

## Re: Metabolism first?

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One more detailed comment: The review accepts uncritically Eigen's assertion that there is an inherent limit on RNA replication fidelity at around 1 error per 100 bases – in the absence of protein catalysts. This is simply not so. In fact, there is no tangible limit to the accuracies which can be achieved, even by simple catalysts, if you are willing to waste some energy. The mechanism is known as 'kinetic proofreading'. It involves the kinetic balance between two competing chemical reactions – a productive one producing template-directed polymerization from activated monomers; and a destructive one (exonuclease) degrading polymers to non-activated monomers. Both processes take place simultaneously. It is assumed that there is some slight preference for the polymerization process to add the right nucleotide over the wrong one. It is also assumed that the hydrolytic exonuclease reaction slightly favors the removal of mispaired monomers. Finally, it is assumed that the two processes are in a close balance with a slight bias toward net polymerization. Under these circumstances, replication fidelity can be arbitrarily high, even with simple catalysts – as long as you are willing to pay the energy cost of repeatedly reactivating the monomers which were degraded by the futile cycle. Therefore, I consider your long review of proposed mechanisms to avert the 'error catastrophe' as something of a 'red herring'.

But I think you are missing the bigger picture and the bigger question

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what is coding for?

Whatever replicant or string of RNA survives IS the selected one, is the one that codes most correctly, is the one that codes best, because it codes for stability in that environment or it would be unstable and wouldn't exist.

Why coding at all? Each and every time to better fit the environment (that's what all the processes of life are).

There is never a time

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when coding would be selected that makes life less stable and less likely to exist in its environment .

And I'll add the reverse rule.

Coding is always for what is most stable in that environment.

This can be confusing because sometimes some parts of life are less stable such that overall other life is more stable – but the stability pluses always outweigh the stability minuses.

Overall every coding is for stability (though over 4 billion years, perhaps the stability is not for that individual organism or even that single species – but for life over