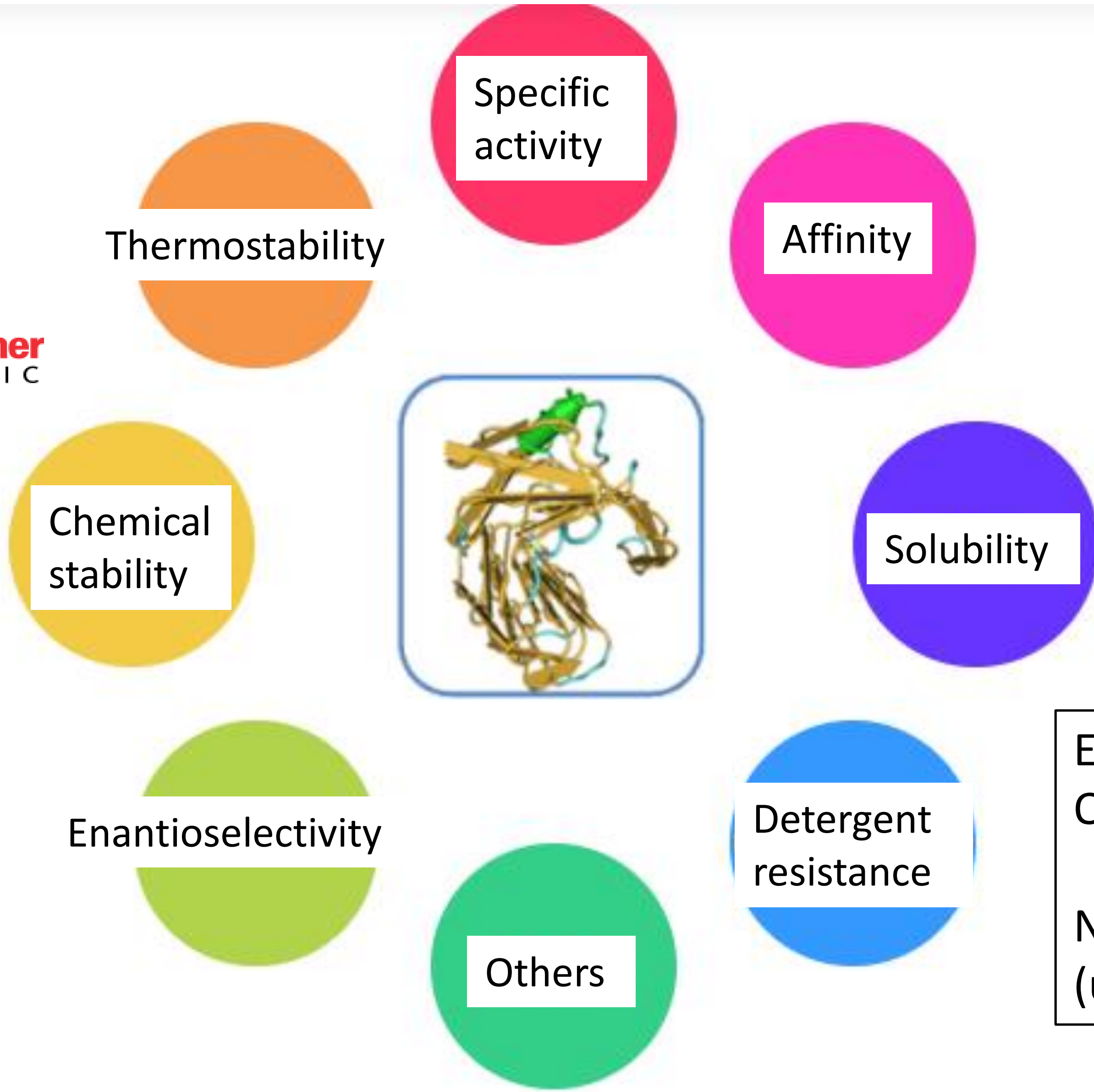
Vídeo #3

<u>Continuação</u>: Enzimas modificadas e não naturais



Enzyme Optimization

Novel Enzymes (unnatural)

“What is directed evolution and what does it have to do with chemistry?”

https://www.chemistryworld.com/news/what-is-directed-evolution-and-why-did-it-win-the-chemistry-nobel-prize/3009584.article

Frances H. Arnold (Caltech-USA): 50 % of 2018 Chemistry Nobel Prize

Directed evolution of enzymes:

Evolution of enzymes to catalyze commercially useful chemical reactions to make biofuels, medicines and laundry detergent, among other things. In many processes, they have taken the place of toxic chemicals (*chemical catalysts*). Bases:

1. it’s easy to understand why chemists like using enzymes to catalyse reactions
2. many bonds chemists are interested in aren’t made by any natural enzyme

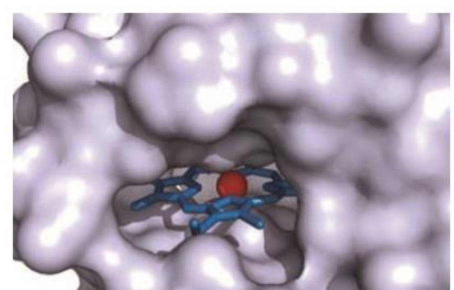
Directed evolution of enzymes tailors them to operate in new reaction conditions, **optimises their catalytic activity towards new substrates**, and **makes them catalyse new chemical reactions**. Directed evolution of enzymes has widely expanded the repertoire of useful biocatalysts. The evolved enzymes offer efficient and environmentally-friendly alternatives to metals and organic catalysts in chemical and biotechnical industries.

NEWS

Engineered enzyme first to forge carbon–silicon bond

BY JAMIE DURRANI

Protein offers new way to synthesise organosilicon compounds



The nature of chemical innovation: new enzymes by evolution*

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Quarterly Reviews of Biophysics (2015), 48(4), pages 404–410 doi:10.1017/S003358351500013X

Abstract. I describe how we direct the evolution of non-natural enzyme activities, using chemical intuition and information on structure and mechanism to guide us to the most promising reaction/enzyme systems. With synthetic reagents to generate new reactive intermediates and just a few amino acid substitutions to tune the active site, a cytochrome P450 can catalyze a variety of carbene and nitrene transfer reactions. The cyclopropanation, N–H insertion, C–H amination, sulfimidation, and aziridination reactions now demonstrated are all well known in chemical catalysis but have no counterparts in nature. The new enzymes are fully genetically encoded, assemble and function inside of cells, and can be optimized for different substrates, activities, and selectivities. We are learning how to use nature's innovation mechanisms to marry some of the synthetic chemists' favorite transformations with the exquisite selectivity and tunability of enzymes.

P450s participate in the metabolism of sex hormones (steroids), vitamin D, and bile acids in mammals, ecdysones in insects and terpenes in plants. P450 monooxygenase systems also participate in the metabolism of a variety of drugs and other xenobiotic substances and provide one of the primary means by which the body rids itself of toxic substances. P450s also participate in the conversion of aromatic hydrocarbons into potent carcinogens → **reações redox!**

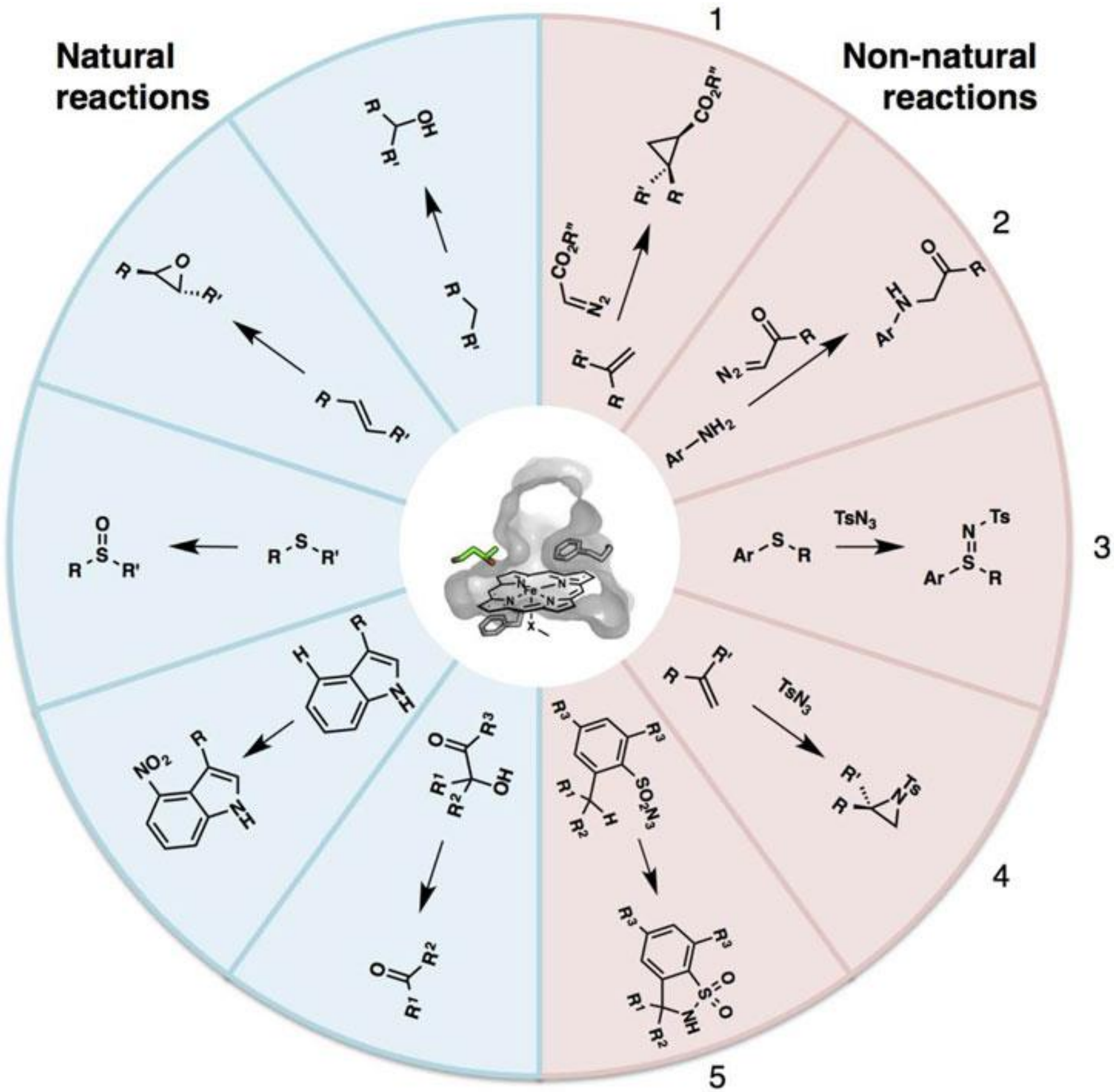

Fig. 1. Natural reactions catalyzed by cytochrome P450s (blue) and new, non-natural reactions catalyzed by enzymes derived from cytochrome P450 by protein engineering and evolution (red).

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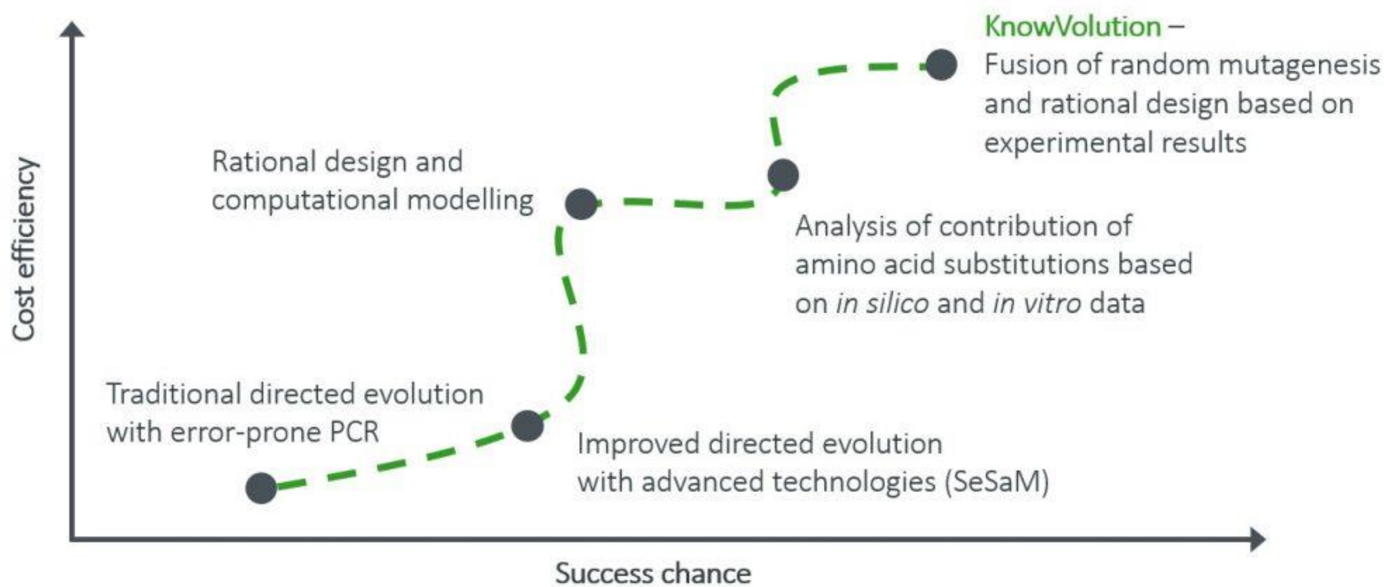
"QuESt employs our protein engineering strategy "**KnowVolution**"



https://www.sesam-biotech.com/enzyme services/quest?gclid=EAIaIQobChMI49e1nNX13QIVhF6GCh2SYwWdEAAYASAAEgJWyPD_BwE

Enzimas naturais e modificadas

Dìaz-Rodríguez & B. G. Davis, (2011) Chemical modification in the creation of novel biocatalysts, Curr. Opin. Biotechnol.,15: 211-219.

H. Yu, Y. Yan, C. Zhang & P.A. Dalby (2017) Two strategies to engineer flexible loops for improved enzyme thermostability, Scientific Reports, 7:41212 | DOI: 10.1038/srep41212