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Evolvability and epistasis studied through the lens of an antibiotic resistance enzyme

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Stellingen

Behorende bij het proefschrift

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1. Mutations of Ile105 are highly beneficial for BlaC fitness. (Chapters 2 & 4)
2. The buffer environment can greatly impact the phenotypic features of BlaC β -lactamase. (Chapter 3)
3. The residue at position 105 is crucial for regulating accessibility to the BlaC active site. (Chapters 2 & 4)
4. Excessive enzyme stability leads to elevated protein concentration in the bacterial periplasm. (Chapter 5)
5. Bacterial transformation efficiency is the major bottleneck in directed evolution campaigns.
6. Understanding the origins of epistasis is the first step toward predicting evolution.
7. Carbapenems are the most promising β -lactam antibiotics for the treatment of bacterial infections.
8. Stabilizing mutations with global compensatory potential are the main source of sequence variability in enzymes.
9. Embracing uncertainty and finding meaning in suffering is essential for conquering your goals.
10. Give it enough time, and evolution will always find a way.

Marko Radojković
Leiden, 12 september 2025