PELE: Protein Energy Landscape Exploration: a la carte drug design tools

Description

Let’s imagine that we have developed a drug with very good potency for some cancer therapy. However, with time, many patients start developing resistance to the drug due to some particular point mutation as a result of the high metabolism of the cancer cells. Or let’s imagine that some specific treatment for a virus has lost its efficacy due to some viral mutation. Those mutations are not largely affecting the protein, since it is obviously still functional, but most likely affect some dynamical aspect of it, such as conformer stabilization, entrance channel, etc… that inhibits the drug binding and/or delivery. Or simply let’s imagine that we are stuck in the development of our drug. To fix theses problems we would like to obtain the atomic mechanism for the drug-protein dynamical behaviour, and modify our original drug accordingly. Such a study, by experimental means, is quite complex, time consuming and expensive.

Now let’s imagine that we connect our computer to a server, that we introduce the coordinates of our protein, the mutation, the drug, and that we go to sleep. The day after we obtain an email: our results are ready. The computer modelling has obtained the drug-protein recognition mechanism, from which we can proceed and design a novel drug, “a la carte novel drug”. With several drug candidates, we repeat the process and obtain one that does indeed bypass the mutation, or has the desired affinity …

We developed such a tool, of such a server. Although it might seem a futuristic view, we have developed technological advances that this is possible today.

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