

Cryptic functions and the need for imperfection

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Can we learn from evolution? Is it possible to design political and cultural roadmaps inspired by what we learn from nature? Neutral Genetic variations expand the conformational landscape of proteins and may underlie cryptic functions that influence protein adaptability under unfavourable conditions. Cryptic functions usually associate with regions of decreased structural stability (frustrated) or even disordered, whose role in evolutionary adaptation is increasingly being recognized. Hence, the balance between protein stability and controlled disorder translates in the dichotomy between the need to allow adaptability (innovation) while conserving functional stability (sustainability). Therefore, the most comprehensive measure of protein fitness is a mix of innovation and sustainability defined as *innovability*. In this context, understanding how genetic variations affect protein fitness is not trivial, since cryptic functions behind frustrated regions are not easily detectable.

In this seminar, we will illustrate the concept of protein fitness using human alanine:glyoxylate aminotransferase (AGT) as a model. AGT is present as a common major allelic form (AGT-Ma) and a minor polymorphic form (AGT-Mi) expressed in 20% of Caucasian population and considered a lower limit of AGT fitness. We will show that AGT retains an high degree of structural frustration, because this likely represents an evolutionary advantage possibly related to protein-protein interactions.

The take home message of the seminar is that naturally occurring genetic variations tip the balance between protein stability and frustration to encode cryptic functions that expand the innovability-potential of the protein. Interestingly, these concepts can be easily translated to a Culture and Society context, as the lesson of evolution is that imperfection is useful. Therefore, a multi-cultural society, although apparently more disordered, has more chances to react and adapt to the global changes that we are facing.

For further reading

<https://pubs.acs.org/doi/10.1021/acs.accounts.0c00813>

<http://www.ncbi.nlm.nih.gov/pubmed/25461797>

<http://www.nature.com/articles/nrg1426>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4737706/>