate things so that goals are achieved at the same or a lower standard. The subfunctionalization of roles need not actually achieve its intended effect. Moreover, the outcome, dependence upon a larger number of roles, was clearly not an intended effect. So this production of essential complexity should not be explained as an effect of beneficent intention.

Here is a similar example of subfunctionalization. Work on gene regulatory networks, modelled as networks of Boolean functions, have shown that network complexity and modularity that appears functional can arise merely from constructively neutral duplication and divergence events (see Wang and Zhang 2007). Though there

¹⁴ Scrambling and unscrambling of exons is also an initial example. There are adaptive explanations of scrambling, such as in Buhrman et al. (2013). However, these seem to provide only moderate advantages (Flegontov et al. 2010) in the biological systems where they have been observed.

¹⁵ Recall the general characterization of subfunctionalization in Sect. 1.

is reasonable grounds for doubt that real gene regulatory networks are strictly Boolean, this can be taken by analogy as an argument that some gene regulatory networks are shaped and complicated by CNE (Brunet and Doolittle 2018). However, it can also be taken directly: CNE processes of subfunctionalization can explain the emergence of complexity in Boolean networks, the objects used as models of subfunctionalization, duplication and divergence. Insofar as Boolean networks are used in technologies, we have direct reasons to believe that CNE processes explain some complexity in those technologies. Indeed, much of the organization of contemporary technosociety is based on Boolean networks, built up using unsupervised methods,¹⁶ so CNE may explain a portion of the complexity in technological arrangements.

Whenever parts or processes are added to systems (biological or technological) with the only requirement for their perpetuation being that they suffice for some task X (are not eliminated by purifying selection for X), interactions between new and existing parts can produce essential dependencies between parts—for reasons having little to do with X. Kitcher's (1993) example of a screw which accidentally contributes to the overall workings of a machine is such a case.

It is possible that you do not know everything about the conditions of operation of your machine. Unbeknownst to you, there is a connection that has to be made between two parts if the whole machine is to do its intended job [X]. Luckily, as you were working, you dropped a small screw into the incomplete machine, and it lodged between the two pieces, setting up the required connection.—Kitcher (1993).

Kitcher intends this example to speak in favour of an account of biological function; I remain ambivalent about whether parts generated by CNE have proper functions. Regardless of their functional designation, it is clear that the capacity for CNE to essentialize initially non-advantageous parts has wide ranging implications, both in biology and technology. Moreover, technologies provide especially compelling examples of what CNE can accomplish.

Consider milking dairy cows. Automated milking has become a staple of dairy farming. Suppose a farmer B operating a farm S must accomplish M, daily milking their cows. Suppose B is just able to do this by hand, given their resources and other necessary task constraints. Now, (1) suppose we introduce A, an automated milking machine. A+B should initially be able to extract more milk or at least accomplish M. However, since A is automated, it presupposes any loss in the ability of B to M. At this point B may discard A with no net negative cost. Over time, (2) B is free to change their practices within S once assisted by A. Suppose they do this by partitioning their time differently, so that they devote less to M and more to some other task T, perhaps the upkeep of another farm animal. After this change to their practices has become entrenched by the addition of many more changes like T, (3) B cannot

¹⁶ Large networks built for some purpose but without supervision naturally tend to contain a large number of features that are unnecessary or redundant for that purpose (Mozer and Smolensky 1989). Contemporary artificial neural networks for example tend to grow large, complex, and difficultly understood, unless something is done to them to make them less so (see Erasmus et al. 2020, Sect. 4.1).

discard A without incurring net negative consequences, since they cannot accomplish both M and these other tasks without automated assistance from A.

In this and similar cases the automation technology A has been essentialized by subfunctionalization¹⁷ of manual labour B, and the techno-system S has increased in dependent complexity by CNE. Although A may have been initially advantageous, after reduction in function of B (by also performing some other task T), the persistence of A need not be explained entirely by that advantage. Indeed, there are ways to intentionally remove or compensate for unintentional loss of automation technologies. Human techno-societies do not need to wait around for complexity-reducing changes to occur by natural mutation, as organisms do. However, when automation technologies have a strong pre-suppressive effect on the redistribution of resources elsewhere in the system then their loss is costly. This makes the intentional reversion to prior, less complex, dependence relationships with these technologies unlikely, or less likely than their continued maintenance.

It is difficult to assess exactly how much of modern techno-society owes its continued existence to dependencies generated by CNE. Perhaps, on the extreme end, the entire edifice of technology might be something that (1) presuppressed or facilitated the loss or reduction of our non-technological capacities, (2) constructed forms of human-technological interaction, and (3) results in complex forms of our dependence on technology (Kaczynski 2016). Perhaps CNE is rarely involved in technological change. I take this section to show that CNE is a good background evolutionary theory in which to situate analysis of the origin of cultural level complexity in some cases.

Conclusion

This essay contributes to the extension of the explanatory scope of constructive neutral processes by examination of cases that sit at higher levels of biological organization. While past biological theory and philosophy has focused on CNE as an evolutionary process important in molecular biology and microbiology, this essay provides cases from physiological ([Neutral evolution of multicellular complexity](#)), ecological ([Neutral evolution of multicellular ecological complexity](#)) and cultural-level complexity ([Neutral evolution of cultural-level complexity](#)).

Here CNE is characterized as a general evolutionary phenomenon satisfying three conditions on the fitness effects of interactions between two sorts of entities (Sect. 1). Once characterized generally and independently of its molecular beginnings, a new variety of examples can be seen as cases of CNE. The examples discussed here are a heterogeneous collection, including duplicate organs, localization of functions, maintenance of vestigial traits, loss of biosynthetic capacities, obligate parasitism, myco-heterotrophy, automation technologies, institutional division of labour and Boolean networks (Sects. 2–4). They were intentionally drawn from different domains of biology, and a rich diversity of cases is what we should expect from an evolutionary process that can take place across levels of the biological hierarchy.

¹⁷ This is properly the closely related process of “subneofunctionalization” (see Lynch and Force 2000).

The rise of molecular biology has encouraged a growing appreciation (and justifiable scepticism) of the use of molecular evidence within more traditionally organismal or ecological investigations. Many are also coming to appreciate that biological theory developed in the context of molecular biology can be brought out and used fruitfully at higher levels of organization in biology (see Gregory 2008). Of particular importance is the neutral theory of molecular evolution (Kimura 1983). The origin and development of CNE within molecular biology was spurred by the important realization that neutral evolution could not only result in an increase in *diversity*, but also in an increase in *essential complexity*, in the number of parts maintained by purifying selection. The mechanisms and processes leading to this neutral construction of complexity are likewise a diverse lot—gene duplication and divergence has not *prima facie* much in common with RNA editing. But this diversity of molecular processes can be helpfully condensed into the tripartite characterization of the conditions for CNE (e.g. Stoltzfus 1999; Brunet and Doolittle 2018; Sect. 1). Once characterized with sufficient generality, CNE is another product of molecular biology that can helpfully be brought into applications within organismal biology and ecology.

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