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RNA's Role in the Origins of Life: An Agentic 'Manager', or Recipient of 'Off-loaded' Constraints?

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Abstract:

In his Target Article, Deacon develops simple models that assist in understanding the role of RNA in the origins of life. However, his models fail to adequately represent an important evolutionary dynamic. Central to this dynamic is the selection that impinges on RNA molecules in the context of their association with proto-metabolisms. This selection shapes the role of RNA in the emergence of life. When this evolutionary dynamic is appropriately taken into account, it predicts a role for RNA that is consistent with the Managed-Metabolism Hypothesis about the origins of life, and inconsistent with Deacon's account.

Keywords:

origins of life; managed-metabolism; offloaded constraints; RNA management; management theory

1. Background

In his Target Article, Deacon sets out to provide an evolutionary account of "how a molecule like RNA or DNA could acquire the property of recording and instructing the dynamical molecular relationships that constitute and maintain the molecular systems of which it is part." To this end, he develops three variants of a model of "minimally complex" molecular processes. The simplest model represents the self-producing system that Deacon refers to as an Autogen. In essence, an Autogen comprises two self-organising components that facilitate each other's survivability: the first is a reciprocally catalytic group of molecules, and the second is a self-assembling capsid that can enclose the reciprocally catalytic group of molecules (the components of the self-assembling capsid are in turn catalysed by the reciprocally catalytic molecules). Deacon's third variant of the model incorporates RNA/DNA molecules. He refers to this model as exemplifying "*template mediated autogenesis* in which catalyst interaction constraints become offloaded onto a molecular structure." RNA/DNA is an example of a molecular structure that can become a recipient of such "offloaded" constraints.

In this commentary I will compare and contrast Deacon's model of the role of RNA/DNA in the origins of life with an alternative model known as the Managed-Metabolism Hypothesis (see Stewart, 1995, 1997, 2000 for the initial description and development of the Managed-Metabolism model. For an article devoted solely to explicating the model in detail and comparing it with other attempts to explain the origins of life, see Stewart, 2019). Broadly, this alternative account argues that the transition from non-life to life occurred when RNA-like molecules began to 'manage' proto-metabolisms. Proto-metabolisms are collectively-autocatalytic sets of smaller molecules, including peptides and eventually proteins. Initially, selection impinging on RNA-like molecules was likely to favour those that exploited autocatalytic proto-metabolisms in their immediate evolutionary interests. This could include the appropriation by RNA of resources from proto-metabolisms and the use of the resources to support the RNA's own self-production. But in appropriate circumstances, selection could also favour RNA-like molecules that actively 'managed' or 'farmed' an autocatalytic proto-metabolism. This involved RNA that intervened in the proto-metabolism in ways that increased the on-going stream of benefits that could be harvested from the metabolism by the RNA.

For example, RNA-like molecules could use their catalytic capacities to constrain an autocatalytic proto-metabolism in ways that enhanced the proto-metabolism's productivity and evolvability. This could boost the benefits that the RNA-like molecules could harvest from a proto-metabolism, and enable the benefits to be harvested on an on-going basis. The potential to increase these benefits was substantial because of the very limited evolvability of un-managed proto-metabolisms. The capacity of the RNA to enhance the evolvability of the proto-metabolism enabled it to unlock these benefits for its own use. In these ways, selection could favour a transition from 'pillaging' to 'farming', eventually tending to align the evolutionary interests of RNA-like molecules with those of the proto-metabolism they constrained.

Furthermore, selection would also tend to favour 'managers' whose interventions were digitally coded rather than analogically-informed. This is because the superior evolvability of digital processes enabled these managers to explore more effectively the space of possible interventions (see Stewart, 2019 for more detail).

2. Discussion

2.1 Commonalities Between the Two Models

The Autogen model and the Managed-Metabolism model share a number of key features. At their core, they both rely on the emergence of autocatalytic sets. These are organisations of molecules that are self-producing because they are collectively-autocatalytic (or reciprocally catalytic in Deacon's terminology). They are collectively-autocatalytic in the sense that the formation of every molecular species in the set is catalysed by at least one other member of the set. The extensive literature on the emergence and evolution of autocatalytic sets indicates that they have some capacity to evolve (see, for example, Kauffman, 1993; Vasas et al., 2012; Virgo and Ikegami, 2013; Nighe et al., 2015; Hordijk and Steel, 2017). As a consequence, autocatalytic sets have some capacity to discover adaptations that enhance their ability to survive. The Autogen model explicitly includes an example of one particular adaptation: the autocatalytic organisation catalyses the formation of molecules that can self-assemble to encapsulate the organisation and enhance its survival in some circumstances.

Both models also highlight the fact that the evolvability of these simple autocatalytic organisations is seriously limited. And both models argue that the existence of these serious limitations is very significant in explaining the role of RNA molecules in the transition from non-life to life. This is because the incorporation of RNA into autocatalytic organisations has the potential to overcome these limitations and can therefore be strongly favoured by selection. Although the Managed-Metabolism model identifies a wider range of impediments to the evolvability of autocatalytic organisations, both models agree that RNA has the potential to overcome those limitations that are due to side-reactions. These impediments are discussed further below.

2.2 Where the Models Diverge

However, beyond these core commonalities, the two models diverge significantly. I will argue that this is due to the fact that the Autogen model insufficiently represents a critically important evolutionary dynamic. Central to this dynamic is the selection that impinges on RNA molecules in the context of their association with collectively-autocatalytic proto-metabolisms. This selection shapes the role of RNA in the emergence of life. As I will show, when this evolutionary dynamic is appropriately taken into account, it predicts a role for RNA that is consistent with the Managed-Metabolism Hypothesis about the origins of life, and inconsistent with Deacon's account.

Deacon's elucidation of the selection dynamics that impinge on the RNA molecules is substantially limited to his statement that "Sequences [of nucleotides] that constrain catalyst interaction probabilities closer to the optimal interaction network will be selectively retained because of higher reproduction and repair rates [of the reciprocally catalytic organisation], and the nucleotide sequences that correspond to this will be more likely preserved and replicated." He seems to be suggesting here that the evolutionary interests of the RNA molecules tend to be aligned with those of the reciprocally catalytic organisation. He does not expand on this selection dynamic in his Target Article. He also seems to be suggesting that the RNA molecules are reproduced through time by a process of replication. Again, he does not expand on this or explicate how RNA replication emerged and evolved. He does not consider the possibility that RNA molecules were initially reproduced not by a process of self-replication, but by a collectively-autocatalytic process that may have been dynamically separate from the remainder of the collectively-autocatalytic proto-metabolism.

The central difference between the Managed-Metabolism model and the Autogen model arises because the Autogen model fails to take appropriate account of the selection impinging on RNA. This selection will tend to favour RNA that acts in its own interests. As a consequence, RNA will tend to act in the interests of a managed metabolism as-a-whole only when it is in the interests of the RNA to do so. If the role of RNA in the origins of life is to be properly understood and modelled, it is essential that the impact of this selection and its consequences are taken into account. When this selection is adequately taken into account, as it is by the Managed-Metabolism model, a role for RNA is predicted that is distinctly different to that envisaged by the Autogen model.

As the Managed-Metabolism model sets out to substantiate, selection impinging on RNA molecules would have tended to favour RNA that interacted with autocatalytic proto-metabolisms in ways that enhanced the fitness of the RNA. In relevant circumstance, this evolutionary dynamic could initially favour RNA that moved between instances of proto-

metabolisms, appropriating resources from them. In these circumstances, selection would have tended to favour RNA that developed agency in relation to proto-metabolisms. This could encompass relationships such as predation and parasitism. However, as the Managed-Metabolism model goes on to demonstrate, selection impinging on the RNA could also eventually favour a form of agency in which the RNA used its catalytic capacity and its dynamical separation from the proto-metabolism to manage a proto-metabolism in ways that enhanced the fitness of the RNA. This could include interventions in the proto-metabolism that boosted its productivity, including by overcoming the very restricted evolvability of un-managed proto-metabolisms.

In this way, selection could have driven the emergence of RNA managers that actively imposed constraints on a proto-metabolism in ways that enhanced the RNA's evolutionary interests. This is very different to the Autogen model which characterises the role of RNA as being the recipient of constraints that are "offloaded" from the proto-metabolism (these "offloaded" constraints begin as the dynamical constraints that constrain interaction possibilities within the proto-metabolism and that are distributed across the metabolism).

2.3 The Capacity of RNA to "Commandeer" and Control a Proto-Metabolism in its own Interests

Both models recognise that the ability of RNA molecules to constrain a proto-metabolism is enabled by the dynamical separation between the processes that reproduce the RNA and the processes that constitute the proto-metabolism. Deacon relies on the seminal work of Howard Pattee to establish this (e.g. Pattee, 1969). But the Managed-Metabolism model additionally draws on the work of Salthe (1985) who extended Pattee's work in a number of respects (e.g. see Stewart, 1995). In particular, Salthe emphasized that a key consequence of such a dynamical separation between processes is that it enables the constraining process to influence the constrained process without being influenced in return. This enables the constraining process to have power over the constrained process. In the case of the evolution of RNA, it enables RNA to have power over and to control a proto-metabolism.

The dynamical separation also means that the RNA can be subject to selection that is different to that impinging on the proto-metabolism and therefore to have different evolutionary interests. This selection will tend to favour RNA that uses its power over the proto-metabolism to advantage itself. Whenever the evolutionary interests of the RNA diverge from those of the proto-metabolism, those of the RNA will tend to prevail. And as the Managed-Metabolism Hypothesis emphasizes, selection can favour RNA that uses its power over a proto-metabolism to unlock the substantial benefits that can be realized once the serious impediments to the evolvability of the proto-metabolism are overcome.

At least implicitly, Deacon's description of the relationship between viral RNA and the cell it infects seems to recognise this kind of power relationship and separation of evolutionary interests (this is significant because Deacon states that his approach is "modelled after virus structure"). In particular, he suggests that when incorporated into a host cell, the viral RNA "commandeers the cell's systems" to make more capsid molecules and more copies of the viral RNA (my underlining). There is no suggestion here that the constraints that are applied by the viral RNA in order to commandeer the cells systems are somehow "offloaded" from the cell's systems to the RNA. Nor is there any suggestion that the interests of the viral RNA and the cellular metabolism somehow coincide. Instead there appears to be at least implicit

recognition that the selection impinging on the RNA virus favours RNA that actively and agentically uses its power over the cell's systems to pursue its independent evolutionary interests. Broadly, this is consistent with the traditional understanding of viruses and their evolution.

The Managed-Metabolism Hypothesis argues that it is equally appropriate to characterise the relevant relationships between RNA and proto-metabolisms as ones in which RNA "commandeers" proto-metabolisms in ways that further the RNA's own evolutionary interests. This characterisation is a much more accurate depiction of the relevant relationships and their evolution than that presented by the Autogen model. Contrary to the Autogen model, the evolution of these relationships is no more driven by the "offloading of constraints" than is the emergence of the relationships between RNA viruses and the cells they "commandeer".

The potential of selection to favour RNA/DNA that uses its power to advance its own interests at the expense of other living processes has long been understood, and is the subject of an extensive literature. Examples include meiotic drive in which DNA competes to bias the reproduction of the organism in its own interests, and, as has been modelled extensively, competition between RNA molecules that undermines the success of proto-cells that contain them. For more detail, see Maynard Smith (1979), Maynard Smith and Szathmáry (1995), and Werren (2011).

2.4 The Limited Evolvability of Un-Managed Proto-Metabolisms

As mentioned briefly above, a further difference between the two models concerns their identification of the limitations of the evolvability of proto-metabolisms. This is an important issue because it is the existence of these limitations that creates the potential for RNA to benefit significantly by constraining a proto-metabolism in ways that overcome these limitations. Both models identify how harmful 'side reactions' can limit the evolvability of a proto-metabolism (e.g. see Stewart, 2019).

But the Managed Metabolism Hypothesis demonstrates the existence of a further class of serious limitations to evolvability. These arise because molecular species that would potentially be able to make a significant beneficial contribution to the survivability of the proto-metabolism, might not be catalysed by any other members of the proto-metabolism. Without catalytic support within the proto-metabolism, they will not be able to persist within it and make this beneficial contribution. As a consequence, the ability of an evolving proto-metabolism to explore the space of beneficial organisational possibilities will be seriously limited. This limitation can be overcome by RNA that uses its catalytic capacity to catalyse the formation of beneficial molecular species that would not persist otherwise (Stewart, 1995, 1997). This limitation cannot be overcome merely by suppressing side reactions that might compete with the beneficial molecular species. This alone will not enable a beneficial molecular species that receives no catalytic support to persist in the proto-metabolism.

2.5 The Managed-Metabolism Hypothesis is Supported by a General Theory of Major Cooperative Evolutionary Transitions

A further strength of the Managed-Metabolism Hypothesis is that an abstract and generalised version (known as Management Theory), can explain not only the origins of life, but all other major cooperative evolutionary transitions. All of these transitions can be explained by the

emergence of Managers that use their power to intervene in collectively-autocatalytic organisations in ways that boost the stream of benefits that the Manager can harvest from the organisation. For detailed discussions of Management Theory, see Stewart (1995, 2020). In contrast, the key features of Deacon's model are not readily generalizable to the major cooperative transitions. For example, consider the case of the major cooperative transition in which complex human societies emerged that are managed by rulers who began as exploiters and plunderers. There would appear to be little justification in characterising this emergence as primarily being driven by the "offloading of constraints" from the societies onto the rulers.

3. Conclusions

Both Deacon's Autogen model and the Managed Metabolism Hypothesis set out to provide an account of the evolutionary processes that shaped the role of RNA/DNA in the origins of life. Both models begin with 'collectively-autocatalytic' systems of smaller molecules that are self-producing, but whose evolvability is seriously limited. Both see an emergent role for RNA/DNA in overcoming these limitations in evolvability. However, after this, the models diverge considerably. Deacon's model omits a critically important evolutionary process. When this process is appropriately taken into account, it reveals evolutionary dynamics that favour a significantly different account of the emergence of RNA/DNA and its role in the emergence of life. Broadly, this alternative account (the Managed-Metabolism Hypothesis) argues that proto-cells emerged due to selection favouring RNA-like molecules that used their power over a proto-metabolism to impose constraints on the metabolism that were in the evolutionary interests of the RNA-like molecules. Initially, selection would tend to favour RNA-like molecules that used their power unilaterally to appropriate resources from the proto-metabolism for its own immediate benefit. However, in appropriate circumstances, selection could eventually favour RNA that managed ('farmed') the proto-metabolism in ways that increased the stream of benefits that the RNA could harvest.

Characterising the evolutionary emergence of a proto-cell managed by RNA as the result of the "offloading of constraints" onto the RNA fails to adequately capture the key evolutionary dynamics involved in this emergence. It provides no basis whatsoever for Deacon's large claim that: "In other words, it might make sense to invert the order of Crick's central dogma when considering the evolution of the genetic code."

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