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1 Executive summary

Evolutionary dynamics is a general mechanism through which nature develops and maintains highly complex adaptive systems. In the first part we review research in how far this mechanism can also explain the human brain's remarkable development and functioning. There is new neurophysiological evidence on structural plasticity as well as new models of learning that show how hierarchical representations of complex actions might evolve, mutate and recombine in the brain. There are also new models of adaptive language processing and problem solving that provide interesting windows on how evolutionary dynamics could be relevant for explaining higher order mental functions. All this raises many fascinating open questions and exciting challenges that we should tackle now in order to understand the full potential of evolutionary neurodynamics to explain our uniquely human capabilities.

The ways in which brains solve problems remain elusive. Two mechanisms are important. First, associations amongst neurons build up by reinforcing synapses that spike together given a stimulus. This predisposes the response to similar stimuli, and emphasizes the role of learning in creativity. Second, given the multifactorial space of possibilities, most random variants over a pattern previously learnt are extremely unlikely to produce a sequence of spikes that approaches a better solution. Hebbian learning addresses the first mechanism whilst evolution in an adaptive landscape addresses the second one. In the second part we investigate a hybrid theory that considers both types of mechanisms. A population of neurons evolves to maximise fitness, while at the same time, it learns the properties of the adaptive landscape. This mechanism results in the maximum speed of response, and reaches a peak with virtually no "mutational" load. This is a possible explanation of how the brain can reach solutions in a vast landscape of possibilities in short time. We also study the effect of distinct neuronal network topologies on this process, and find that highly connected networks provide the best response. By employing modifier allele theory we also study synaptic plasticity. That is, the change in network topology driven by long-term learning. By imposing fitness costs on the number of neuronal connections we constrain the system to evolve topologies that maximise learning with a possible minimum of neural connections.

Cognitive processing in the brain may occur in a massively parallel way. Parallelism is necessary (though not sufficient) for effficient evolution. Evolution via mutation and selection provides a very efficient search method over a rugged and complex fitness lendscape. It has been suggested multiple times that the brain solves certain highly complex problems, mostly during insight and language learning, in a parallel way that utilizes such Darwinian dynamics.

A model is presented in the third part that will allow comparison of evolutionary search algorithms and theory-search during human learning (as hypothesized by e.g. Tenenbaum). The model simulates Darwinian search for tRNA structure and sequence over a population of random RNA molecules. The search is restricted by a limited set of "servers" (evaluators) that could fold RNA sequences and assign fitness to them according to the folded minimum free energy structure being closest to the cloverleaf of the tRNA. The inherent parallelism of the population and the architecture of shared servers provide an efficient search method over a hierarchical fitness landscape that performs better than a population of independent stochastic hill climbers of the same size. Relationships to theory-search are discussed.

2 Hebb, Bayes and Darwin: Evolutionary neurodynamics (an Insight manifesto)

Chrisantha Fernando, Michael Öllinger, Luc Steels, Gábor Tamás, Eörs Szathmáry

In this paper we examine the idea that Darwinian dynamics possibly plays a crucial role during development of the brain and in cognition. If this idea holds, then cognitive development consists of, at least partly, the evolutionary origin, maintenance and elaboration of different coevolving populations of neuronal representations and their associated support structures in the brain. This evolution, as evolution by natural selection in general, is thought to generate complex adaptive solutions through cumulative selection. This idea is by no means new: it can be traced back to some passages in the classical work of William James[1], and has been explored in the neurobiological context, especially by Changeux[2-4] and Edelman[5]. There are other sporadic attempts to explore this idea[21-24], but they have failed to root themselves deep enough in neurobiology and cognitive science. There are three related questions that we wish to address here: Why are we dissatisfied with the older, allegedly 'Darwinian' approaches? What makes us believe that a fresh start is not only welcome, but also timely? How would this approach change our understanding of higher cognition and thinking?

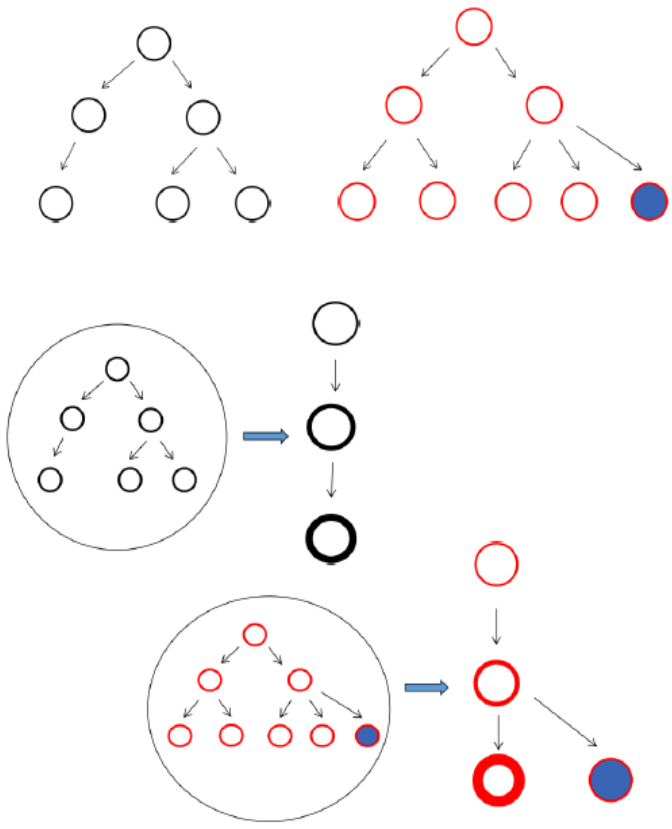


Fig. 1. Classical and compressed units of evolution

Our analysis is structured as follows: First we explain critical features of evolutionary dynamics that we think are relevant for a new approach to the brain. Then we survey possible mechanisms by which selection of heritable variation at various timescales could contribute to adaptive brain function. We consider then the examples of Bayesian inference, reinforcement learning, language development and insight problem solving, in which an evolutionary component is either already apparent or at least covert. We close by outlining a research programme that might lead to the success of a truly Darwinian view of cognitive processes in the brain.

2.1 Essential evolution: natural and artificial

It is instructive to start with the criteria for evolutionary units as summarized by

Maynard Smith[6]: units of evolution must multiply, show heredity and variability (meaning that heredity is not exact; Fig. 1). If among the hereditary traits there are at least a few which affect the chance of survival and/or reproduction of the units bearing them, then in a population of such units, evolution by natural selection can take place, and possibly lead to complex adaptations. Note there are quantitative conditions that must be met, e.g. small selective differences result in adaptive evolution in large enough populations only. It is striking that essential Darwinism can be summarized this shortly. The main message is so simple that some find it difficult to understand. Note that in this formulation there is no reference to any particular level of organization, which we regard as an asset. IF the conditions are satisfied, THEN a Darwinian dynamic can unfold. Of course Darwin was mostly concerned with organisms (he could not know about molecular replicators or genes, for example), but we today are not so restricted. Evolutionary thinking has been applied with varying success to almost anything, from molecules and algorithms to cultural items (memes) and even cosmology. We shall return to the example of the adaptive immune system below.

It is important to spend some time on aspects of search that an evolutionary mechanism can explain. Evolutionary dynamics is particularly effective at finding good solutions in very large combinatorial spaces. This becomes clear when looking at two different search procedures for chemical functionality: combinatorial chemistry[7,8] or in vitro evolution.[9,10] The former works if the combinatorial space is small enough and one can perform an exhaustive search, meaning that all possible molecular sequences of a certain size can be synthesized, functionally tested and selected. But this method does not work well with polymer molecules of even modest size. There are 20^{100} possible proteins composed of 100 amino acids, which roughly equals 10^{130}. Only a tiny fraction of these possible structures could be realized using up all the known available matter in the Universe[11]. It is true that many variants are as good as others, but such selective neutrality merely reduces the problem of search space size from hyper-astronomical to astronomical in the best case. *In vitro* evolution, such as the SELEX procedure, uses replication with errors and recombination. It works with population sizes around 10^{10} in about a dozen generations but can nevertheless generate catalytic RNA molecules (ribozymes) with pre-determined function.

It is noteworthy that Darwin got his idea partly from artificial evolution, namely animal breeding. Various types of evolutionary algorithms are also examples of artificial evolution, and arguably the adaptive immune system is also a kind of breeding with goal functions set by the breeder (the organism). This observation is important. In artificial evolution one can apply component processes and selection schemes that cannot happen in the wild because of constraints on either the genetic system or selection. For example, one can use unconventional mutation operators or unnatural selection schemes (such as elitism, whereby some of the best individuals are copied into the next generation unchanged). A further important difference is that in the wild whole distributions of organisms survive, while the breeder can just throw away what he or she does not like to propagate.

Let us take a look at a didactic version of breeding from the point of view of population dynamics. Begin with a number of animals that fill a stable of *N* slots (the size of the population). A subgroup selected according to the breeder´s criteria is selected for breeding, and the rest of the individuals are removed from the stable. Empty slots are filled up with offspring of the breeding

subpopulation. Thus individuals *compete* for leaving offspring in the next generation, and slots occupied first by inferior individuals are populated by offspring of the superior ones later. From the slots´ point of view, there is *information transfer* from slots with good content to those with bad content, and the bad content is erased. From the selected individuals´ point of view, information transfer is mediated by *inheritance*. Recombination and mutation generate *hereditary novelty* in the system, and the novel variants also enter the competition. All this happens in a population *in parallel:* thus we can summarize that the Darwinian dynamic rests on parallel, competitive search with information transfer and hereditary variability[12]. *All these components are necessary to have the full power of evolutionary search for complex adaptive solutions*.

There is a variant of the basic Darwinian logic (Fig. 1a) that qualitatively preserves the essential feature of evolutionary search leading to cumulative adaptation (Fig. 1b). First of all, there is in general *no need for multiplication*, but there is a need for strengthening or weakening in some measure the different variants according to fitness criteria. Note that strengthening requires autocatalysis (leading to growth), but not necessarily a copying of replicators at the level of the strengthened structure, so that they would become separated in physical space. It is only when *a novel variant* is generated that copying must happen: information from the source is transferred to the new unit with "mutation". Applying the famous definition of information: "the difference that makes a difference"[13], it is crucial to have a distinct representation of the "mutated" part; the invariant part can be shared with the old unit, provided the old and new pieces of information can be evaluated for fitness effects independently (see the path evolution algorithm below).

It is important also to consider the distinction between units of selection and units of evolution[6]. Crucially, the former type of unit shows heredity but not variability (the production of novel variants). Selection acts on the variation that is provided by the initial conditions. This way the population ultimately settles down to some attractor (such as a stable distribution of types), which is the "end" of selection. We explore the hypothesis of evolution in the brain do exist.

The seminal works by Changeux[2-4] and Edelman[5] were the first attempts to apply evolutionary thinking to brain dynamics. However these are examples of selection, not full open-ended evolution[12, 14-17]. In Changeux´s classic picture there is overproduction of neurons and connections in development, out of which a considerable fraction gets eliminated according to functional criteria[4]. This view is valid and important, but one is missing the ongoing generation of novelty from this picture. Or could it be that the initial variation in the population is sufficient to solve any problem? Does moulding of the brain follow the 'algorithm' for sculpting given by Michelangelo, namely pruning away from the block of marble everything that does not fit? Note that apart from the required expertise, it is indeed true that the statue could be thought of as embedded in the marble block: production is by elimination (Fig. 2). This is made possible by the fact that the block has no holes in it: it is as dense as crystal structure allows. The brain is far from that: even transient redundancy around year two in child development is very far from complete overall connectivity. Globally, one can say that there is sparse activation (spiking) in an already sparsely connected network[18] (apart from local networks, e.g. Ref. 19). It would thus be very surprising to find everything in the initial population of pre-representations that would be useful later in the life of the animal. Developmental overproduction and subsequent pruning under functional criteria are established and they are very important components of neuronal development, but we need more: *ongoing production and testing of novel variation*. In the case of humans, cumulative selection of novel variants looks to be massive. As Rossi aptly wrote: "... the main goal of neural adaptation is to allow individual organisms to cope with changing environmental conditions. A closer examination of neural development and plasticity in this perspective actually suggests that the nervous system must be endowed with an intrinsic capability to construct neural circuits so to create novel functional properties, beyond the original set of potentialities. As a consequence, both selective and constructive mechanisms participate to determine neural ontogenesis and plasticity. Constructive strategies, however, prevail over selective ones when the individual nervous system has to face contextual environmental demands" (Ref. 20, p. 154-155). This aspect is related to the *open-endedness* of natural evolution. The environment can always change, which translates into change of the fitness landscape on which the population evolves. New variants must be produced and tested. Without ongoing construction, heritable variation gets exhausted and evolution comes to a halt.

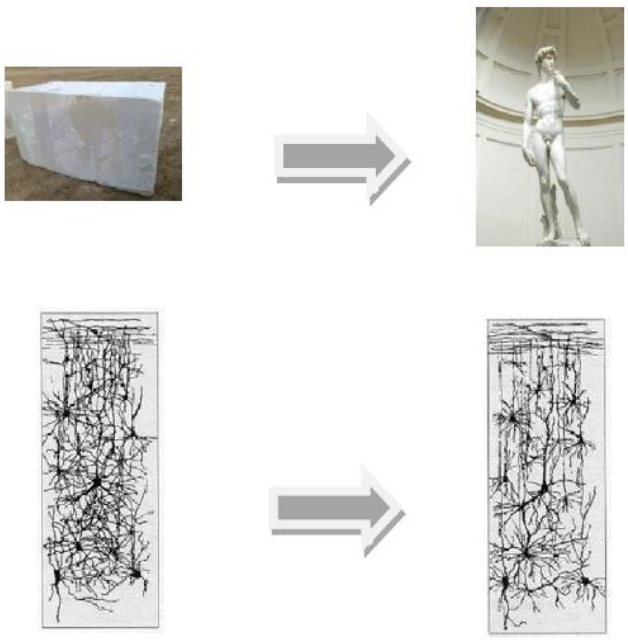


Fig. 2. A view of brain development: functional pruning of transient redundancy

Finally, one should be aware of the limits of evolution by natural selection. Although it has produced a huge number of spectacular solutions, there is no guarantee that it would solve any problem that is in principle solvable, or that it would solve it in reasonable time; actually, theory tells us that this would be impossible for any algorithm. When solutions are found, they frequently (but not necessarily) deviate from the engineering optimum, being often only approximately correct[25]. Such evolutionary optima have lower fitness than "perfect" solutions (i.e. the engineering optima) and the reason for this limitation is in population dynamics: the smaller the difference in fitness between two states, the larger the population size that allows natural selection to "feel" this difference[26]. Since every real population is finite, variants with small enough fitness differences remain "effectively neutral". (Thresholding in neural systems might alleviate this problem. By adjustment of the firing threshold a subpopulation of a small group of neurons may emit as strong a signal as that of a larger one.) Despite all these limitations, evolutionary search remains the "Swiss army knife" of algorithms[27] to look for complex solutions in huge combinatorial spaces in reasonable time and for open-ended criteria. Let us therefore consider further what it can bring us in the brain.

2.2 Hebb and Darwin

The exciting results about structural plasticity of neuronal networks in adult animals calls for an evolutionary interpretation, which goes back at least to the pioneering paper by Adams[28], appropriately entitled "Hebb and Darwin". Adams draws some useful analogies between classical evolution and some brain processes. In particular, he notices that synaptic strengthening is like increase in frequency of a certain allele, whereas the formation of new connections can be regarded as 'synaptic mutation' (Fig. 3). Adams is right in stating that a novel hypothesis, if we expect it to be productive, should generate novel insights and predictions. He boldly suggests that Eigen's insight into the error threshold of molecular replication might be relevant here. Briefly, Eigen calculated that if the mutation rate increases steadily, there is a critical point (the error threshold) beyond which selection cannot maintain information in the system[11]. By analogy, the prediction is that too much synaptic plasticity should melt neuronal information. (It would be excellent to demonstrate that this transition is really sharp, and functional systems might be close, but still safely below, this level of 'synaptic mutation rate'). Structural plasticity seems to be important in finding new solutions, but not for their maintenance, as is proposed in Kilgard's

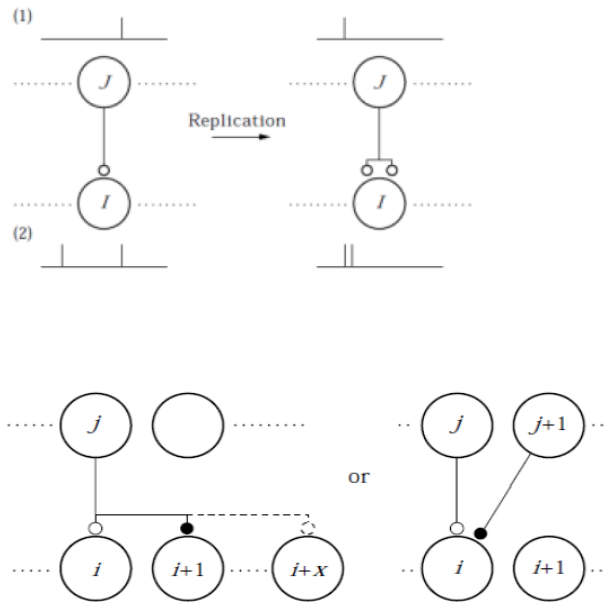


Fig. 3. Synaptic replication (top) and synaptic mutations (bottom), after Adams

cortical map expansion-renormalization model[29]. The proposal that a rather small number of new but enduring synapses are sufficient for memory is important (Fig. 4), consonant with facts, and testable[30]. As Kilgard[31] observes: "The Expansion–Renormalization model is based on principles of Darwinian selection. In ecosystems and market economies, the Darwinian two-step model [i.e., (i) replication with variation; and (ii) selection] is highly effective at generating robust and complex networks" (p. 717).

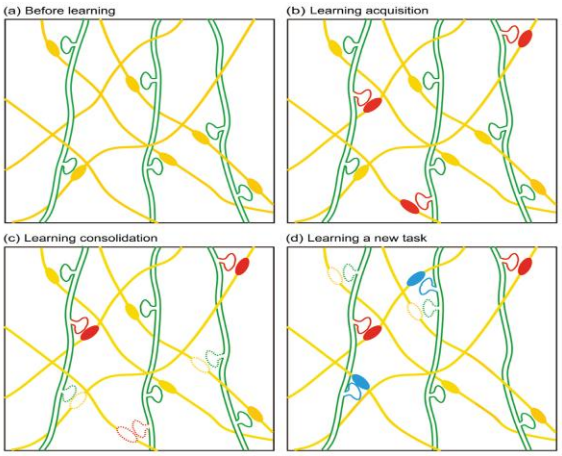


Fig . 4. Expansion and renormalization: an explicitly Darwinian view of synaptic plasticity (Kilgard's view)

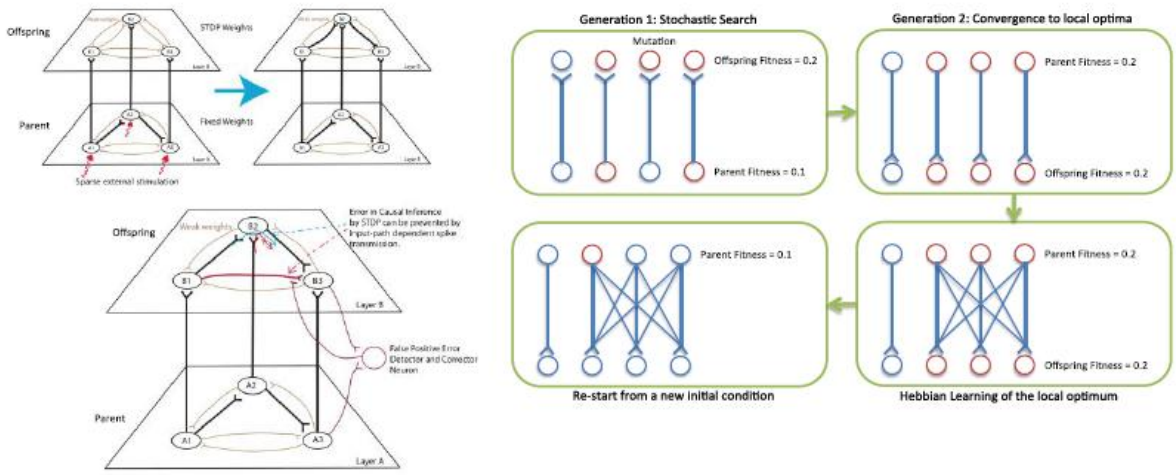
Synaptic mutation and selection operate on the timescale from minutes to days and weeks. Is there a possibility for faster evolutionary neurodynamics? One suggestion, at the millisecond timescale, is the copying of bistable activity patterns from one array of neurons to another (synfire chains)[32,117]. Such a process could realize something like a genetic algorithm provided copying of the patterns is gated so that better candidate solutions are copied into the arrays of inferior solutions

Another possible candidate for a unit of evolution in the brain is a local connectivity pattern (synaptic weights) in a group of neurons (the 'teacher'), which can be copied to a neighbouring one (the 'student'), connected to each other by a topographic map[33]. A student network would then inherit the weights of the original network by causal inference, see Box 1a. Synaptic mutation and selection operate on the timescale from minutes to days and weeks. Is there a possibility for faster evolutionary neurodynamics? One suggestion, at the millisecond timescale, is to copy bistable activity patterns in an array of neurons to another (synfire chains)[32], see Box 1b. Such a process could realize something like a genetic algorithm provided copying of the patterns would be gated so that better candidate solutions are copied into the arrays of inferior solutions. The proposed mechanisms require Hebbian learning, spike-time dependent plasticity (STDP) and gating. The copying shown would naturally occur with a certain error rate, so hereditary variation, on which selection could act, would be guaranteed. It is in this context that a remarkable synergy between Hebbian learning and replication-based evolution has been demonstrated. Whereas in genetic replication the identity of the nucleotide in the copy is influenced predominantly by the nucleotide facing it in the template strand, such a constraint does not apply in neural tissue. In short, for "neuronal replicators" the mutation matrices become evolvable. This effect has already been shown to confer a distinct computational advantage on the neuronal implementation, relative to a classic genetic algorithm[16].

One of the reasons why people may feel uncomfortable with the idea of evolutionary neurodynamics is that neurons do not reproduce. But, as shown in Box 1, patterns of activity and connectivity might reproduce. Another objection could now be raised: especially the mechanisms mentioned above look too much like a mechanistic (and low-dimensional in the neuronal context) analogy of nucleic acid replication. We agree with this criticism (even though these mechanisms

might be realized as special cases). However, the relevant question is this: how could functionally similar mechanisms be *embedded* in realistic neuronal networks? In order to tackle this question, we look closer at one possible implementation, the path evolution algorithm (PEA), proposed by some of the authors[34].

BOX 1a (Left) Two candidate neuronal units of evolution that replicate in a way analogous to DNA template replication are shown. On the left is a mechanism for copying of patterns of neuronal connectivity between neurons. The parental circuit is shown on the bottom sheet. It consists of neuron A1 connected to neuron A2 which is connected to neuron A3. The parent undergoes low frequency spontaneous activity due to homogeneous external stimulation. A topographic map connects the parent to its offspring neurons in the sheet above, which are initially only weakly connected to each other. This mapping transmits the spike-time correlations that arise in the parent to the offspring. The synapses connecting offspring layer neurons are subject to spike-time-dependent plasticity that undertakes causal inference to reconstruct the parental circuit. Of-course some strengthening between B1 and B3 is expected, which could remain at the sub-threshold level resulting in effect in copying with mutation. 1b (Right). Another possibility is the copying of bi-stable activity patterns between arrays of neurons. One array is randomly initialised with an activity pattern which is copied by a topographic map to an offspring array. There are errors (mutations) in the copying of the bi-stable activity array. Both arrays have their fitness assessed. If the offspring has higher fitness it becomes the parent, and makes a copy that overwrites the parent, else the parent makes another offspring. This process continues in the fashion of a 1+1 Evolution Strategy (REF), until convergence at which point a small amount of Hebbian learning takes place between the parent and offspring. The process is then restarted from another random initial condition. This time, copying is biased by the Hebbian off-diagonal weights that have formed which 'remember' previously visited local optima. It has been shown that this mechanism can solve certain deceptive problems in polynomial time that could only be solved in exponential time with mutation only genetic algorithms[16,35].



2.3 Path evolution and its possible embedding in realistic neuronal networks

Imagine a network of nodes with an initial connectivity pattern (Fig. 5a). Nodes are meant here to represent neurons and edges the synapses between them, emphatically, at a very abstract level. We assume that new nodes can be generated with a certain probability (this may simply mean that nodes from a hitherto indifferent part of the network get connected), thus allowing for the generation of more paths (Fig. 5b). Similar processes can generate, for example, a 2-point crossover between existing paths. The phenotype in this abstract model is defined by the identity of the nodes: they could send efferents do different extensor and flexor muscles, for example. The weight of edges is a random variable. A first stimulus spreads probabilistically across the network, at every node the outgoing edge is selected proportional to the weight of that edge relative to the weights of the other outgoing edges. Once a path is being traversed, it is given an eligibility trace, and the phenotype of the visited nodes defines the value assignable to this path. Then a second stimulus is sent, and if the path taken probabilistically is different from the previous one, it also gets an eligibility trace. Then the fitness values (assumed to be linked to some functions) of these paths are compared, and the edges specific to the winning and losing paths are strengthened and weakened, respectively. Weights get normalized and eligibility traces are erased. Mutations and crossovers are generated with fixed probability. Inactive nodes and weak edges undergo decay.

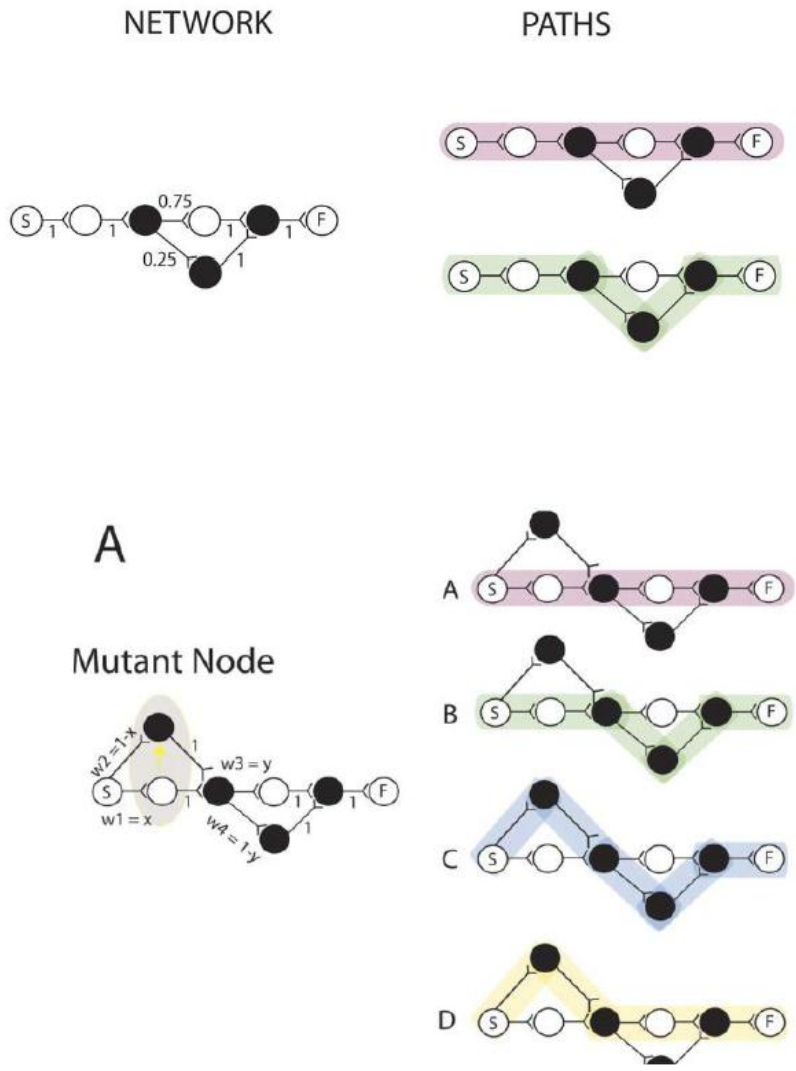


Fig. 5. Elements of path evolution

PEA performs as well as classical genetic algorithms on various combinatorial optimisation problems, and performs significantly better on the very rugged fitness landscape of the HIFF (Hierarchical If and only IF) problem with many local optima (cf. Ref. 35). The population size of the

paths belonging to the network show expansion-contraction dynamics: during search, parallelism is increased in a self-organized way and decreases once the solution has been found. This kind of dynamics has been described in detail to take place in cortical map plasticity[29]. A slightly more neuronally realistic version with spiking neurons, activity-dependent synaptic mutation and winner-take-all lateral inhibition has also been worked out[34], but this model is still more algorithmic than implementational.. Nevertheless, it shows that something like PEA is a powerful computational method for adaptive search in large combinatorial spaces.

Intensive research must be carried out for embedding of PEA in realistic neuronal networks; we propose two possible lines of investigation. One is the embedding of PEA in spiking networks with STDP but without structural plasticity. This may sound awkward since the PEA has been proposed with the latter in mind, but a way to embed the PEA in a structurally stationary network would look as follows. Consider a recent cortical model[36] in which groups of neurons self-organize into assemblies under different kinds of repeated input. A crucial element is stochasticity, whereby different paths can be traversed during repeated runs with the same initial conditions and input. Thus there is a stochastic exploration of different paths, and selective amplification of certain assemblies due to STDP. This suggests that evolutionary dynamics happens already within this model. This idea needs testing; for example by following of transients during which the responsive assembly forms. Visualization of different paths with large-scale population imaging methods during the transient could provide evidence for an embedded PEA. A further experiment could mimic a process of "sympatric speciation", the latter meaning the split of a species into two within the same habitat in evolutionary biology[37]. Suppose the network forms assembly *A* under input *a*. Now we retrain the network with randomly repeated inputs *a* and *a',* where *a'* is similar, but not identical to *a* (e.g. two similar, but recognisably different variants of the same tune). Two corresponding assemblies *A* and *A'* will arguably be formed. If the two assemblies emerge by some form of splitting (division) of the original assembly A, then the speciation analogy holds and this would strongly support evolutionary neurodynamics. Alternatively, should *A'* self-organize somewhere else, essentially unrelated to assembly *A,* then this we would find discouraging.

A test of PAE should also be carried out using a neuronal model such as SORN[38,39], involving also structural plasticity, essentially along the lines described in the previous paragraph. An obvious extension is the examination of the role of embedded PEA in combination with reinforcement learning (see below). If the underlying dynamics turns out be Darwinian, reward would provide the appropriate fitness landscape, on which the transitional assemblies would climb. It is possible to use any of the dopamine-mediated temporal difference error signals from in the domain of reinforcement learning to define the fitness of path-based units. We note that evolutionary assembly dynamics governed by reinforcement would establish a unit of selection that is definitely above the level of "selfish synapses" that are programmed to undergo strengthening if the rules acting locally permit[28,53]. It is a major issue in evolutionary biology how replicator dynamics at lower levels (e.g. genes) does not disrupt higher level units (e.g. cells). Egalitarian mechanisms (such as Mendelian segregation) have repeatedly evolved that keep internal competition at bay[40,41]. Eligibility traces would mark synapses that could systematically and functionally be linked together:

the set of synapses thus bound together would be analogous to genes sitting on the same chromosome.

2.4 Bayes and Darwin

There are two striking quotes: "Inductive inference is the only process known to us by which essentially new knowledge comes into the world", from Sir Ronald Fisher[42]; and "The theory of evolution by cumulative natural selection is the only theory we know of that is in principle capable of explaining the existence of organized complexity", from Richard Dawkins[43]. Given the fact that organized complexity represents knowledge about the world, are we dealing with two different mechanisms or only just one? Work by Shalizi[44] and Harper[45] argues for at least a strong mathematical isomorphism between these two processes. In fact it is not counter-intuitive to think of different replicators in the population as alternative hypotheses for success across generations in the given environment; in this case it is the sampling of the fitness landscape that provides the evidence whereby one arrives at the posterior distribution of replicator frequencies. Fig 6 shows that this relationship is remarkably deep. This is impressive, but it is selection, and not yet evolution! Evolution comes into play when we are interested in the innocent-looking questions: where do alternative and novel hypotheses come from and how does the brain search among them for better ones?

$$P(H_i \mid E) = \frac{P(E \mid H_i)P(H_i)}{P(E)} \qquad x'_i = \frac{x_i f_i(\mathbf{x})}{f(\mathbf{x})},$$

Bayesian Inference	Discrete Replicator
Prior Distribution $(P(H_1), \ldots, P(H_n))$	Population state $x = (x_1, \ldots, x_n)$
New Evidence $P(E\|H_i)$	Fitness landscape $f_i(x)$
Normalization $P(E)$	Mean fitness $\bar{f}(x)$
Posterior distribution $P(H_1\|E), \ldots, P(H_n\|E)$	Population state $x' = (x'_1, \ldots, x'_n)$

Fig. 6. Comparable Bayesian and selection dynamics (Harper, 2010).

In this context we remind the reader of combinatorial chemistry *versus in vitro* evolution. If the combinatorial space is modest and the selection criteria do not change, any generative mechanism can do, and a simple brute force search process (such as greedy search) will also do. As we learnt from the chemical example, efficient search in large spaces will require something like a genetic algorithm, also utilising recombination, to arrive at reasonably good solutions in reasonable time.

Bayesian approaches have proven tremendously successful in explaining learning in various contexts. Recent examples include, among others, concept formation and theory construction. Remarkably, essentially the same formalism can describe finding the right kind of theory and within this kind the right model that fits the data[46,47]. Such hierarchical models are very impressive, and we concur that they conceptualize the problem to be solved nicely at the computational level. Due to computational limitations of real organisms the authors suggest that the hypothesis testing is done by a sequential Markov model[48], which is an admittedly cumbersome and slow search, and does not scale well with the number of dimensions. As they write: "these algorithms are slow, unreliable,

and unsystematic (indeed often random), but with enough patience they can be expected to converge on veridical theories" (Ref. 48, p. 16), and "*Moving forward, a broader range of algorithmic approaches, stochastic as well as deterministic, need to be evaluated both as behavioral models and as effective computational approximations to the theory search problem for larger domains.*" (p. 44, our italics). We agree, especially with the second sentence, and suggest that one of the alternative stochastic search dynamics to be evaluated is a kind of evolutionary dynamics, since we expect it to reduce the degree of slowness and unreliability.

The crucial elements of symbolic representation, some form of generative mechanism and a "knowledge landscape" (that may be often rugged with several local optima) of the hierarchical Bayesian approach[48] are shared with our evolutionary interpretation. In the latter case the landscape becomes a fitness landscape, the search is evolutionary. Local search would rest on mutations, whereas escaping from local optima would be made possible by finite population and recombination. Incidentally, we see recombination, in line with Monod, as a major source of evolutionary innovation in a space of ideas of all sorts[50], as have other authors[106]. Ullmann et al. in their Bayesian framework propose that "Our algorithm proposes variants to the current hypothesis by replacing a randomly chosen part of the theory with another random draw from the probabilistic generative grammar for theories (that is, the prior over theories)" (Ref. 48, p. 17). Notice that this describes recombination. But we suggest that recombination between hypotheses *at the same level* can also be very rewarding, this is in fact what happens in biological evolution; we shall see a linguistic case below. It could also be one of the mechanisms of transfer learning between different domains.

2.5 Evolutionary tools in cognitive architectures

Development of behavioural patterns in individuals has the crucial component of trial and error. It has been repeatedly noted that Skinnerian operant conditioning and natural selection are formally isomorphic[6]: alleles are to fitness as behaviours are to reward. It is not surprising that a replicator-based formalism for reinforcement learning has been suggested[52]. However, such general isomorphism is of limited utility in making predictions about the capabilities of specific learning systems. Consider the case in biology that whilst DNA was discovered in 1953 we still only have a limited understanding of the function of most DNA. The isomorphic problem is as follows. If evolutionary neurodynamics happens and neuronal replicators exist, how could they operate within the cognitive architecture of the brain and what extra functionality could they provide? The question is a rather hard one because we do not yet understand the cognitive architecture of the brain. We emphasize again (cf. Ref. 12) that it is one (albeit important) thing to cast synaptic function[53] and reinforcement learning in very general selectionist terms[54], and it is quite another to consider how units of evolution could contribute to learning and cognition with their full capacity. In this vein, at least three areas exist in which evolutionary neurodynamics may be expected to contribute to a cognitive architecture.

i) *Evolutionary neurodynamics may allow the hierarchical representation of complex actions to evolve, mutate, and recombine in the brain.* Compositional and hierarchical action representation

has been studied both in reinforcement learning[55] and in neuroscience[56], and in both domains the question of how an unlimited number of complex actions, especially for tool use[57], can be generated and flexibly recombined remains a mystery. Both robotic control problems and human experiments lend strength to the concept that actions are learned in conjunction with the goals to which they are directed[58,59].

ii). *Evolutionary neurodynamics may facilitate the generation and selection of inductive models of the world*. There is too much raw sensory data to model and predict, as evidenced by the surprising results of change blindness experiments in which for example a gorilla can walk in full view in between a group of basketball players and not be noticed by an observer[60]. We model, predict, and experience only a very sparse subset of our raw sensory input. What determines this subset? Thinking about the brain from an evolutionary neurodynamics perspective allows us to take a more sophisticated approach to this question: the subset is determined by the constraints on generation of models and the criteria for model selection. In terms of this approach fitness cannot simply be achieved by minimizing prediction error[61]. If this were so then models of trivial, easy to predict events would dominate the brain. A variety of other model fitness criteria are suggested by work in intrinsic motivation, e.g. prediction progress[62], compression progress[63], empowerment[64], and predictive information [65]. Conversely, action selection may be carried out to improve model learning, for example in a recent robotic simulation it was found that the best kind of motor babbling is that which is likely to produce most disagreement between predictions in a population of models[66]. Fisher's fundamental theorem of natural selection states that the rate of increase in fitness of any population at any time is equal to its genetic variance in fitness at that time[26]. This suggests a very general (tentative) intrinsic motivation-like meta-heuristic for neuroevolution: allocate more neuronal resources to populations with higher standing fitness variance, because these are predicted to improve the most.

iii) *Evolutionary neurodynamics may provide a powerful ensemble learning method for boosting supervised and unsupervised learning processes taking place in the brain*. It would be foolish to use evolutionary methods where the desired targets of a function are already known, or where an unsupervised learning algorithm such as Hebbian learning, or Self-Organising Maps are effective. Allowing multiple models to exist that compartmentalize and segment tasks, permits weaker individual models to be combined in an open-ended manner. The advantage comes in the coupling of efficient methods of local search (effectively a kind of Lamarckian directed variation, such as the delta-rule[107] with the evolutionary processes capable of stochastically shuffling information between simultaneously maintained populations of solutions, and improving this shuffling by a process known as the evolution of evolvability[67]. It is exciting that the brain has far more capability for learning to structure exploration than genetics does. The use of Hebbian learning and more sophisticated methods such as deep belief networks[68] to learn to bias 'mutations' so that a variant is more likely to be fit is probably a core feature of evolutionary neurodynamics. In short, a role of Evolutionary neurodynamics is to make blind but intelligent guesses that channel powerful local learning methods through specific paths of problem domains.

2.6 Can language learning be viewed as an evolutionary system?

We believe the development of language in humans offers a window on evolutionary neurodynamics at work. Language learning results in a complex representation and communication system that shows cumulative adaptation for communication. It takes several years for children to develop this competence[100]and it keeps expanding and adapting throughout adult life[101]. In this process, combinatorial construction and feedback through communicative success play a crucial role. There is no general agreement among linguists how to describe language in detail and there is no consensus on how language gets processed by the brain, but we suggest that for linking language to its biological foundations, linguistic theory has to meet a number of criteria, such as (i) account for linguistic variation underlying the fluid and adaptive nature of language in populations and within individuals; (ii) offer a computational account how language learning and use are carried out by individuals; (iii) scale well with respect to the true complexity of language in realistic communicative situations.

The theory and the computational platform of Fluid Construction Grammar (FCG) is an attempt at fitting the above criteria[102]. FCG is a symbolic-computational model of language processing and language development. FCG follows a trend in current linguistics to use constructions as the core unit of linguistic knowledge[103]. A construction implements a set of constraints on well-formed meaningful utterances. For example, the causative construction regulates how to express that a causing agent is making another agent do something (as in "Eörs made Chrisantha burst out laughing"). The construction constrains the sentence structure, the verb sense ("make"), and the case roles of the participants. In many instances, a construction also constrains some of the morphological and phonological properties of the utterance and incorporates discourse issues. The construction inventory of a typical language user is estimated to contain at least 100,000 constructions[115], ranging from lexical constructions constraining the use of words to very specific idiomatic or ready-made constructions and then more general ones (such as the causative construction). Some constructions are in competition with others, either because they express similar meanings in different ways (e.g. "burst in laughter" versus "burst out laughing"), because the speaker is still learning the language and therefore not yet sure how something is expressed, which implies that he has to store competing hypotheses, or because there is genuine variation in the population and speakers have to be able to recognize them. Empirical studies of language change and language learning show that populations and individuals tend to converge, retaining the constructions that have most communicative success, require the least cognitive effort, and provide adequate expressive power[104]. All this is consistent with the hypothesis that evolutionary neurodynamics underlies the language faculty. Although many details, particularly the neural implementation, are not yet worked out, current computer simulations[102] give already clear confirmation that this hypothesis is a viable track.

Constructions and transient structures. A transient structure in FCG contains all information assembled about an utterance (semantic, syntactic, etc.). In comprehension, the initial transient structure contains information about the surface form of the utterance itself (words and their ordering and intonation) and constructions add partial descriptions until the meaning could be reconstructed. In production, the initial transient structure contains the meaning to be expressed

and then constructions add partial descriptions until the form of the utterance is completely determined. Each construction has a score reflecting the success of the construction in previous language interactions. Due to the ambiguous nature of language, transient structures can often be expanded in multiple ways, leading to a search space with competition between transient structures, possibly explored in a parallel fashion.

Copying within FCG. In order to so see how and why evolutionary neurodynamics is appropriate, we must first make a distinction between (i) the routine process of applying a construction C to a transient structure T to generate an expanded transient structure T' and (ii) the formation of new constructions.

(i) Applying constructions: C x T => T'. This happens in two phases. First a matching phase where compatibilities are tested between C and T and then a merging phase in which the elements of C which are not in T are added to T to yield T'. Before merging, copies of T and C are made. A copy of T is needed because the original may possibly merge with other constructions. C has to be copied because all internal variables (= open slots) need to be made unique and elements of the copy of C are used to build T'.

(ii) Creating new constructions. New constructions are formed by abstraction from transient structures or by modifying or combining existing constructions. The latter implies that the old constructions are copied first. They stay around, and the new ones have to compete with the old ones for survival in the construction inventory.

The generation of variation through repair strategies. In current models of FCG, new constructions are created based on learning/invention strategies. These are executed when the language user encounters missing elements in his own language (for example an unknown word or a new use of a syntactic construction) or failures in communication (for example, inappropriate use of a word). The strategies are very similar to error correction in the genetic system, except that strategies carried out by the speaker or hearer *create new constructions or change existing ones.* Repair strategies are 'smart' and driven by concrete cases. They are often based on re-entry (i.e. re-producing a sentence that was parsed from input or re-parsing a sentence that was self-produced). Some of the different repair strategies are:

(i) Take a construction and make it more abstract (by introducing variables for some units, leaving out some of the details, etc.).

(ii) Take an existing construction and add additional constraints, narrowing its scope of application.

(iii) Re-categorise existing words so that they get coerced into new functions. For example, re-categorise the noun Google into a verb as in "he googled him".

(iv) Combine a number of constructions into a single construction, possibly leaving out some of the components (chunking).

Thus, in FCG the creation of new constructions is like site-directed mutagenesis, induced by stress (demand). This is rare but not unheard of in the context of bacterial evolution[116], for example, but it is possible and indeed expected to be typical in the case of cognitive development.

Fitness. As mentioned above, communicative success and minimisation of cognitive effort (e.g. damping combinatorial search, avoiding articulatory effort) give the direction of selection to the population of linguistic constructs in FCG (105). Scoring of constructions implements selection

dynamics not unlike that in population dynamics: the score of a successful construction goes up, whereas those of competitors (other forms with the same meaning and same forms with other meaning) go down.

We point out that FCG combines *a kind of replicator dynamics with Hebbian learning* because some new constructions are formed by chunking and these chunks then start to behave as a unit of their own[188]. Note that this is analogous to a major transition in evolution, namely the linking of previously independently segregating genes on a chromosome, whereby competition between the different genes is suppressed as they are "sitting in the same boat"[40,41].

2.7 Insight problems and parallel search

Massive parallel computations followed by slow and sequential processing were shown in the perceptual domain[109]. We propose that similar processes take place during human creativity, which is likely to be the highest human intellectual faculty. Although there is some progress in understanding the underlying mechanism, it is still unclear how novel solutions to difficult problems are produced in the brain. In particular, it remains unclear what causes the transition between having no idea how to solve a given problem and suddenly knowing the appropriate solution. We suggest that evolutionary neurodynamics might help answer this question, by providing a fundamental principle by which novel information can be generated and tested. We suggest that the interplay of parallel and sequential processing in our evolutionary neurodynamics model helps to integrate already existing psychological theories that postulate parallel, subconscious processes[69,70], with evolutionary theories of creativity[71], and neuroscientific findings that coarsely assume generative mechanisms before the moment of insight[72,73]. An optimal solution would be that some representation of a problem and its match to candidate solutions should be achieved with some degree of parallelism. How this could be done we do not yet know, but it has been adapted to the generation and testing of a large body of alternatives and hypotheses, that brings us back to hierarchical Bayesian networks that might play an important role (see above).

We propose to put some limitations of existing psychological theories of insight problem solving in the context of evolutionary dynamics and explore how this might contribute to the solution of these problems. For a number of insight problems it is well known why they are difficult, and that often a representational change is the key element for the solution. For example in the nine-dot problem (Box 2) it is crucial to draw lines outside the given square. A burning unanswered question is what exactly happens before a representational change occurs relaxing self-imposed constraints. One answer to this question might be that upon an impasse *parallel search processes can take place* that generate and test candidate solutions. It is conceivable that these processes might be widely unconscious and potentially will come up with the solution to the problem, before it goes beyond the threshold of consciousness[69,84]. "Insight is sudden, but it is preceded by substantial unconscious processing" (Ref. 85, p. 88). Figure C in Box 2 depicts an exemplary parallel search for the first move of the nine-dot problem.

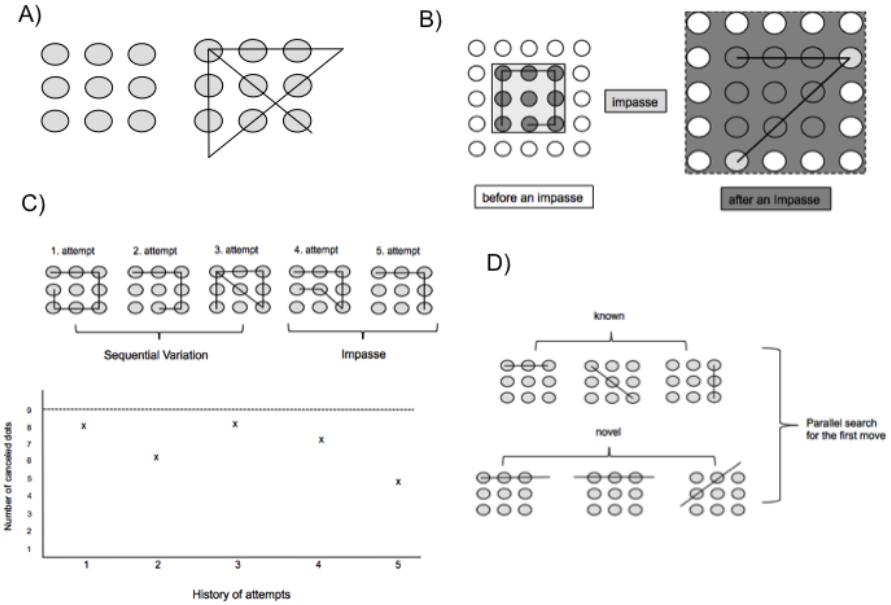
Box 2. The Nine-Dot Problem

The nine-dot problem (Fig. A) is one the most famous and most controversially discussed insight problems[74,75]. The solution of the problem stands often *pars pro toto* for creativity, innovation, and "out of the box" thinking. There are a number of factors explaining the problem difficulty and the peculiarities of the nine-dot problem[76-81-78]. An important role is played by moves that end and turn at non-dot locations, which requires one to overcome the initial perceptual grouping of the given nine dots.

The first computational model that attempted to explain the underlying processes was provided by MacGregor et al.[80]. The authors extended problem space theory[82] to explain insight problem solving. They assume that search guided by heuristics is the key element for solving the nine-dot problem. The first heuristic following a *maximization criterion* that implies in the case of the nine-dot problem to connect as many dots as possible with each line (hill climbing). The second heuristic is a *progress monitoring* heuristic. It monitors the ratio between the remaining dots and the remaining lines for an attempt; e.g. cancelling out three dots with the first line, results in a situation where six remaining dots have to cancel out with three remaining lines. Therefore, the model assumes phases of generation and testing. Variation occurs in this model when problem solvers realize that no further progress can be made with the applied strategy. Now, successful solvers start to search for new and *promising states*. Promising states elicit new solution possibilities that finally support a solution.

Öllinger et al.[81] elaborated on this account and suggested a model of consecutive stages where the applications of heuristics *sensu* MacGregor et al. play an important role before and after an impasse (Figure B). Sticking within an impasse increases the likelihood that a *representational change* relaxes the self-imposed constraints on the search space. After the impasse efficient strategies are necessary to restrict the even larger combinatorial state space.

An evolutionary model can shed light on the different phases of the model. An assumption is that a successful solver starts with a sequential search approach that shows variation in terms of starting points and move configuration (see Figure C) for a hypothetical problem solver, and the fitness-function). The first attempt showed the maximum number of dots that can be cancelled out within the over-constraint search space, namely 8 dots. After a number of attempts the solver is idling around and an impasse is reached. Within an impasse *parallel search processes can take place* that generate and test candidate solutions (Figure D). It is conceivable that this processes might be widely unconscious and potentially will come up with the solution to the problem, before it goes beyond the threshold of consciousness[84].



We stress that parallel search is a broader category than evolutionary search. There is some behavioural evidence for unconscious, parallel search in solving anagram problems[70]. In the particular case, a parallel constraint satisfaction search has been suggested without considering any alternative and its

behavioural testability, however. Parallelism is necessary but not sufficient for evolutionary search. Parallel search is known in auditory and visual processing—the question now is how much parallelism there is in complex thinking, e.g. involving language. This relates to the general problem that there is invariably a serial bottleneck, since behaviour (including language) is serial: one cannot utter several different sentences at the same time, or do several different movements simultaneously by the hand, for example. If there is parallel search, then it is covert rather than overt. One should also mention that in order to search in hypothesis space in parallel, the brain must be able to assess the alternative solutions also in parallel, although the channel for parallel assessment might be considerably narrower than that for the production of variants.

It is conceivable that in humans the right hemisphere is better wired for parallel search possibly facilitated by its cytoarchitectonic features, such as the larger synaptic input fields of dendrites and longer axons[85]. Exactly *because of parallelism, this search cannot be conscious.* The idea that there is ongoing, possibly massively parallel search for insight problems (which include scientific ones, such as the solution of the structure of benzene by Kekule in the form of a ring of carbon atoms[86]) is consonant with the finding that sleep promotes insight[84], but a lot more targeted work should be done to move from the suggestive to the conclusive.

2.8 What makes us human: evolutionary neurodynamics evolves

People have been puzzled by the nature of the apparent gap between humans and the rest of the animal kingdom. Arguably, the emergence of the capacity for natural language was the last major evolutionary transition with a solid background in genetic evolution. Yet, it has been heavily contested what exactly is innate as a result of past selection on genetic variation. Opinions have ranged from an innate universal grammar to a universal language of thought. We cannot analyse this complicated issue in this article, but we would like to state that undoubtedly there is a qualitative change in the complexity of adaptive behaviour from animals to humans, and this change must somehow rest on distinct neurobiological mechanisms ("original resources" in the words of Ramón y Cajal[87]) conditioned by genetic changes affecting the development of the brain. What constitutes the "language readiness"[108] that you apparently do not find in avian and other mammalian brains?

Although we argue that evolutionary neurodynamics emerged in brains before the origin of humans, only the human brain is capable of unlimited heredity. The theory of the major transitions in evolution[40,41] highlighted the facts that (i) novel forms of storing heritable information did appear a number of times during evolution, and that (ii) such evolution typically proceeded from limited to unlimited heredity. Limited heredity means that the number of possible replicator types is much lower that the allowed number of individuals on which selection can act. In the case of unlimited heredity the number of possible types is for all practical purposes hyper-astronomically larger than that of the number of individual in any realistic system. (As an example, think of short pieces of DNA versus genes. Whereas nucleic acids built of say, 10 nucleotides can all be physically realized in parallel , they can carry only limited information. In contrast, genes carry a lot more information but parallel realization of all sequences is firmly excluded; c.f. the previous example of

combinatorial chemistry). Unlimited heredity is necessary but not sufficient for open-ended evolvability. It is in this sense that we suggest that evolutionary neurodynamics, to the extent it exists in other species, rests on limited hereditary mechanisms in those brains. Put differently, the units of evolution in other brains have limited complexity, thus the complexity of representations is also limited.

The next question is whether there is a physiological basis for the capacity of unlimited heredity. Recently, exciting evidence has appeared differentiating human cortical dynamics from that of rats and monkeys. Contrary to animal studies showing relatively high firing rates and infragranular dominance in determining rhythmic cortical activity, assessment of human oscillations using intracortical electrodes revealed a marked decrease in neuronal firing rates and identified a governing role of supragranular layers and weak infragranular contribution[108]. This suggests structural elaboration of the underlying microcircuits and a potentially increased signal to noise ratio in the upper layers of the human cortex. Enhanced anatomical complexity of the human microcircuits has been initially suggested by Cajal[92]. He observed a greater variation in human vs. rodent interneuron types. In addition, a striking increase was found in the complexity of dendritic organization of individual pyramidal neurons at the single cell level in humans compared to primates[109]. Activation of single neurons in the human brain demonstrated a high sensitivity of cortical networks to the action potentials of some, but not all, single neurons[89] and it seems that the human cortex is especially sensitive to perturbations

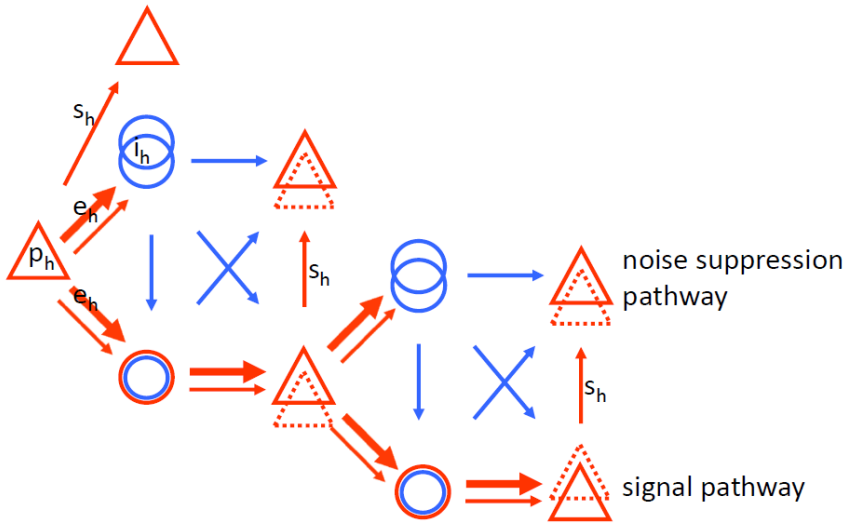


Fig. 7. Some crucial differences in human microcircuits to those of other animals. Potential elements of pathway evolution in human microcircuits. Human-specific increase of variation in pyramidal dendritic complexity (p_h) and number of inhibitory interneuron types (i_h), altered rules for STDP on inputs arriving to pyramidal cells (s_h), and strong synapses linking pyramidal cells (e_h) might contribute to unique features of signal propagation in human microcircuits. Spikes in an individual pyramidal cell (red triangle) trigger postsynaptic action potentials in some inhibitory (blue circles) and some inhibitory/excitatory GABAergic cells (chandelier cells, red and blue circles) through strong synapses (thick arrows). In contrast, single pyramidal cells cannot fire postsynaptic pyramidal cells (weak synapses, thin arrows) and both inhibitory and inhibitory/excitatory GABAergic cells also respond to pyramidal cells with subthreshold EPSPs. Simultaneous triggering of inhibition (noise suppression pathway) and excitation (composed of alternating glutamatergic and GABAergic steps, signal pathway) could increase signal to noise ratio. Pathway evolution might involve groups of pyramidal cells dynamically recruited through repeated motifs of feed-forward spike propagation depending on their membrane potential, GABAA reversal potential and combination of inputs.

triggered by a single cell[110]. In other words, experimental investigation of the synaptic effect of individual action potentials of identified human pyramidal cells revealed complex events triggered in the human neocortical network. Compared to occasional polysynaptic events reported from other species[90], single action potential triggered human event sequences lasting an order of magnitude longer. Importantly, some of these long lasting sequences showed a very precise and repeatable temporal structure unprecedented in recordings studying nonhuman networks to date. Human event series required selective spike-to-spike coupling from pyramidal cells to GABAergic interneurons and resembled Hebbian or Lego-like neuronal assemblies that are proposed to be building blocks in cognitive processes[111,112]. We think the importance for our topic of this finding is that complex patterns can be ignited by minimal regulatory action, which is consonant with what researchers believe about the triggering and application of linguistic constructions. If the cell assembly is the basic unit of "neuronal syntax"[91] then the demonstrated mechanism offers a unique way of linking them. In the footsteps of Cajal, who proposed that the complexity of circuits formed by "short-axon" cells (GABAergic interneurons) increases as with brain complexity in evolution[92] we suggest further that relatively minor differences might have pushed human neuronal network action above thresholds, whereas non-human cortical systems could not cross them. In addition to potential differences in the number and sophistication of cell types, small changes in the magnitude and routing of strong versus weak synapses have a profound effect on signal to noise ratio and spike propagation[93]. Compared to rodent networks human short-term dependent plasticity rules are altered and operate in a wider temporal window due to differences in intrinsic ion channel distributions[94]. Finally, relatively moderate changes in presynaptic neurotransmitter production and postsynaptic alterations in receptor composition or in the recruitment of voltage gated ion channels might prime human patients to illnesses like schizophrenia which are difficult to elicit in nonhuman individuals[95].

2.9 Conclusion and open questions

Evolutionary neurodynamics as a concept is old and new at the same time. It is old because its roots go back to thoughts of Williams James[1]. It is new because it pursues a firmly evolutionary research programme about brain function at various spatial and temporal scales, consistently applies this hypothesis to cognitive phenomena including Bayesian and reinforcement learning, natural language and insight problem solving, and rests on species-specific dynamics of neuronal networks including cell assemblies. We emphasize that we are still at the exploration rather than exploitation stage, but we think that this exploration is very worthwhile. The recent results on structural plasticity are especially encouraging, but there are other highly promising areas for evolutionary neurodynamics. In the best case, aspects of brain function will turn to be more powerful than evolution by natural selection in the wild; a prime example for this perspective is the possibility of evolvable mutation rates by Hebbian plasticity.

We especially draw attention to the application of the evolutionary dynamics to understand the adaptive immune system. The generation and affinity maturation of antibodies has two distinctive features: there is a generative system (as a result of past genetic evolution) and a Darwinian

evolution of the functional products thus generated. Note a few critical features. Not all of the immune system is Darwinian, only an important component of it, which works in synergy with other component mechanisms. Evolutionary dynamics is embedded in a complex network with the associated properties, including immunological memory[96]. The system is open-ended because at least in mammals the antibodies can nearly fully cover the shape space of antigens[97]. In short, evolution by natural selection has reinvented itself in the form of a complex information-gathering and storing device with open-ended search possibilities.

Due to the complexity of the whole problem of evolutionary dynamics in (as opposed to of) the brain, it should be attacked simultaneously at different fronts. Open questions are naturally legion. A few critical open issues are the following:

- What are the most important manifestations of evolutionary neurodynamics, and at what spatial and temporal scales?
- We share the view that concepts and grammatical constructions (among other mental things) have identifiable neuronal representations. Currently various cell assemblies are the best candidates[91] for the physical carriers of these representations. This raises the question whether concepts, hypotheses, rules and policies evolve at this level. Alternatively, does evolutionary dynamic contribute at some lower level, and is the change of the mentioned entities a result of this underlying evolution?
- In organismal evolution the separation of genotype and phenotype is an enabling constraint. Not unrelated to this issue, the division of labour between nucleic acid genes and protein enzymes, along with the emergence of the genetic code, was an enabling constraint[4ö,41]. Is there anything like this in evolutionary neurodynamics? One way for this would be that entities that vary ("mutate and recombine") are "translated" into entities that are tested and do the work. Were such a two-level neuronal representation system active, then the "neural code" would be not one thing but at least two.
- This raises the question of the evolvability of neuronal representations. Imagine a genetic algorithm for making designs for tables. One could encode the length of the legs separately, in which case the legs would mutate independently from each other. Undoubtedly, another coding that would regulate the lengths of legs together would produce more useful (fitter) designs more often. What are the evolvability components[67,98,99] of the units in evolutionary neurodynamics?
- Is the difference between us and other animals, at least in part, due to some crucial differences in the implementation of cerebral evolutionary mechanisms, including that between limited and unlimited heredity?
- Another aspect of evolvability is more subtle, but critical for our case. Natural evolution does not solve predetermined tasks; it finds its tasks by itself: this is in contrast to the area of genetic algorithms. Evolutionary dynamics is very opportunistic: it produces all kinds of variants, some of which turn out to be useful in the given environment: what we see are mostly the success stories. We suggest that evolution within the brain unfolds along similar lines: during the maturation of each brain variants get selectively fixed with opportunistic functions. (In order to see this both the environment and the internal mechanisms must be

sufficiently rich, which is a challenge to modelling.) There are two important constraints, however. The first is the set of innate initial conditions. The second is communication by language. Since mental information can be passed from brain to brain, and this has got survival value (proximately as reward, distally as fitness), language is a mechanism that grossly constrains individual development, and ensures a considerable degree of parallel evolution in different individuals. This is yet another interesting possibility to verify or reject.

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3 The evolutionary basis of neuronal learning

3.1 Introduction

The mechanism through which a brain solves problems remains elusive. On the one hand, associations build up by reinforcing synapses that spike synchronously given stimuli. Without doubt, this predisposes a response to a similar stimulus, emphasizing the role of learning on creativity. On the other hand, given the multifactorial space of possibilities, most random variants of a learnt pattern are extremely unlikely to produce a sequence of spikes that approach a better solution.

This bears some analogies with neutral evolution. Imagine a population that stands at a fitness peak. Suddenly, the optimum fitness value is displaced by, say, ecological factors and the population is left at a neutral, sub-optimal plateau. It will be unlikely that only due to random mutations the population will approach the fitness peak.

In both problems the concept of selection applies. In evolution, selection needs no introduction, and understanding how the interplay between selection and mutations leads to adaptation is one of the central goals of population genetics(Crow & Kimura 1970; Fisher 1958). In neuroscience, the concept of selection is less widespread and less accepted, although not at all absent. Edelman proposed a selectionist framework to brain function(Edelman 1987; Fernando et al. 2012). He noted that selection is essentially analogous to the preferential reinforcement and stabilization of some synaptic patters over others by neurotransmitter rewarding mechanisms (e.g. dopamine).

Edelman's idea, neural Darwinism, is not incorrect. However, it is incomplete if we want to make something of that analogy(Fernando et al. 2012). Neural Darwinism lacks two critical components: the mechanisms for generating the variation over which this selective mechanisms acts, and an interpretation of heredity in terms of neurophysiology. This is at the essence of Crick's criticism, that is, the lack of a unit of selection.

The mechanisms for generating variability are relatively simple to rationalize, and there are many models in the literature that take this aspect as modelling objective in terms of stochastic processes and by drawing analogies with statistical mechanics(Ullman et al. 2012). But it is less obvious, of deeper implications and of far-reaching consequences to realise that a mechanism of "neural heredity", or anything analogous to it can and in fact does exist.

In this work we investigate how reinforcement learning and hill-climbing (i.e. selection) work together to drive the system to the optimum. This is a first formalization of the analogy between neurodynamics and evolution. We will show that for eyes educated on evolutionary biology, the equations that describe the whole process are astonishingly similar to the mutation-selection equations, albeit with a twist. That is, the mutation rates are not constant. Rather, they are functions that depend on the state of the population in a peculiar way. The relevance of this difference is that such a "learnable" mutation rate is able to learn the local properties of the fitness landscape, and direct bias mutations towards the direction of fitness increase. In this way, the joint action of selection and learning facilitate reaching the fitness peak.

We will study how different neural architectures facilitate or compromise evolution, and show (somewhat expected) that higher connectedness results in better adaptation. However, by imposing a certain cost per connection we are able to trade-off the benefits that a highly connected brain brings by the elevated metabolic, physiologic and anatomic costs that this might have associated.

After analysing this first level of the analogy, we will incorporate a pioneering construct. That is, mechanisms of synaptic plasticity that affect the neural network topology. This is a crucial factor since it models the mechanisms behind specific neural architectures, and relates these architectures to the specifics of the process that are being solved.

At the end, we discuss the opposite direction: the "learning basis of genetic systems". Although this can sound preposterous, we will show that this is essentially analogous to the problem of evolvability in quantitative genetics systems (Jones et al. 2007).

3.2 Analogy between neutral evolution and neurodynamics

A simple stochastic model of neuron is the Boltzmann machine (MacKay 2003), where spiking of a neuron *i* follows an update rule of the form

$$P[X_i(t') = 1|\mathbf{X}(t)] = \frac{1}{1+\exp(-E_i)}$$

where $E_i = \sum_j \phi_{ij} X_j$ is the "energy" or current of the input neurons, and w_{ij} are the weights determining the associations amongst neurons, that is, the network. These weights change according to the correlation amongst spikes by a reinforcement model such as Hebb's rule(MacKay 2003):

$$\Delta\phi_{ij} = \lambda X_i \sum_k \phi_{kj} X_k$$

where λ is the learning rate. Alternatively, any other suitable weight reinforcement mechanism can be assumed (e.g. Oja's rule, which has normalised weights; see Box 1). Note that in this formulas the representation of the state of the neurons is X=1 if the neuron fires and X=–1 if it doesn't. This choice ensures that the weights associate all neurons that spike, and all neurons that do not, and at the same time dissociates spiking from non-spiking neurons. The update rule above defines a transition matrix for a Markov chain describing the stochastic change in time of spiking frequency. However, the trajectories that this system can take are directed only by the topology of the network as well as random events.

Box 1: Oja's rule. Hebb's rule is problematic because it allows weight to increase unboundedly. A bounded version, known as Oja's rule is a simple variant where weights are normalized:

where , and the normalization condition is required, namely, , for . In most examples of this article, and unless otherwise stated, we employ a Euclidian norm, α=2.

Retaking the analogy with evolution, we can interpret that if $X_i = 2p_i - 1$, where p_i are allele frequencies at locus *i*, a Markov chain that describes the probabilistic changes in a similar way as above would represent a neutral process. This choice for X ensures that X=–1 when p=0 and that

X=1 when p=1. In particular, the conditional probability $P[X(t') = x|X(t) = y]$ is precisely the substitution rate of allele *y* for allele *x*. For diallelic loci, that conditional probability is precisely the mutation rate. Clearly, in population genetics or molecular evolution these rates are typically assumed to be state-independent, reflecting, for example, substitutions due to copying errors of the polymerases that replicate the genetic material, or other sources of errors that do not depend on the genetic states of the population.

For neuronal dynamics this update rule, which replaces the mutation rate, still describes a process that is selection-free. However, unlike in population genetics model, the update is state-dependent and directional. These two properties of the update rule, together with the reinforcement rule, constitute one of the underlying processes of learning and memory. But, by making use of the evolution analogy, despite the plastic directionality of these "mutation rates", there is no selective process assumed on these models of learning.

3.3 Neural Darwinism revamped

The previous analogy shows that the selection component is lacking in the Boltzmann machine model. If we want to take seriously the Neural Darwinism idea, we must consider selection. In fact, having noted that the update rule is analogous to a mutation rate, what we lack is incorporating the update due to selection. The marginal probability $P[X_i = 1] = p_i$ is analogous to the frequency of allele '1'. Therefore the change in time of p_i is given by

$$\frac{dp_i}{dt} = p_i\left(\frac{w_i}{\bar{w}} - 1\right) + M_i(2p_i - 1)$$

where W_i is the fitness, and $\bar{W} = \sum_i p_i W_i$ the mean fitness. The function $M_i = 1/(1 + \exp[E_i])$ is dependent on the state of the system, and follows directly from the update rule. Written in such a form, the dynamics seem identical to a selection-mutation equation. However, as stated above the update rules *M* are state-dependent, and due to the reinforcement of the weights, it is also changing in time.

Beyond the cosmetic similarity between the replicator equation and neural dynamics, the underlying difference is that the update rule is able to learn the local properties of the fitness landscape. By doing so, hill-climbing towards a fitness peak is facilitated by generating mutations that are preferentially directed towards the optimum.

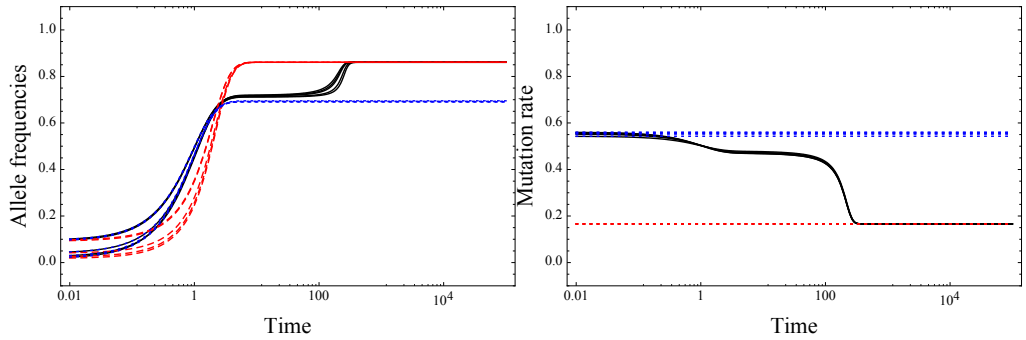

Figure 1. (A) Example of selection-learning dynamics (black lines) compared to standard mutation-selection with naïve mutation rates (M~1/2; blue) and learnt mutation rates (red). (B) Evolution of the mutation rates in time. n=5, s=1, λ=0.01, α=2. Initial conditions for allele frequencies and for initial weights are randomly sampled from a uniform distribution U[0,0.1]. The learning network is fully connected.

In Fig. 1 the dynamics of the neuronal replicators is compared to that of a simpler standard selection-mutation equation. In this case we employ Oja's rule (normalized weights; Box 1), and a directional selection landscape, $\bar{W} = \exp(s\sum_i p_i)$. In general, we assume that $\lambda << \alpha$. For our examples we will keep all factors equal (initial condition and directional adaptive landscape). Two interesting results are conspicuous. First, an equilibrium point between mutation and selection exists. This equilibrium is determined by the properties of the fitness landscape and the learning rule. However, unlike in population genetics, the mutation rate is adaptive and cannot be tuned independently. Curiously, the equilibrium point is independent of the learning rate λ (in as long as this is much smaller than selection). Second, mutation rates that have been learnt in a previous run provide the fastest speed of convergence to equilibrium.

We find that the initial conditions (of both weights and allele frequencies) do not affect the equilibrium state of the system. However, we suspect that this can change under a more complex fitness landscape (we discuss this below).

Paradoxically, we find that mutation rates decrease with the strength of selection, s, and with number of loci, n (Fig. 2). More specifically, we can show that fully connected networks converge to per-locus mutation rates of $\mu \simeq \exp[-n^{\delta}]$, where $\delta = \frac{\alpha - s}{\alpha}$ (note that this implies $0 < \delta < 1$). This is in sharp contrast to polygenic systems under mutation-selection balance, where the genetic load increases linearly with the number of loci(Crow & Kimura 1970). For neuronal replicators the load in equilibrium is $L = ne^{-n^{\delta}}$. Hence for large n the load will decrease quickly with the number of loci, becoming vanishing as $n \to \infty$. Thus, *neuronal population become very well adapted with many loci*. Notice that this asymptotic result depends neither on the learning rate nor on the strength of selection.

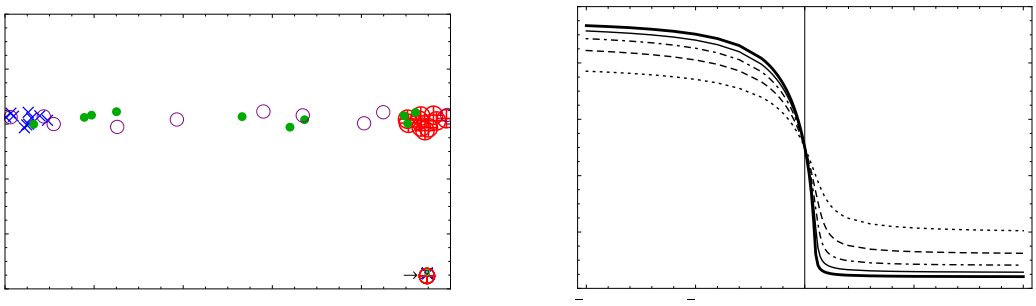

Figure 2. Dependency of the learnt mutation rates on (A) initial conditions of weights and allele frequency, drawn uniformly: p_0~U[0,0.1], ϕ_0~U[0,0.1] (blue crosses), p_0~U[0.9, 1], ϕ_0~U[0,0.1] (red targets), p_0~U[0,1], ϕ_0~U[0,0.1] (purple rings), p_0~U[0,1], ϕ_0~U[0,1] (green dots). (B) Equilibrium mutation rate, strength of selection s and the number of loci; n= 2 (dotted), 4 (dashed), 6 (dot-dashed), 8 (solid), 10 (thick). Otherwise as in Fig. 1.

3.4 Topologies of the neuronal networks

By relaxing the assumption of full connectedness, the equilibrium mutation rates and spiking probabilities become spread to an extent determined by the connectivity patterns of the underlying network . Figure 3A presents some examples of the outcome of evolution using topologies drawn randomly from the Erdős-Renyi model (Erdös & Rényi 1959; Erdős & Rényi 1960) with various degrees. Poorly connected nodes maintain high polymorphisms and high mutation rates, whereas highly connected nodes have frequencies close to fixation and small mutation rates. As a general trend we find that the mean and variance of the mutation rates decrease with the degree of the network and the specifics of the topology don't seem to be highly relevant (Fig. 3B). For instance in Fig. 4 we plot the mean mutation rates from networks with topologies according to Erdős-Rényi, Barabási-Albert (scale free) and small world topologies. The only parameter that seems to matter is the degree of the networks (Durrett 2007).

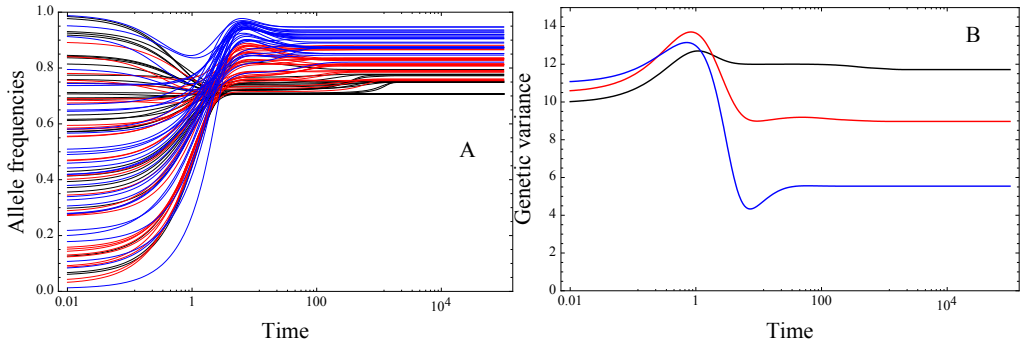

Figure 4. Evolution and learning under differently connected networks. (A) Allele frequencies, (B) genetic variance. Topologies are drawn randomly from an Erdős-Renyi model with degree of 10 (black), 50 (red) and 100 (blue). n=30, s=1, λ=0.01. Initial conditions for allele frequencies and weights drawn from

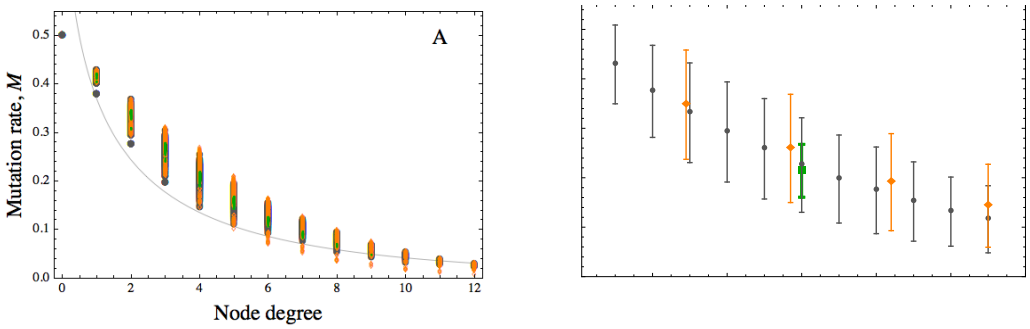

Figure 3. Dependency of mutation rates on the connectedness of a network. (A) Individual mutation rates vs. a node's degree, and (B) mean and spread of mutation rates as a function of the degree of the network for distinct topologies: Erdős-Renyi random graphs (gray, bullets), Barabási-Albert scale free networks (orange, diamonds), Watts-Strogatz small-world networks (green, squares). Each point contains 30 replicas with randomised topologies. The small-world networks cluster has 180 replicas including a range of rewiring probabilities between 0.05 and 0.5 (all have the same degree = 2n=60). Otherwise as Fig. 3.

3.5 Asymmetric landscapes

In the landscape of directional selection studied above there is a single peak where the alleles X=1 are all equally favoured. We first relax such a degree of symmetry by allowing each locus or neuron to have a different weight s on fitness. The interplay between asymmetric landscapes and network learning topologies is non-trivial to anticipate. In flatter regions of the fitness landscape there is less to learn. Also, from mutation-selection models we know that weaker selection allows more variability to be maintained. Do we expect that larger node connectedness will compensate this load, and enhance learning on the flatter regions of the fitness landscape? Or, given that selection is weak, there is no way out from staying poorly adapted because the landscape is "non-learnable" along some directions?

Mean fitness is defined as $W = \exp\left[\sum_i s_i p_i\right]$. We allow negative selective values so that the fitness peak is not necessarily a (1,1...,1), but that it can be arbitrarily at any corner of the n alleles hypercube. As with the symmetric landscapes, we find that the learnt mutation rates provide the quickest response to selection (data not shown). The Hebbian weights, in this case, can evolve to be negative, even if the initial weights are positive. (For some reason that we still do not understand, if initial weights are allowed to be negative, the system evolves to a suboptimal solution). Unlike in the case of a symmetric landscape, the weights are not all equal. Instead, we find that there is a strong correlation between the weights and the selective value.

In Fig. 5A we present the outcome of a model run. The first row of the array shows the selective values (which are sorted increasingly), and the rest of the matrix shows the weights in equilibrium (diagonals are zero as we don't allow self-connections). The figure clearly shows that the system learns to discriminate the gradient of the landscape and thus directs mutations accordingly. In this textbook example the outcome is very satisfactory. However, some times the weights evolve towards an anti-correlation, although still a very strong one.

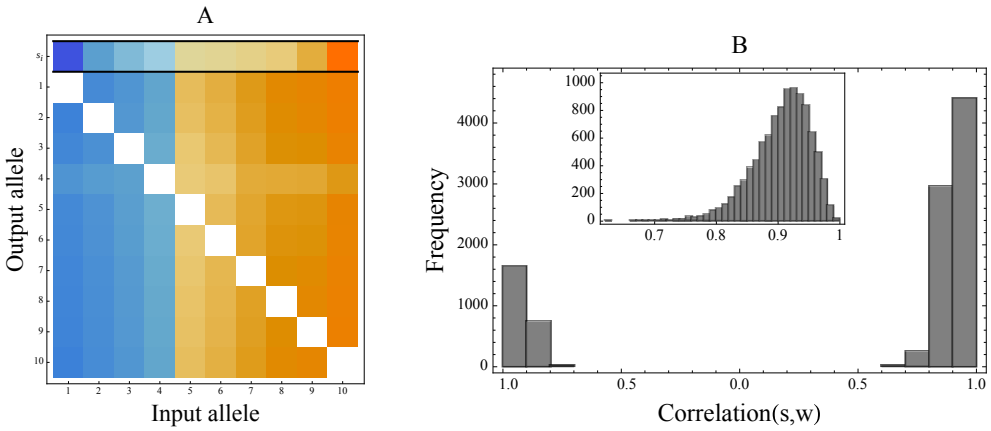

Figure 5. Outcome of evolution and learning under an asymmetric landscape. (A) Hebbian weights of a sample run. (B) Correlation between equilibrium Hebbian weights and selective values for 1000 different runs with randomly chosen selective values. The selective values are chosen independently from a U[-1,1] and then normalized with an Euclidean norm. The inset shows the distribution of the absolute value of the correlations. n=10, λ=0.01, p_0~U[0.4,0.6], ϕ_0~U[0,0.1]

This is summarized in Fig. 5B, for 1000 random choices of vectors of selective value. In most of the cases the learning of the landscape is optimal. Figure 5B implies that the average of the absolute value of the correlation, i.e. can be used as a measure of the discriminating capacity of the network.

We now turn to study the effect of network topologies. We will employ the absolute correlation average ρ as an additional tool to evaluate how distinct topologies allow adaptation. For the moments we will focus only on Erdős-Rényi graphs with varying degrees of connectivity.

Figure 6A presents the absolute correlation averaged over several replicas, for various numbers of loci and different network connectivities. First, we find that the correlation is higher for larger number of loci. This makes sense when we think that more neurons are better at discriminating and learning patterns. Second, we note that the correlations initially decrease with

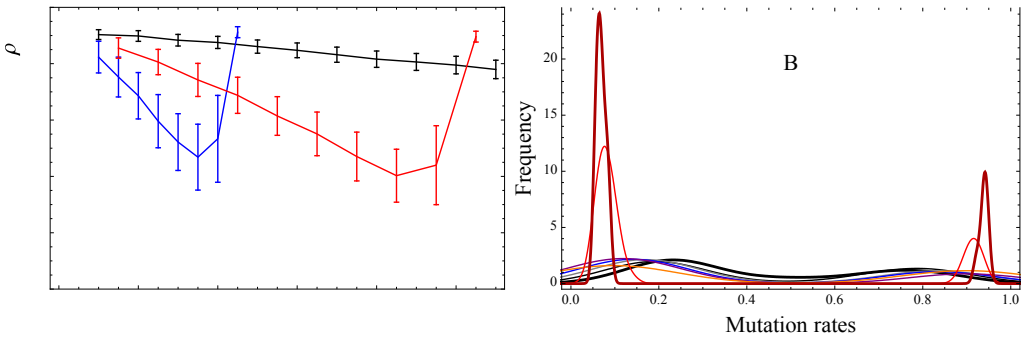

Figure 6. (A) Absolute correlation n=30 (black), 15 (blue), 10 (red). (B) Distribution of mutation rates for networks with different degrees: 15 (black), 20 (gray), 25 (blue), 30 (purple), 35 (orange), 40 (red), 45 (thick red); n=10. Topologies randomly drawn from Erdős-Rényi graphs. Otherwise as Fig.5.

the degree, but once the network becomes populated, there is an abrupt increase in the correlation. In other words, *the most discriminating networks are those of low degree, or of high degree, but those with intermediate degrees are less able to learn the asymmetries of the adaptive landscape*. In Fig. 6B we find that low degree networks have mutation rates that are spread, whereas networks with high degree have a bimodal distribution: one peak (the highest) close to zero, and one smaller peak close to one. The latter probably correspond to those weights that result anti-correlated with the selective values.

3.6 Future directions

A. Complex landscapes

The next relevant extension will be to study the performance of the neurodynamics under more complex adaptive landscapes. By complexity we refer to including non-additive fitness effects (epistasis, in population genetics) that make the landscape rough. These kinds of landscapes are "hard" in that there are many local peaks or solutions, and a simple hill-climbing algorithm can get

stuck in one of such landscapes. In this case, one of the many interesting questions is whether learning on one peak will help to climb other peaks. Another relevant question is whether learning mechanisms can help overcome local peaks and make it easier to find global solutions (Ullman et al. 2012).

B. Synaptic plasticity

Although the advances above are novel and very encouraging, these neurodynamical aspects are describing the simpler level of learning, which is reinforcement learning. The next step is to consider the evolution not only of the allele frequencies (analogous to neuron spiking), but how the connections amongst the neurons are established (Fernando et al. 2010). That is, synaptic plasticity. This describes another type of learning, which, although it is not independent from the previous one, it incorporates mechanisms for long-term memory. To achieve this we will employ the same system described above, but where we will allow that, with certain probability, the network can add or remove nodes. Then, we will study the evolution of this system. In other words, we will study how changes to the network topologies that are themselves neutral, are fixed in the population due to the advantage that they give in finding the solution of the neuron spiking probabilities (and weights) in a given fitness landscape. Technically, this is known as "invasion analysis". With this model we will then study what are the kinds of topologies that evolve to facilitate learning.

However, above we reported that highly connected networks are best in finding the solutions. But, establishing neural connections in the brain is energetically costly, and spatially constrained. Therefore we will add a fitness cost, $\bar{W} = \bar{W}_0 e^{-\beta\delta}$ where β is the cost of each connection in the network, and δ is the network's degree. This factor does not make any difference for the calculations above, since evolution occurred only given a common network topology (we varied topologies, but not across runs). However, a mixed population where there is more than one topology will provide another factor that is expected to optimize connectivity given the constraints of numbers of connections.

C. Relationship to evolvability

Evolvability is understood as the potential of a population to respond to selection. How fast the response to selection is depends on the amount of genetic (or heritable) variation that can be produced. This can be given by standing variation, cryptic variation (due to epistasis, for example), or due to mutational variance. Although high mutation rates will provide source "material" to respond to selection, these will also create load that keeps the population maladapted. However, the optimal scenario is achieved if mutation rates can be increased as selection is started, and tuned down once the population approaches adaptation.

As we saw above, this is precisely what happens with the neurodynamics we have described. Of course, genetic systems do not have a learning mechanism as the brain does. Nevertheless, these are totally analogous. We want to bring the analogy further and interpret that the input current *E* as a quantitative trait, with the weights *w* taking the role of additive effects.

A previous model in quantitative genetics has taken an approach very similar to ours (Jones et al. 2007). They did not apply a learning mechanism, but they considered modifier alleles for the mutational effects which are selected indirectly increasing the mutation rate in the direction of the highest increase in fitness. Thus, there seems to be a niche in order to apply what we have learnt in neurodynamics back to evolutionary biology.

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4 Parallel search for RNA cloverleaves and active sites with shared server architecture: an analogy to mental search for form and structure

4.1 Introduction

Human cognition, while on the surface level seems to be a serial process, runs in fact, for a large extent, in parallel under the hood (e.g. visual parsing, grammar parsing [4], [8], etc.). Some think that learning, theory formation, and hypothesis-generation are all parallel processes of which we can only observe the serial output on the behavioural level. As a matter of fact, a parallel architecture is a necessary pillar of Darwinian search: a population of ideas entertained in the brain might be subject to the same dynamics as a population of species undergoing selection and evolution. This line of thought was proposed by many, most recently by Fernando and colleagues, as the Neuronal Replicator Hypothesis [3, 1]. According to the NRH, Darwinian dynamics of neurons, groups of neurons, connective topology, spike paths or spike patterns (responsible for cognitive processes) are perfect candidate units of selection and evolution in the brain. Darwinian search is known to be a very effective optimization algorithm for rugged, hierarchical fitness landscapes with many local suboptimal solutions, i.e. for complex problems.

Insight learning is a prime candidate for a heavily parallelized cognitive process that could benefit from evolutionary search. Though there are algorithmic models that can be used for some extent (see Tenenbaum [5]), insight learning in general is more complex and less understood. It is a special form of learning where theory generation is nontrivial, involves lots of trial and error, the learner usually sticks with suboptimal solutions for an indefinite time (impasse), and the impasse is overcome with a sudden insight that must be the result of low-level cognitive processes.A low-level process that could explain the sudden insight is recombination of candidate solutions and/or frames in the evolutionary approach.

There is an obvious algorithmic analogy between insight learning (theory acquisition) via parallel processing in the brain and evolutionary search over structure and sequence of polynucleotides, for example. Stochastic search processes were already suggested by Tenenbaum (MCMC [7]) to approximate more abstract "ideal learning" in a Bayesian framework. Lower-level stochastic models might be able to bridge the gap between high-level abstractions (modelling theory learning in adults and children) and low-level neuronal components of the system.

Also, there is an important question: is the observed serial nature of the output the result of the modality of the way it was externalized (e.g. speech) or is it serial because the cognitive process itself becomes serialized *before* any utterance is made? For example, Zylberberg and colleagues [8] have argued that surface-level serialization in human brain (the psychological refractory period) could be the result of a decision bottleneck when *recombining* parallel solutions, something that provides the high level of flexibility of the human brain. Clearly, there is a very important aspect of such considerations: while parallelism seems to find a solution faster than a serial method for most cognitive tasks, there are obvious costs for maintaining such parallel architectures and – more

importantly – costs of evaluating, comparing and recombining results of parallel searches through a bottleneck "router" that might also bound the efficiency of any parallel subsystems. Accordingly, if the limiting number of shared bottlenecks is increased, the efficiency of parallelism can be restored.

A simple model is presented here, simulating parallel, shared, stochastic evolutionary search. Individual solutions to a problem (represented as RNA sequences) are maintained and evaluated in parallel over a shared architecture of fitness evaluators ("servers") and those with higher fitness after evaluation have higher chance to replicate and become dominant in the population than inferior sequences with low fitness. Such shared architecture is called "processor sharing" in queuing theory: any waiting process (sequence in this case) can enter any of the shared processors (servers); a server usually chooses randomly from the processes wating.

If parallelism and Darwinian search is indeed exploited in the brain, the model presented here could serve as an analogy: it provides a computational example that contains all the necessary components of Darwinian dynamics (cf. [2]) that can be compared to components of cognitive processes and that of the neuronal structures:

- **Population**: the model has a population of individuals performing search in **parallel**. The brain contains millions of neurons and many cognitive functions are known to be performed in parallel, e.g. visual or auditory processing.
- **Variation**: since mutations can happen, the population is likely to be diverse, on which **selection** can act.
- **Competition**: slots in the population can be **redistributed** among individuals according to their fitness, as after replication, offspring is generated at the expense of other, existing individuals. The NRH assumes that units of selections (neuronal connectivity or activity patterns) exist in the brain competing with each other for resources (e.g. space in the memory).
- **Shared architecture**: shared servers could account for both increased parallel efficiency (any server can be accessed by any individual) or severe serial bottlenecks (if there are many fewer servers to share than individuals, queues are formed).
- **Recombination**: a population of individuals could recombine to produce offspring that share features of their parents (will be implemented in the near future).

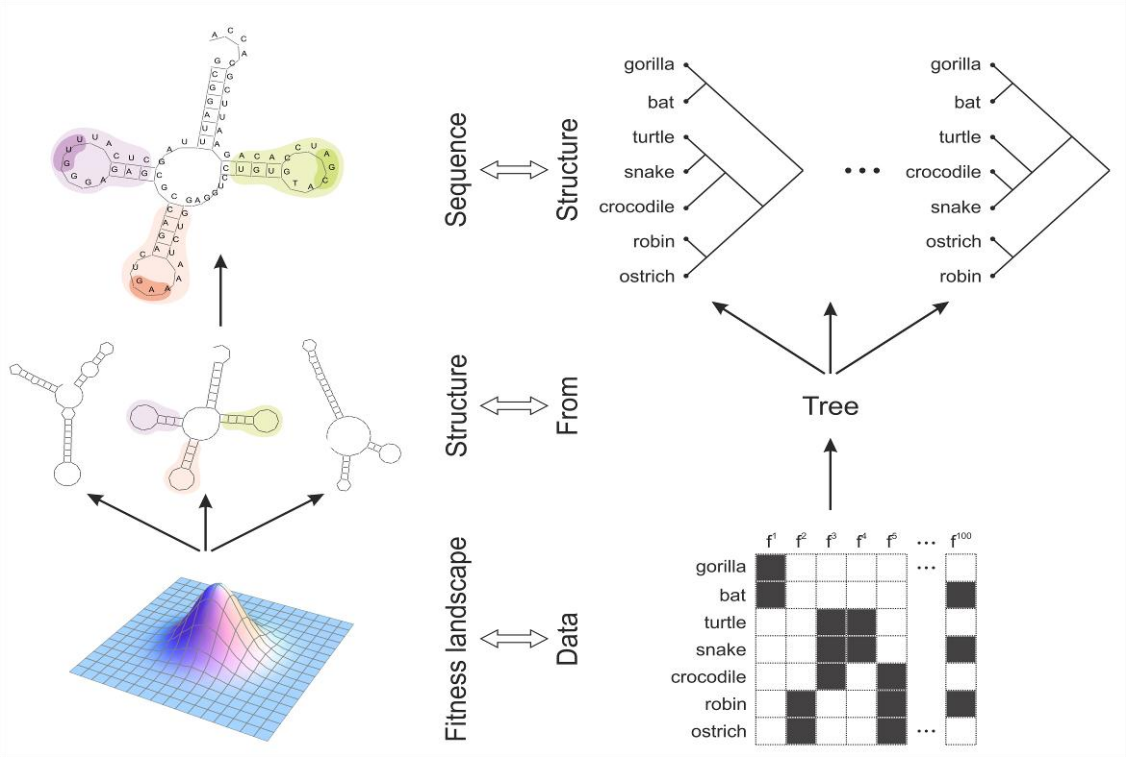


Figure 7. Analogy between finding structure in data according to Tenenbaum (right) and Darwinian search for tRNA (left). The model on the right panel (modified from [5]) performs a search based on a dataset to find the best *form* that describes the data (a hierarchical tree in this case) and the best *structure* that instanciates the form, i.e. the tree that is parameterized optimally to account for the data. In case of search for RNA functionality (left panel), first the appropriate structural form has to be found (three loops in the cloverleaf, larger coloured blobs) and only if the appropriate structural form is encountered will parallel search go on to fine-tune the active site-sequence in each loop (the three triplets emphasized with deeper colors).

A hierarchical fitness landscape is used, where sequences first have to find a given structure (loops of the canonical tRNA structure) and only if the structure is already found will they further adapt to find the optimal active site triplet for each loop. This hierarchy is in coherence with Tenenbaum's assumption [5]: during the structuring of a discovery process (i.e. a child learns or a scientist develops a new theory) the higher level feature of the theory (the *structural form*) is explored and discovered *before* fine-tuning it and finding the best fitting *instance* of the given form. The relation of the two models is illustrated by

Figure 7.

The hierarchy in the fitness landscape dramatically changes the performance of different optimization processes. As there is no selection for the active site *until* the structural loop has been found, an individual can be stuck in a local optimum (a found loop is better than if there is no loop at all) but since the correct active site is to be found, most mutations would ruin the structure. This makes the search for the second adaptation (finding the active site) a notoriously hard problem; it is assumed that parallel searchers without redistribution (a population of independent SHC-s) cannot solve it easily.
The major questions asked and intended to be answered in this report are:

- Does the parallel architecture perform better than a serial one?
- Does the parallel architecture with shared evaluation perform better than independent evaluators?

4.2 Methods

The model consists of a population of RNA sequences undergoing exploratory stochastic search in a mutation-selection regime. Sequences are folded into their minimum free energy structures (folding done by the ViennaRNA Package version 2.0 [6]) by a limited number of "servers" that are shared within the population. Folding takes time (more complex structures having more paired bases require more time) and when folded, the 2D structure is assessed for fitness and the sequence can replicate according to the assigned fitness by the server. *The main focus of the experiment is to monitor when the population achieves certain milestones of adaptations while under selection on a fixed fitness landscape.*

4.2.1 Fitness landscape

A smooth but hierarchical fitness landscape with a single peak is assumed. The target optimal structure that must be reached is the canonical 76 nt tRNA: during evolution, the population has to acquire the three structural tRNA loops Furthermore, for each loop, when it is stably found, evolution has to finetune the active site of it (active sites are arbitrarily fixed triplets, one for each loop, at fixed positions). A population of independent hill climbers is expected to easily find the optimum – the question is: would the parallel architecture with shared servers provide any advantage compared to a (parallel) population of independent hill climbers?
Addition and deletion is allowed during mutation (sequences can grow up to length 100 or shorten to 50), thus Hamming distance-comparison of structure (or sequence) is not available. The distance of the i^{th} sequence from the optimal structure and active sites is defined as:

$$D_i = (1-(1-\frac{\min(L, D_{ST})}{L})(1-\frac{D_{AS}}{9}))$$

where D_{ST} is the tree-edit distance of the secondary structure compared to the standard 76-nt tRNA secondary structure (truncated at a maximum distance of L = 100); and D_{AS} is the Hamming distance of the three active sites (9 nucleotides in total at fixed positions) compared to the corresponding triplets of an arbitrarily chosen tRNA sequence. Note, that the j^{th} active site is only

checked for $D_{AS,j}$, if the corresponding j^{th} loop+stem structure is at the right position. Thus if only the third loop+stem is at the right place and it has an active site with one mutation, the Hamming distance from the target will be $D_{AS} = D_{AS.1} + D_{AS.2} + D_{AS.3} = 3 + 3 + 1$.

The fitness of the i^{th} sequence is a function of D_i:

$$w_i = \max(1 - D_i^e, w_0),$$

where $e \in (0,2]$ and $w_0 = 0.01$ is the baseline fitness. By increasing e, the fitness function becomes more tolerant toward mutations (see Figure 8).

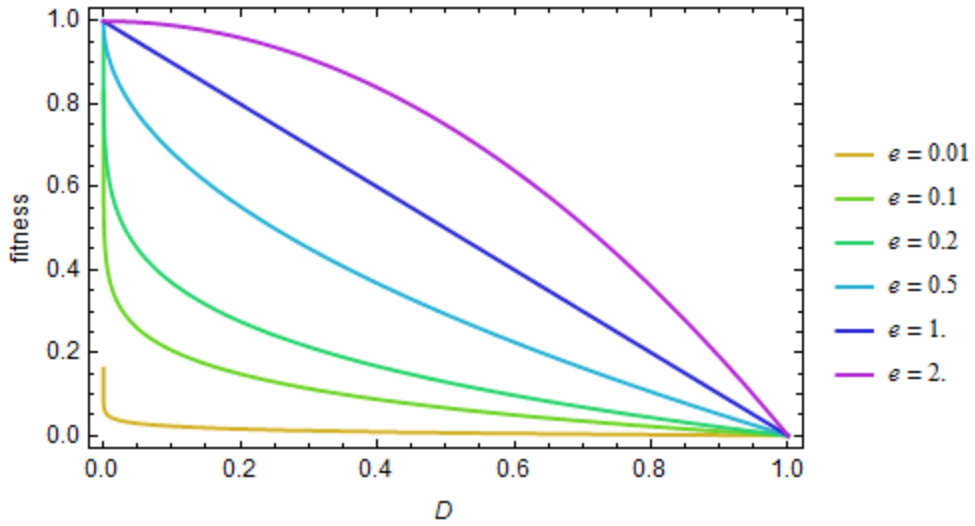


Figure 8. Fitness functions for different exponent values (e) depending on the distance D measured from the target structure and sequence.

The initial population is randomly chosen from low-fitnessed sequences, usually having a uniform fitness of w_0. A single optimal RNA sequence is arbitrarily chosen as target, adopting the standard tRNA secondary structure (the cloverleaf). In summary, the fitness landscape is smooth and single-peaked. Though it is also hierarchical: at a coarse level, structural elements must be found and, as a second stage for each structural element (i.e. *only* when a loop has been found), finetuning is done on the sequence level.

4.2.2 Parallel architecture with shared servers

The parallel search is simulated by implementing fitness-evaluation as a time-dependent, asynchronous process. The number of "free" individuals at time t is $N_t \leq N_{max}$ and the system has a fixed number of S slots ("servers") to evaluate S sequences in parallel (sequences allocated to servers are not free). Any sequence can enter any server when available. The total population size is thus maximized in $N_{max} + S$.

A server can be empty or occupied by an RNA sequence. At each time step, $0 \leq s \leq \min(N_t, S)$ number of sequences of the population is randomly allocated (regardless of their fitness) to the s empty servers. Sequence i at a server spends t_i time steps to be folded, t_i equalling the number of base pairings in the 2D structure, i.e. the evaluation time increases with structural complexity. After

t_i time steps, D_i and w_i are calculated and assigned, and the sequence is replicated and added to the population with its potential offspring.

With a certain probability (proportional to fitness), sequence i is replicated (with possible mutations), and a single offspring sequence is generated with mutation. If the population is smaller than N_{max}, parent and offspring (if exists) replace randomly chosen members of the population, so that the population cannot grow over N_{max}. Due to the asynchronous nature of fitness evaluation and offspring production, accumulation of sequences over the initial population size N cannot be avoided. Accordingly, after some time, total sequence count in the system will be close to $N_{max} + S$, therefore the *rate of parallelism* ($R = S/N$) cannot be higher than ½.

4.3 Results

Results clearly show that the population can converge on the target sequence. Interestingly, the structure can tolerate as high as 14 neutral mutations ($D_{ST} = 14$) while the active sites remain un-mutated with D_{AS} being 0. Majority of neutral structural mutations are accumulated at the right flanking region, because 1) addition can remain neutral at the right end (left additions would shift loop positions) and 2) changes made to the flanks are less probable to alter the optimal minimum-free-energy structure. However, no addition/deletion is welcome in the left flanking region, in the loops and stems, and between the loops, as such mutations would cause a shift in one or more of the loops' positions, effectively setting $D_{AS} = D_{AS.max} = 9$ and thus D to its maximum 1 (with $w = w_0$). A fitness close but not exactly 1 is more probably due to structure being shifted, than because of mutation in the active site: any mutation has a higher probability to hit the structure (usually 76 possible positions) while the chance to mutate the active site is much less (9 positions only).

Since absolute positions of loops are checked from left to right in the dot-bracket structure representation, the leftmost loop (L_1) is usually found first, and is maintained at higher abundance, as any other loop can be freely appear/disappear without affecting the first loop. If, however, the first loop shifts, it will probably ruin any other loop being downstream.

Characteristic results for R = 1/3 server ratio and shared servers

Starting from $N_{init} = 200$ randomly chosen 76-nt RNA sequences, with S = 100 slots to evaluate fitness and $\mu = \mu_{sub} + \mu_{ins} + \mu_{del} = 0.002 + 0.002 + 0.002 = 0.006$. Fitness function exponent is $e = 0.5$, number of time steps is 100 000.

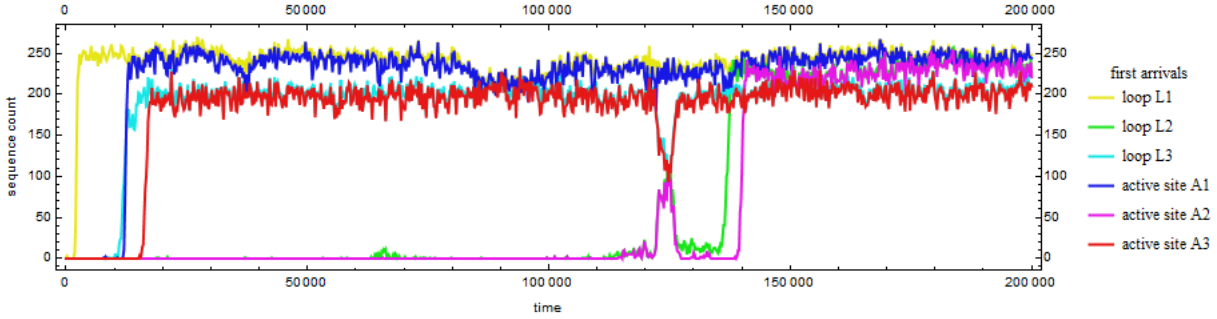


Figure 9. Number of individuals with given structural loops and active sites in the population. Note that an active site (a 3nt-long subsequence) is only registered if the loop that contains it is at already the

right position in the structure. Due to the artefact of reading positions from the left, the leftmost loop (L_1) is usually found first and is maintained at higher abundance, as any other loop can be freely appear/disappear without affecting the first loop. If, however, the first loop shifts, it will probably ruin any other loop downstream. Vertical lines indicate the first point when the given loop/active site is stable appearing (i.e. its abundance never drops to zero anymore). Note that even if all three loops are present in the population it does not mean that all three are present in the same individual. The next figure informs about that

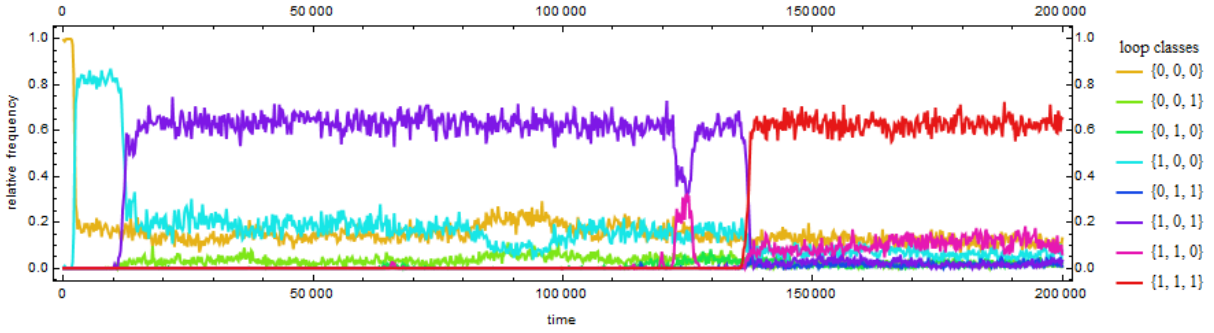


Figure 10. Relative frequency of loop classes. {1, 0, 1} for example means that the first and last loops exist at the right places (with correct stem lengths) but the second loop is missing or shifted to wrong positions in the structure. Existence of active sites is not shown here.

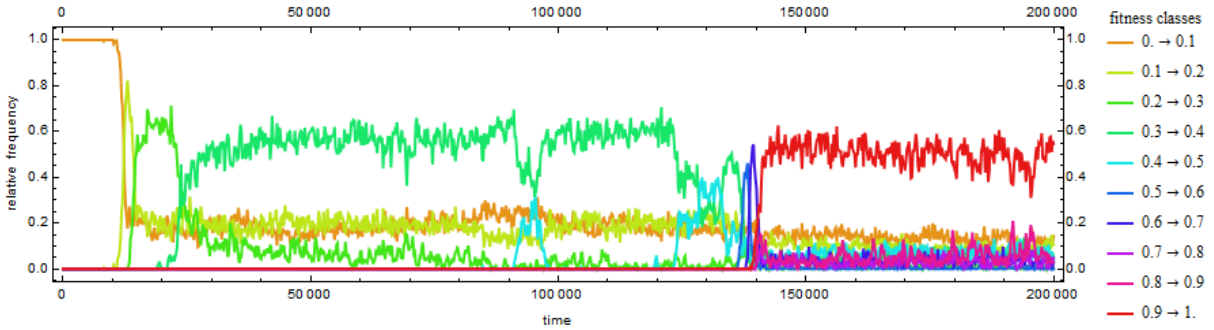


Figure 11. Relative frequency of fitness classes. Red indicates best class containing the optimal structure.

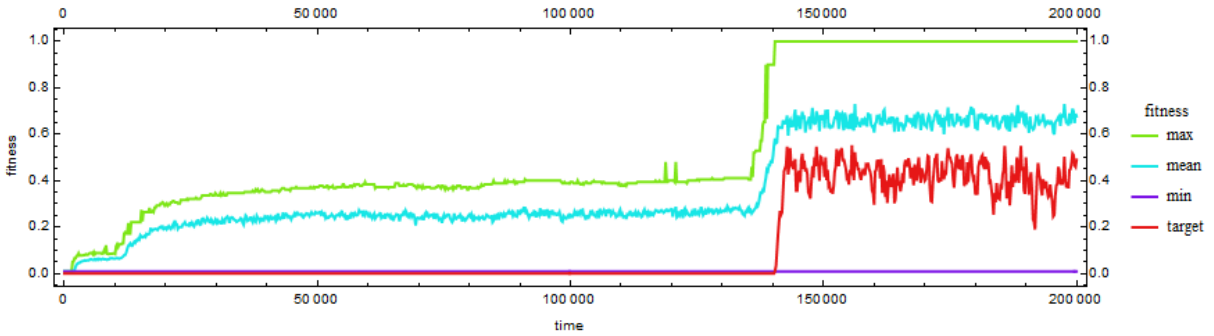


Figure 12. Fitness statistics. Maximum (green), mean (cyan) and minimum fitness (purple) and relative frequency of the best sequence of $w = 1$ (red).

Averaged results for increasing server ratio and shared servers

In this experiment, the number of servers was increased from S = 1 to 200, all other parameters are the same as in the previous experiment (initial population size N = 200, e = 0.5). Each figure is an **average of 100 independent simulations**. The larger S gets, the more evaluations happen during a simulation, thus the population converges faster on the optimal structure. The found loops and the relative frequency of 3-looped structures increases in the population, until they dominate over 2-looped suboptimal structures. If the target sequence is found (i.e. loops with stems are found **and** active sites are aligned correctly, i.e. fitness is $w = w_{max} = 1$), it remains and cannot be lost from the population. With a less strict fitness landscape (e > 0.5, figures not included), this is not the case, and the target - once found - cannot spread as effectively, thus inferior competitors can exclude it from the population. Nevertheless, the target sequence can be easily found in those cases again.

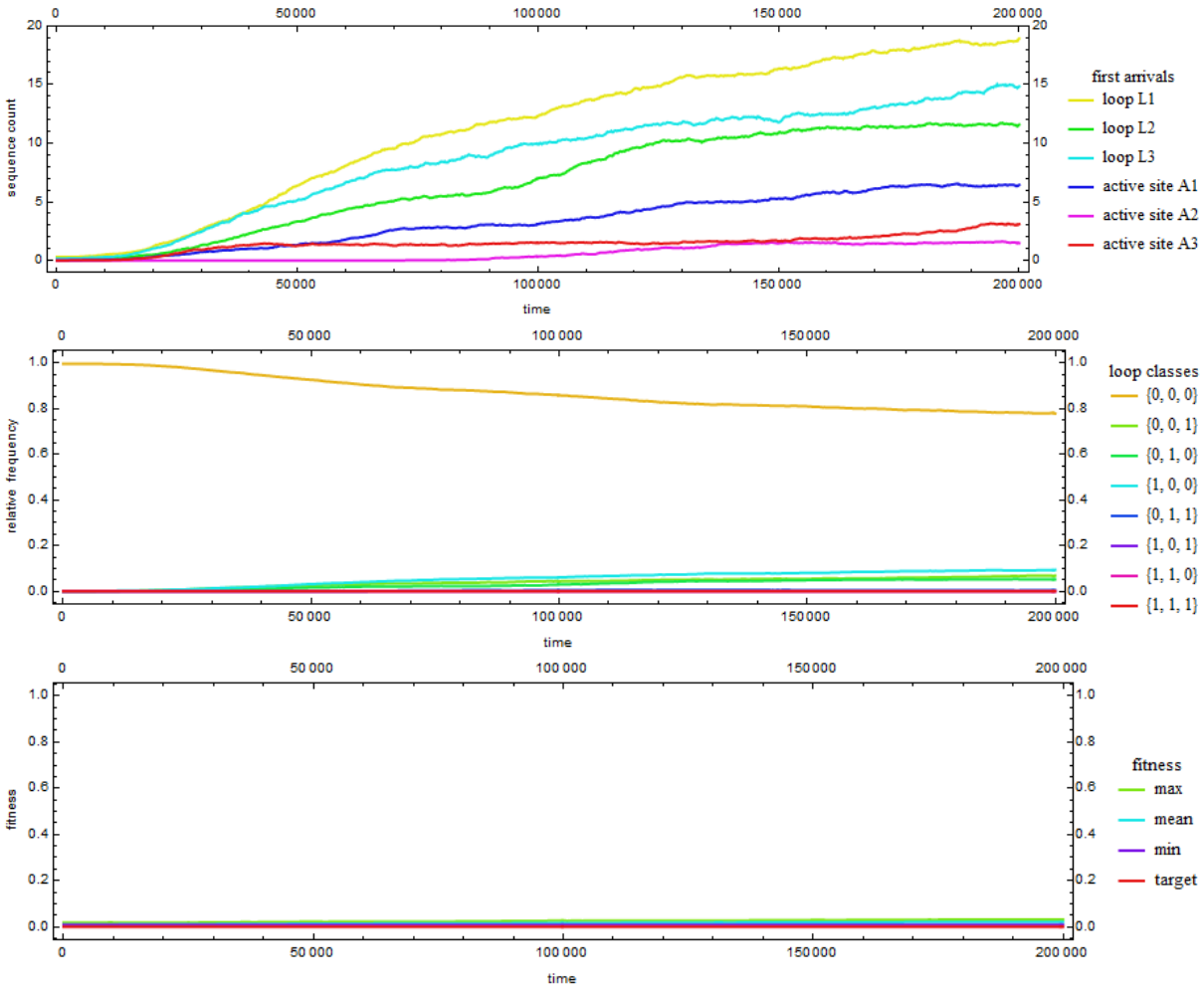


Figure 13. Server number S = 1 (R = 1/201). Loop and active site counts (top), relative frequencies of loop classes (middle) and min-max-mean fitness (bottom).

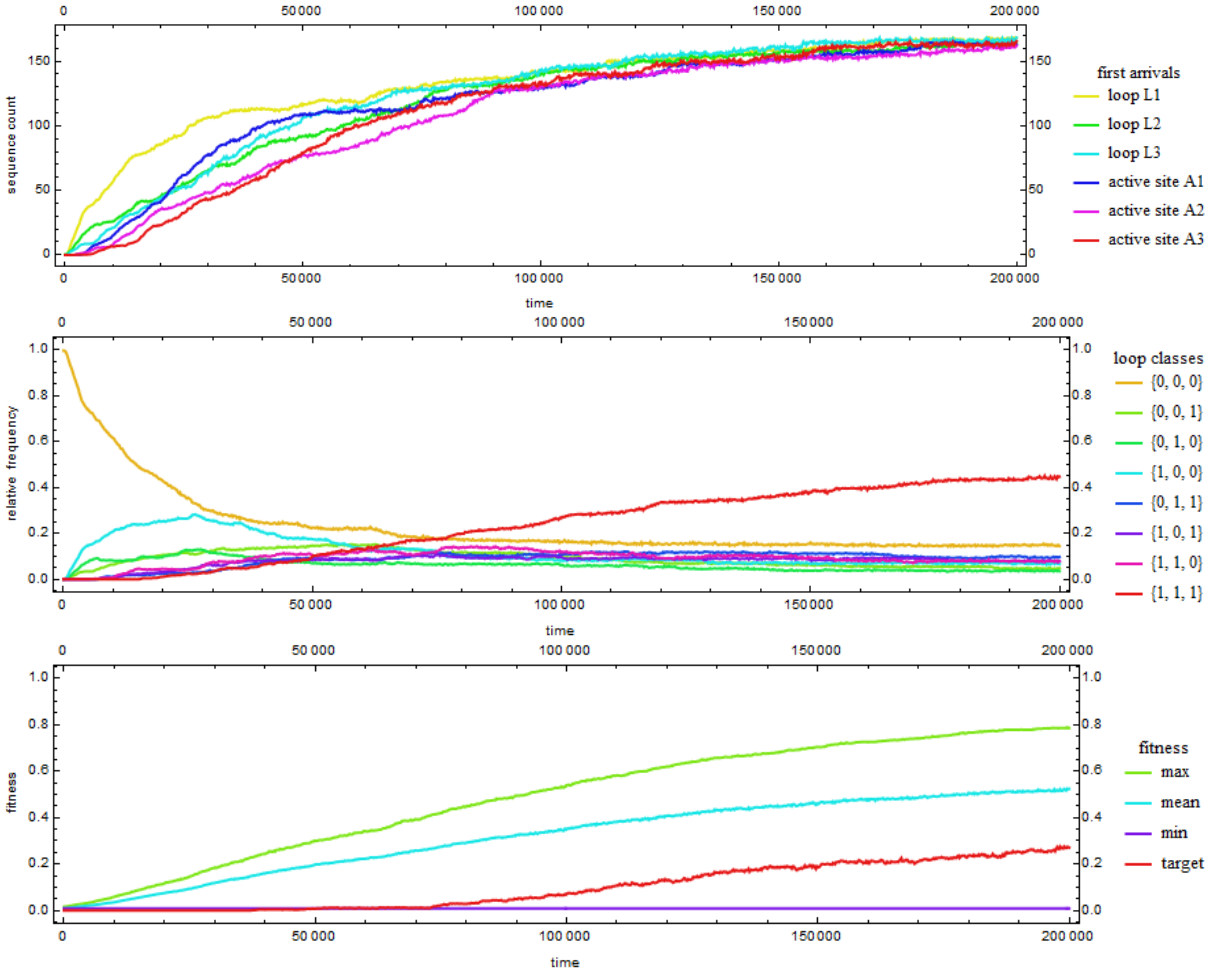


Figure 14. Server number *S* = 50 (*R* = 50/250). Loop and active site counts (top), relative frequencies of loop classes (middle) and min-max-mean fitness (bottom).

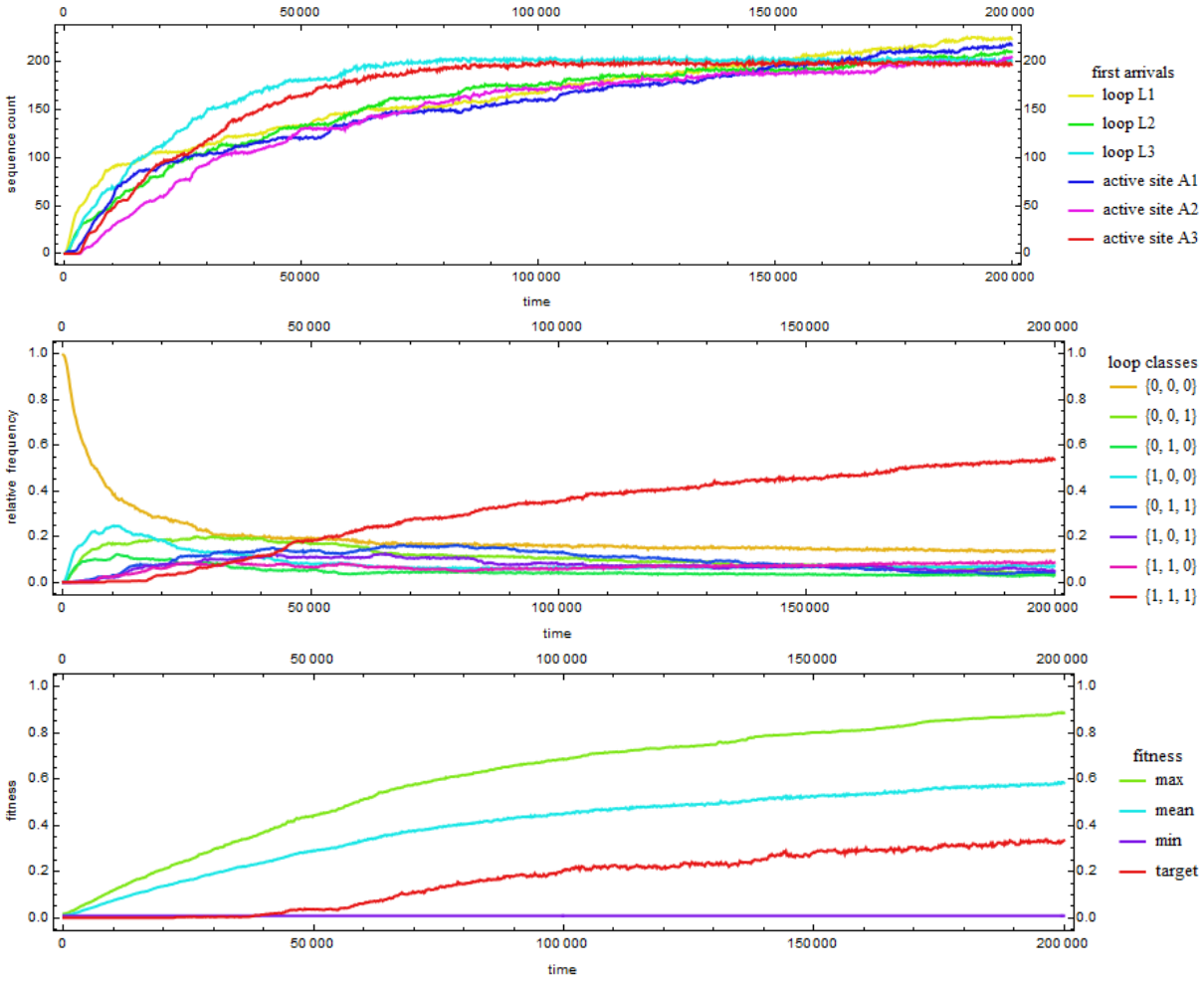


Figure 15. Server number *S* = 100 (*R* = 1/3). Loop and active site counts (top), relative frequencies of loop classes (middle) and min-max-mean fitness (bottom).

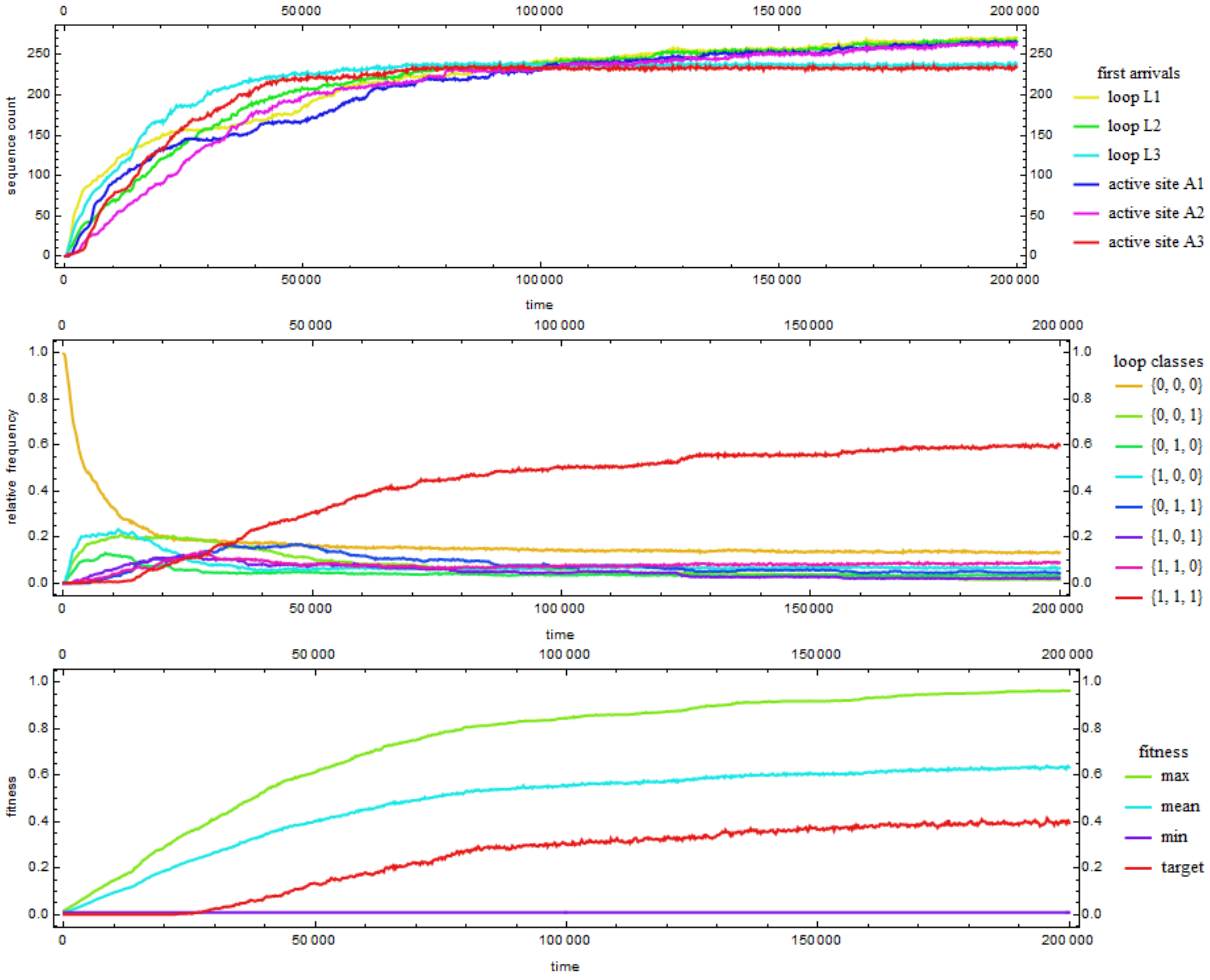


Figure 16. Server number *S* = 150 (*R* = 150/350). Loop and active site counts (top), relative frequencies of loop classes (middle) and min-max-mean fitness (bottom).

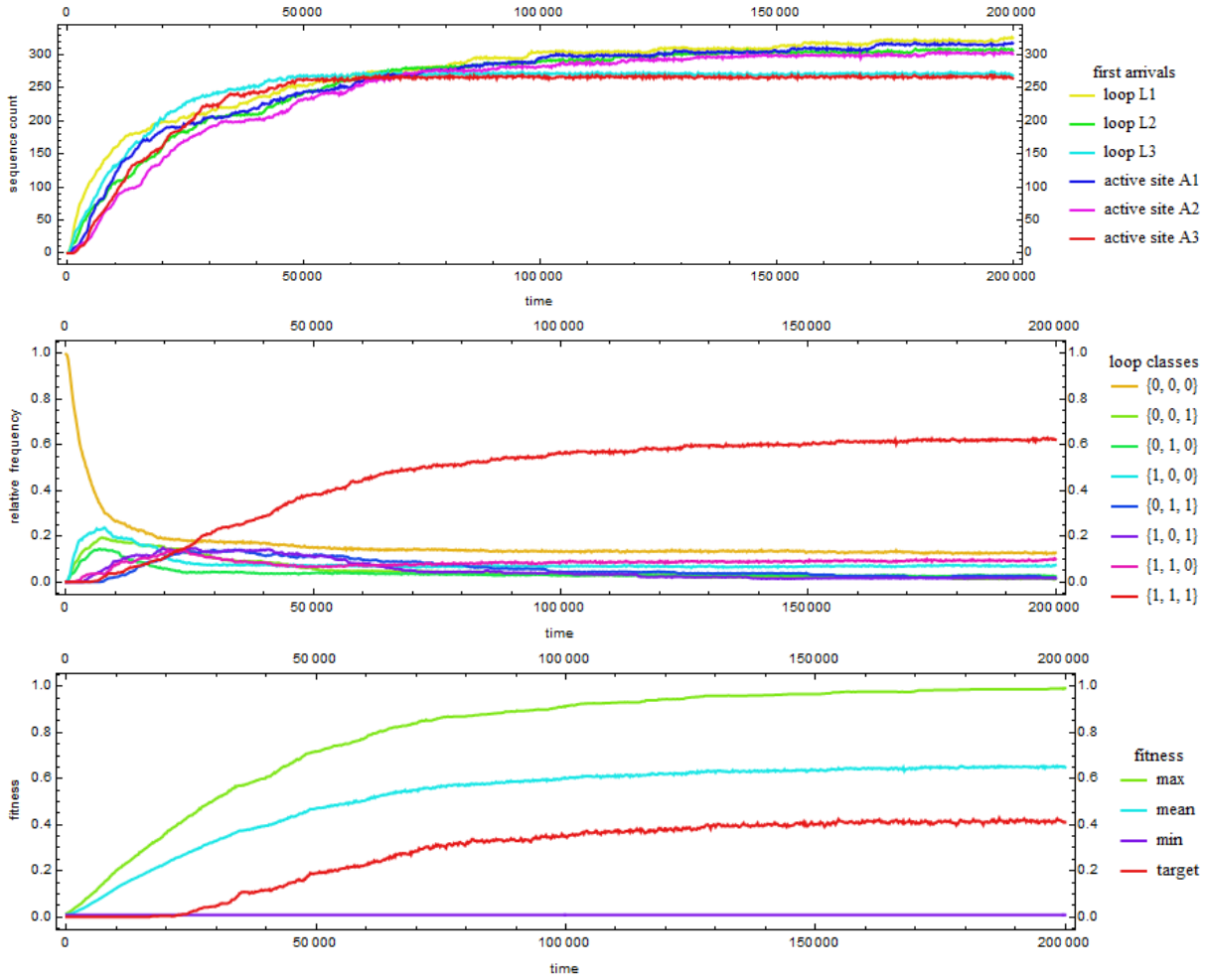
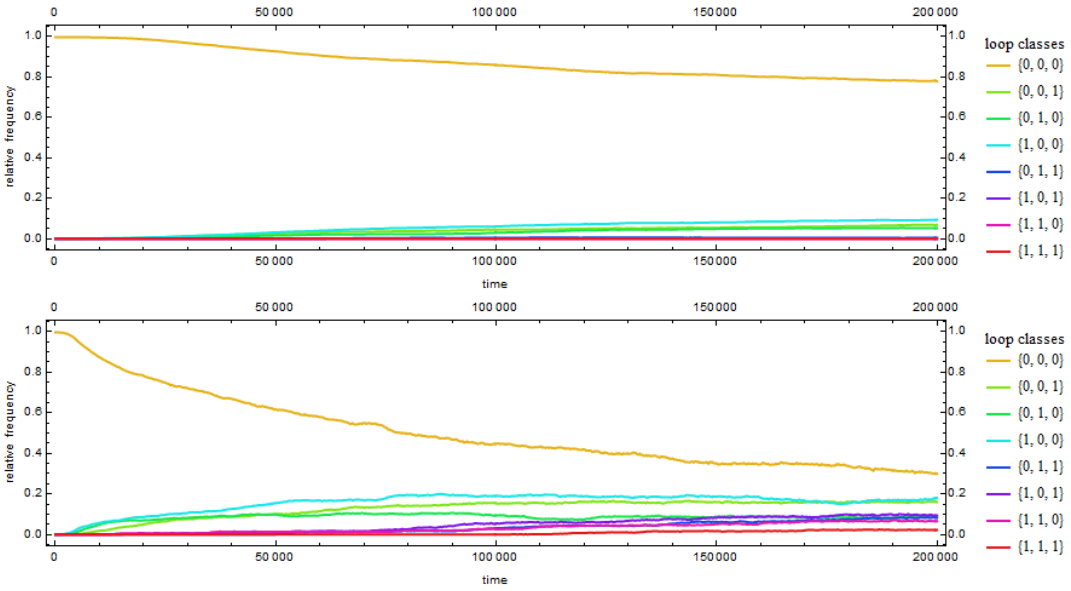


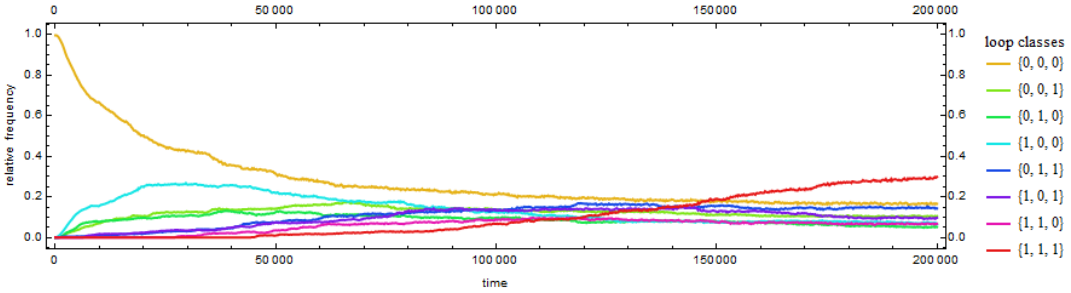
Figure 17. Server number S = 200 (R = ½). Loop and active site counts (top), relative frequencies of loop classes (middle) and min-max-mean fitness (bottom).

S = 1

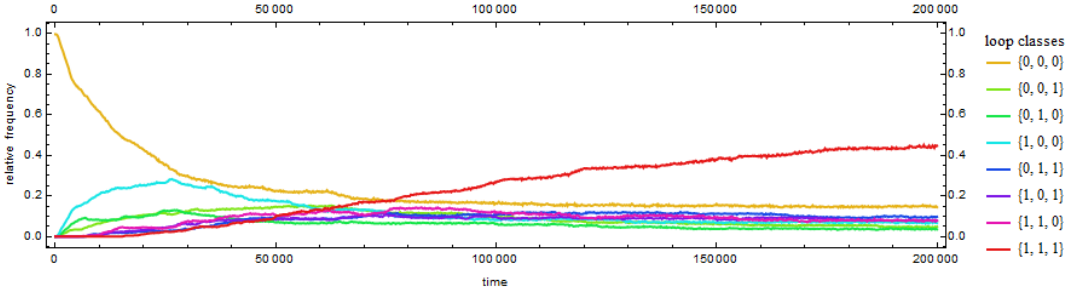
S = 10



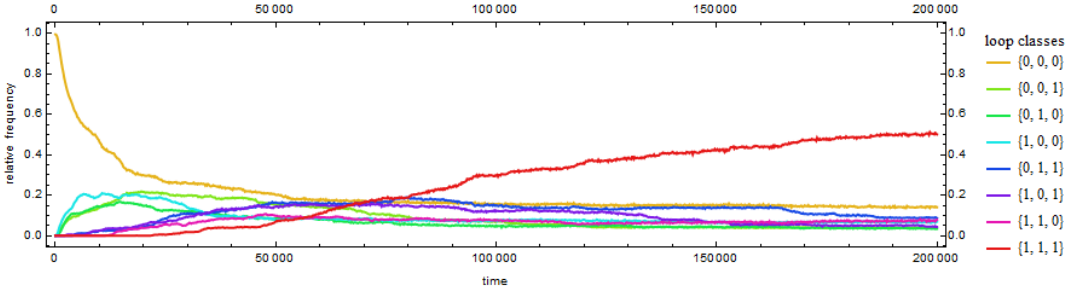
$S = 30$



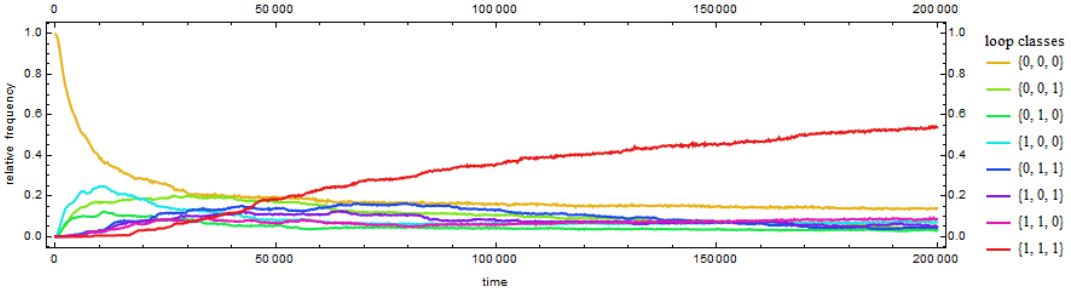
$S = 50$



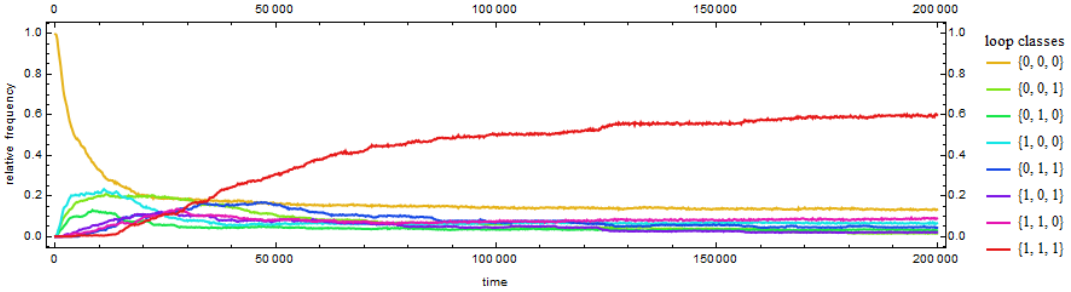
$S = 70$



$S = 100$



$S = 150$



$S = 200$

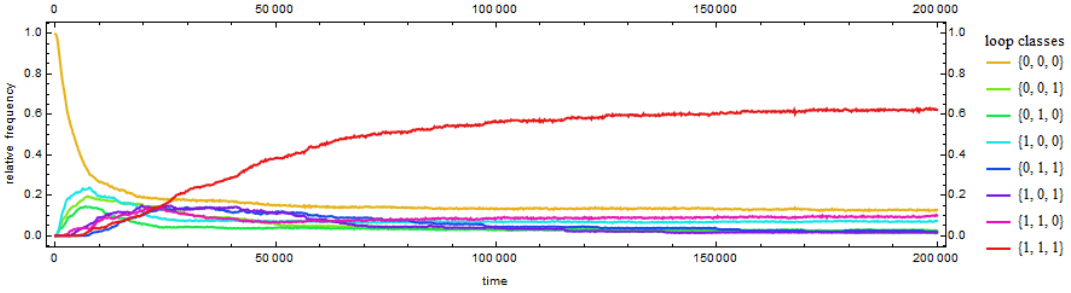


Figure 18. Averaged loop class frequencies for increasing server ratio with finer *S*-resolution. Each figure is an average of 100 independent simulations. Results indicate that loops are found earlier if more servers are available, i.e. when parallelism is more prominent.

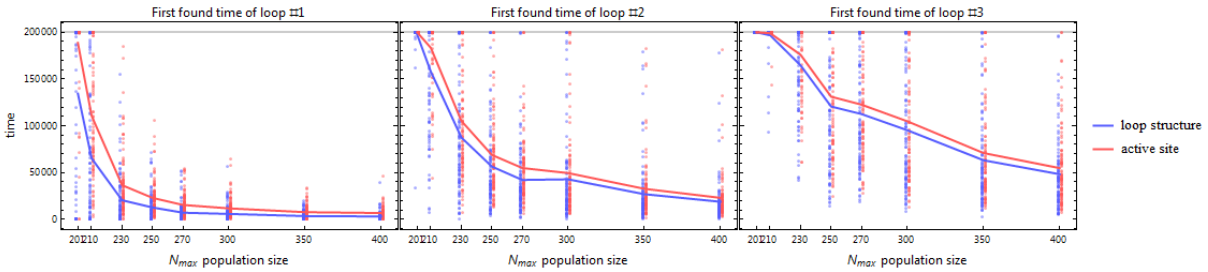


Figure 19. First arrival times of found loops (blue) and active sites (red) depending on the number of servers.

While initial population size is constant N = 200, as the server number increases over the range S = 1..200, the total population size increases from N_{max} = 201...400. Accordingly, the rate of parallelism increases from R = 1/201 to R = 200/400 = ½. Dots indicate the results of 100 independent simulation, continuous lines denote the average of these simulations (blue for loop structure, red for active sites). Note, that the number of a found loop (#i) does not necessarily equal to its position in the structure (L_i, counting from the left; see

Table 1 for more details). Since each simulation was run for a maximum of 200 000 time steps, longer first-arrival-times were not recorded. Accordingly, the N_{max} = 201 average value for the third found loop (#3) should be above the hard limit, the observed plateau is just an artefact.

A **B**

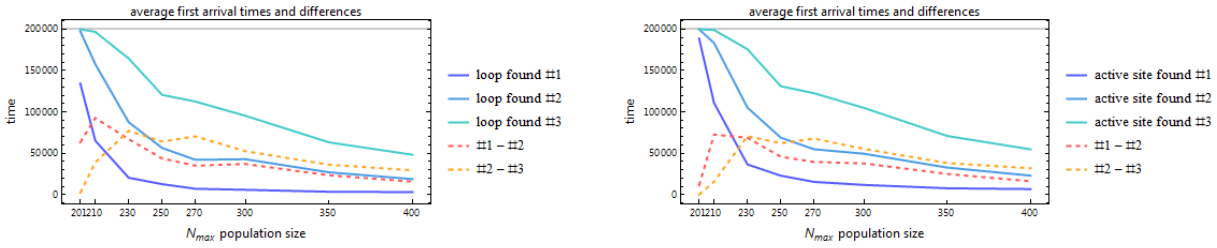


Figure 20. Superimposed average first arrival times (solid) and their differences (dashed).

The number of cases of all simulations where the first found loop is L_1 has the highest probability (314 cases, see

Table 1.). This is expected because of 1) the artificial *sequence effect* (i.e. leftmost loops are more stable against frameshift mutations than downstream loops); and 2) the first loop L_1 is the shortest (16 bases) compared to L_2 and L_3 (both being 17 bases long). Interestingly though, the second most common loop that is first found is not L_2 but the rightmost L_3 (with a total of 244 cases), which contradicts our expectation (L_2 with 176 cases) predicted by the sequence effect. To fully explore the underlying causes of this distribution, an even more artificial experiment has to be run where each loop would have the same length and each flanking and joining non-loop region would also have identical lengths.

Table 1. Number of simulations where the first found loop was L_i (L_1 being leftmost in the sequence, L_3 rightmost). "none" indicates that no loop was found during the 200 000 time steps, a combined L_i & L_j means that the loops *i* and *j* were found simultaneously.

S	**L_1**	**L_2**	**L_3**	**none**	**L_1 & L_2**	**L_1 & L_3**	***total***
1	20	9	16	55	0	0	**100**
10	42	24	26	8	0	0	**100**
30	43	28	29	0	0	0	**100**
50	50	26	24	0	0	0	**100**
70	36	29	34	0	0	1	**100**
100	39	22	39	0	0	0	**100**
150	43	28	39	0	0	0	**100**
200	41	20	37	0	2	0	**100**
total	**314**	**176**	**244**	**63**	**2**	**1**	

4.4. Independent stochastic hill climbers – servers are not shared

A parallel architecture with dedicated (i.e. not shared) servers provide an appropriate comparison against previous results. The model of non-shared-servers consists of $N_{max} = S = 1...400$ independent stochastic hill climbers (SHC), 100 iterations for each server number. A single SHC equals to a "population" of a single sequence with a single server that evaluates the offspring and keeps it if it is better than the parent or (with a low probability of $\sigma = 0.01$) keeps it even if it is inferior. Individuals cannot share servers, each server is asigned to a single SHC lineage.

Note that a population of *N* independent SHC-s are not equivalent to a population of *N* replicators with a single server within the shared architecture: while any population of independent SHC-s always has a parallelism ratio of $R = 1$, individuals cannot share their servers. Thus while server numbers are the same for both architectures (i.e. S = 20 means in both cases that there are 20 servers performing parallel evaluation), the population sizes are not the same: in the shared architecture (due to the asynchronous evaluation of sequences), it cannot be avoided that while a

sequence is assigned to a server and waits for evaluation another sequence, just evaluated, adds an extra offspring to the population. Therefore in case of shared servers, the population number increases over time and will converge to $N_{max} = N + S$, and parallelism cannot increase above $R = ½$ (when $N = S$). Since sequences cannot be assigned freely to any server in case of SHC-s, the ratio of parallelism is always 1, and **only the absolute population size and number of parallel threads are comparable**. This allows us to identify the difference between the two architectures (shared and not shared servers).

First arrival times (Figure 21 and

Figure 22) indicate that the finding of the structural loops might be faster than for the shared architecture (dues to the gradient hill climbing required by the smooth fitness landscape *for the structure*), though the appropriate active site is found less efficiently (and time scales linearly with population size). This is because the fitness landscape becomes rugged when the structure is found: sequences could easily get trapped in local optima where from the correct active site is less probable to be found via mutations than to destruct the loop structure. Contrary to the SHC-s, the distributed population and shared architecture allows for a buffering effect: even if the structure is ruined, there is a population which probably stores at least one good individual that can be further replicated.

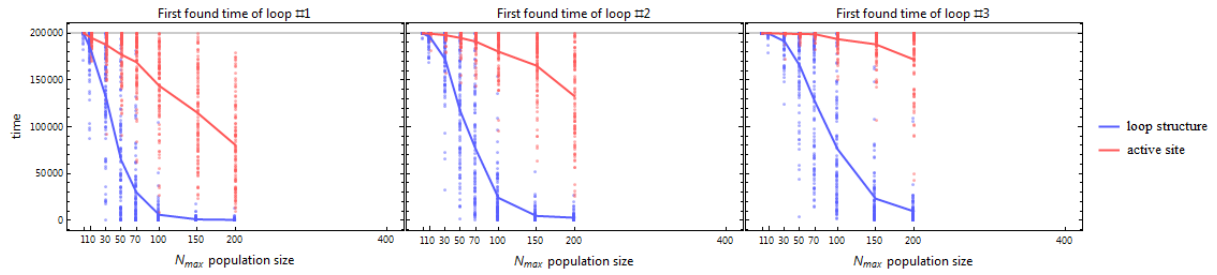


Figure 21. First arrival times of found loops (blue) and active sites (red) depending on the number of servers in case of independent stochastic hill climbers. Results for higher population numbers are still under analysis.

A **B**

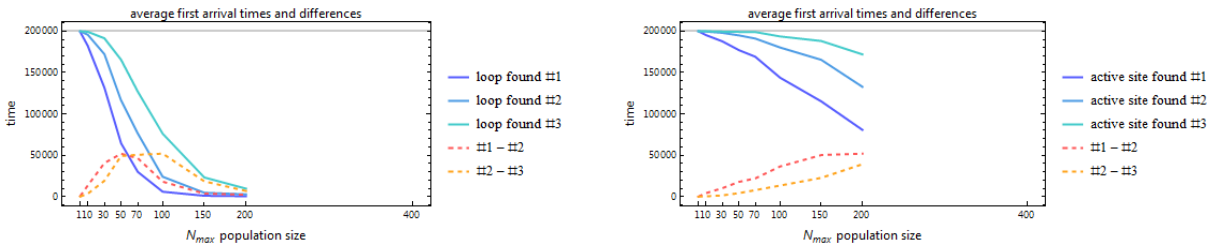


Figure 22. Superimposed average first arrival times (solid) and their differences (dashed) in case of independent stochastic hill climbers. Results for higher population numbers are still under analysis.

4.5 Conclusion and outlook

Parallel search scales better with parallelism (i.e. with number of servers per individuals) then linear: the time required for finding the first loop (#1, irregardless of which loop it is exactly in the structure) decreases faster than linear with increasing parallelism. This was expected and found for the SHC model as well.

Times required to find further loops/active sites (higher numbered #-s) are closer to the linear. This is expected (and found) for the SHC model as well.

Active sites are quickly found after the structure is found in case of the shared architecture. This is not expected for the SHC model, and results indicate that indeed independent SHC-s struggle finding the active site after the loop structure is found. This is because the shared parallel architecture allows both for redistribution of population slots to allow faster evolution and for buffering: even if a mutation (while searching for the correct active site) ruins an already found loop, the population might contain copies of the original parent that can be restored.

Further research should clarify why the second loop (L_2) is found usually at last instead of the rightmost L_3. For this, a special RNA target is going to be chosen where each loop, flanking and linking regions has equal lengths, to rule out any effect that might come from the fact that L_1 is the shortest in the standard tRNA.

Recombination is known to have a highly beneficial effect on search times. At the moment the shared architecture lacks this important component of true Darwinian evolution: individuals cannot recombine to produce better fit offspring. It is expected that allowing recombination of successful molecules would further decrease search times and would make the fine tuning of the active sites a much easier task. Finally, a *bona fide* evolutionary approach will be worked out for the Tenenbaum problem.

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