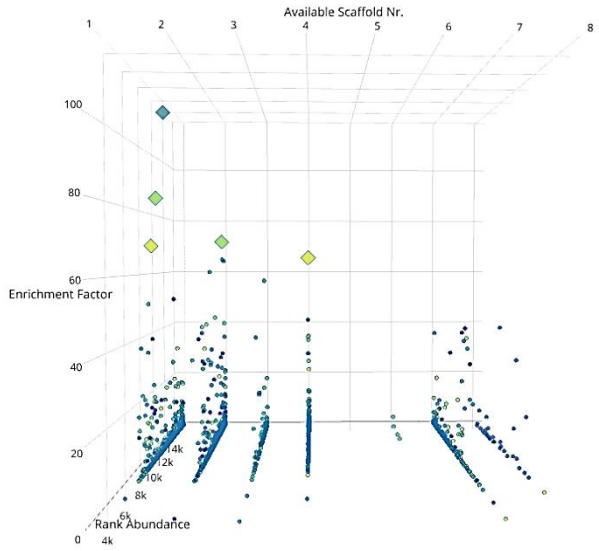
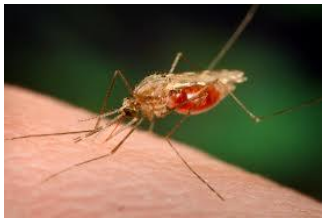
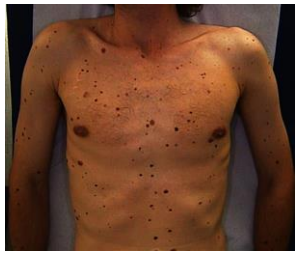
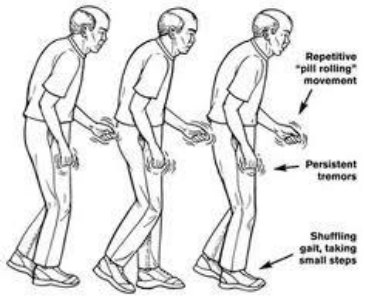
Wirkstoffsuche mit DNA-kodierten Molekülbibliotheken – von der Romantik zur Ratio



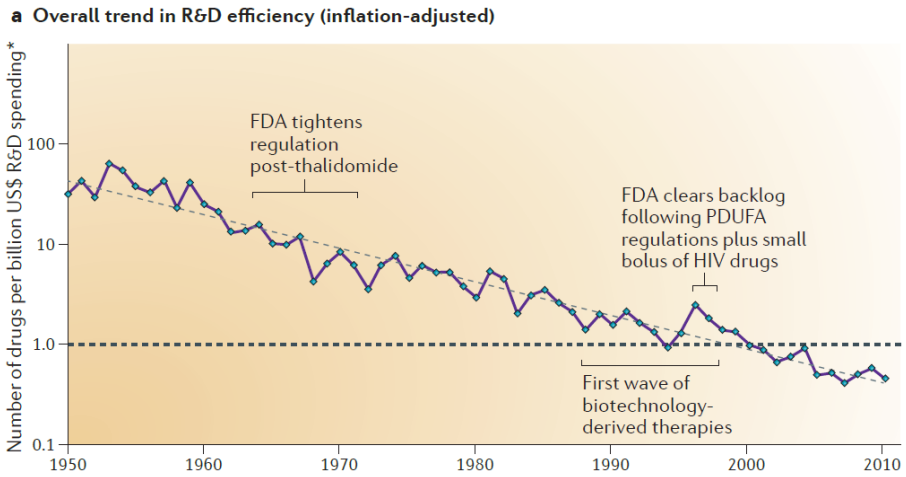






Diagnosing the decline in pharmaceutical R&D efficiency

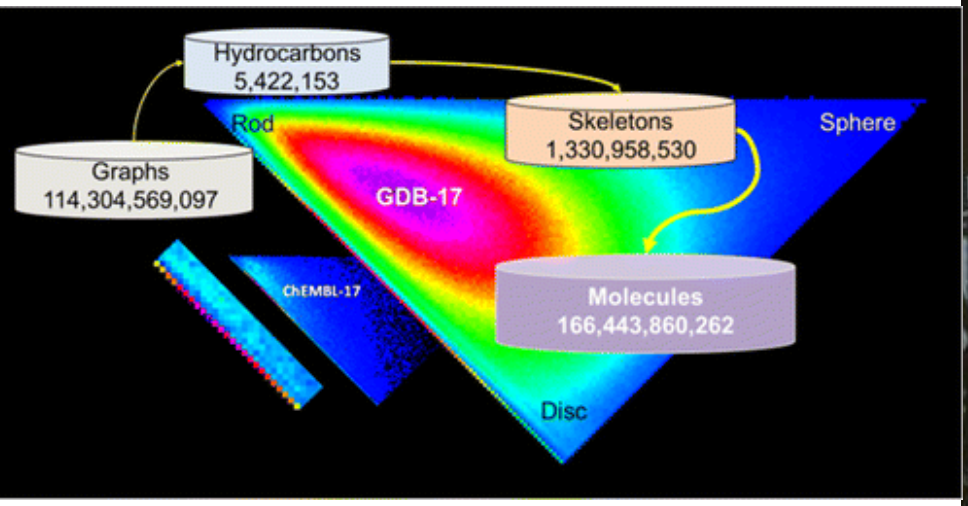
NATURE REVIEWS | DRUG DISCOVERY



Entwicklungskosten eines Medikaments: 1,6 Mrd $

Technologien für die Arzneimittelentwicklung: gesellschaftlich relevant

Wirkstoffsuche



Wirkstoffsuche

- Screening von Molekülbibliotheken (**≈1 Mio.**)
- Warum nur und warum diese 1 Mio. Moleküle?

Abdeckung des chemischen Raums?

Follmann, Drug Disc. Today, 2018; Reymond, Acc. Chem. Res. 2015, „**The chemical space project**“

DNA-kodierte Molekülbibliotheken

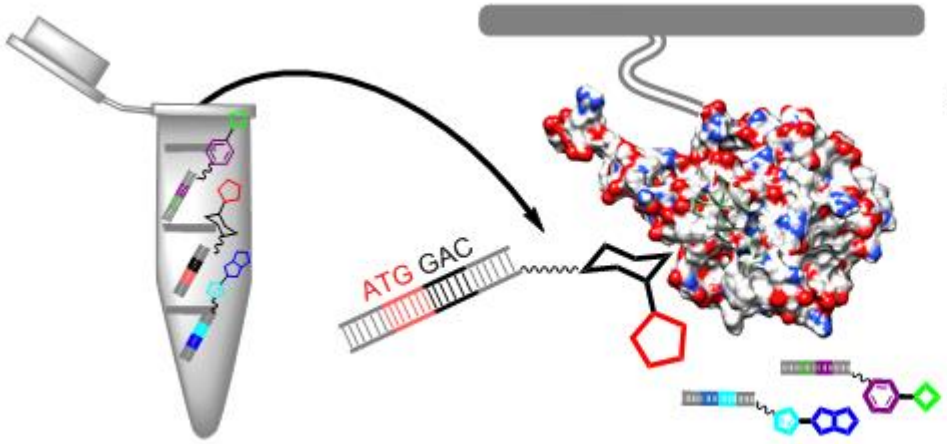
Phänotyp-Genotyp-Kopplung

DNA-kodierte Molekülbibliotheken

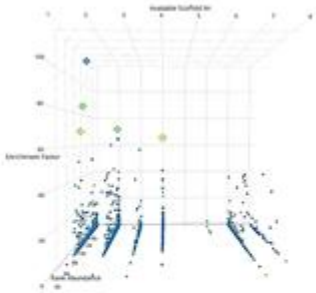
DNA-Encoded Libraries, „DELs“

Skalierung von Screeningbibliotheken

DNA-kodierte Molekülbibliotheken



DNA sequencing



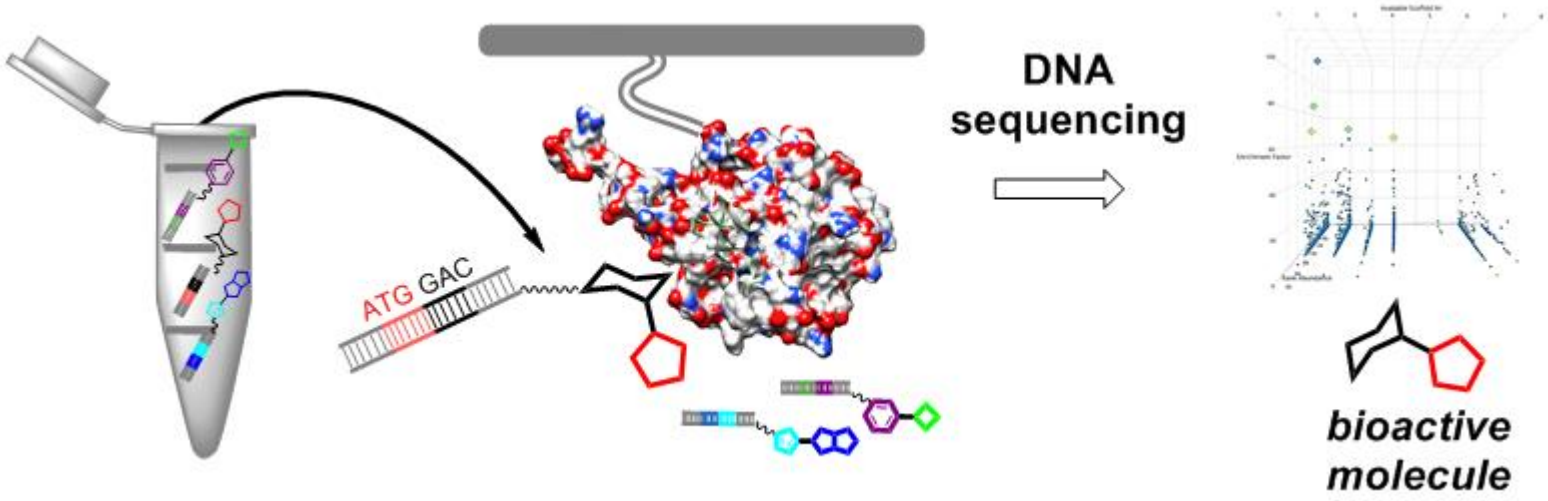
bioactive molecule

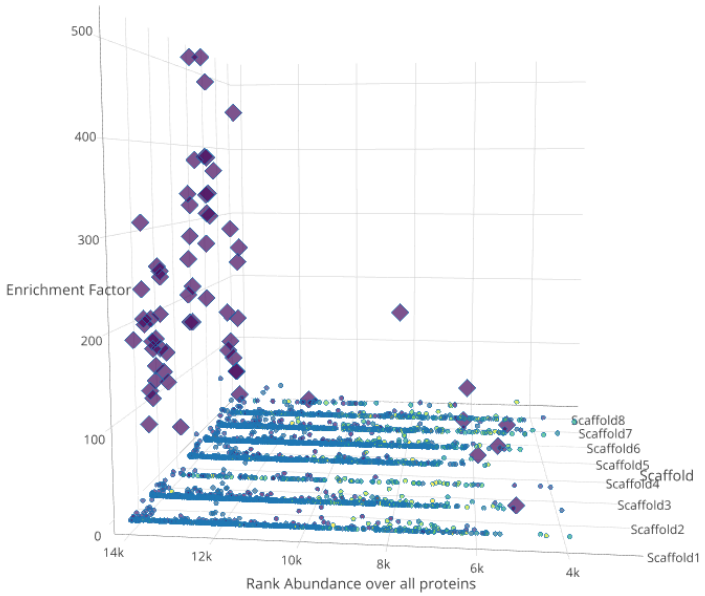
Wirkstoffidentifizierung durch Selektion

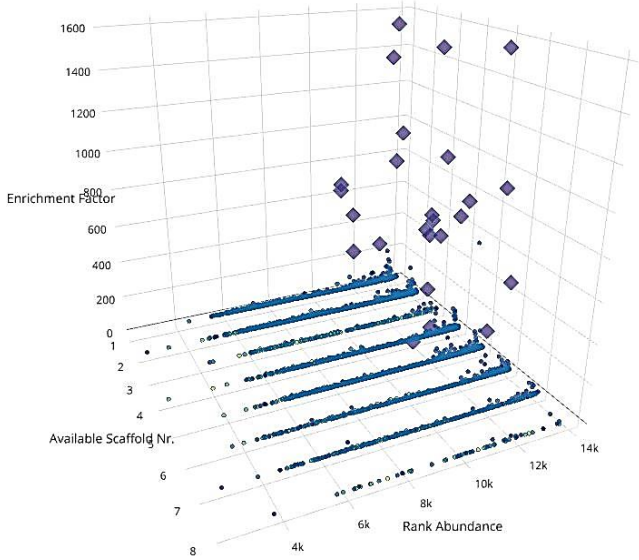
- generisch, effizient
- DNA-Sequenzierung
- bis 300 Mio. Datenpunkte
- Statistik!

Salamon, ACS Chem. Biol. 2016; Harris, J. Med. Chem. 2017

DNA-kodierte Molekülbibliotheken

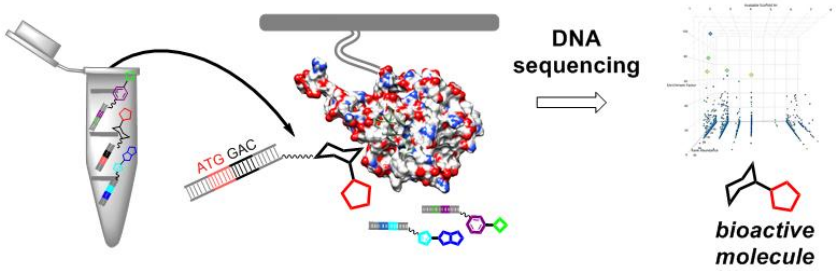


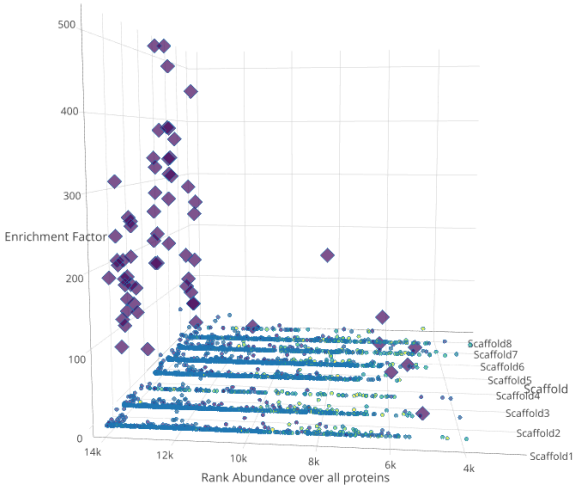




8.000 Moleküle – 20 Mio. Datenpunkte – Wirkstoffkandidaten

DNA-kodierte Molekülbibliotheken





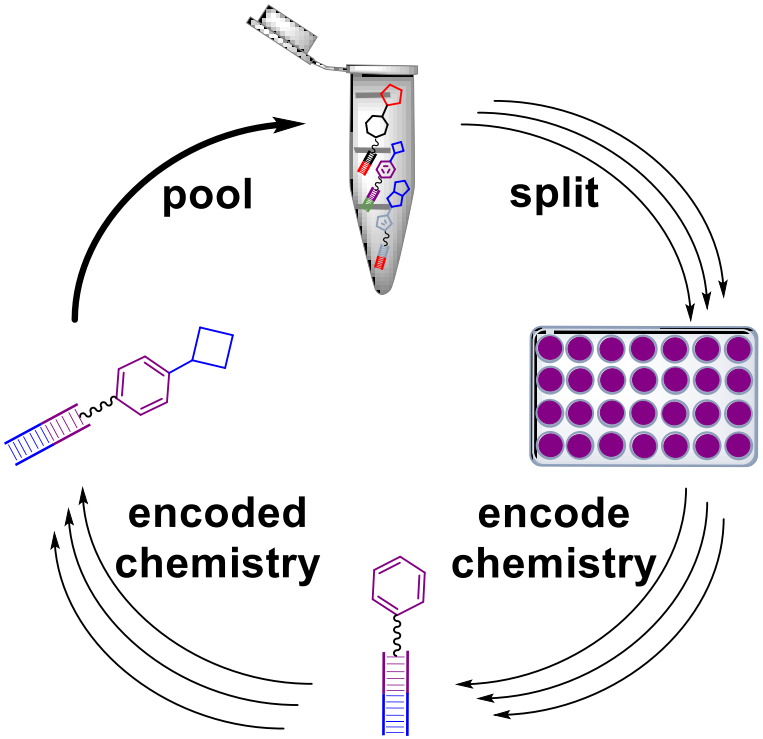
Problem 1:

Schnellere Datenverarbeitung von 300 Mio. Datenpunkten

Problem 2:

Statistik zur Identifizierung von spezifischen Wirkstoffen

DNA-kodierte Molekülbibliotheken



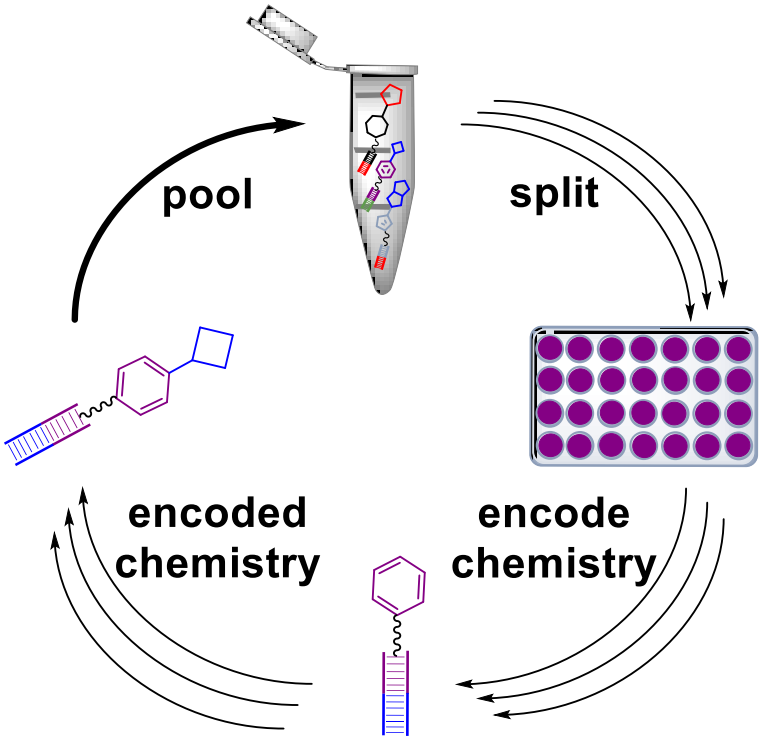
Synthese von DELs: Kombinatorik

Chemoresistentes Genom: *Chem. Sci*. 2017

Mizellare Katalyse: *J. Am. Chem. Soc*. 2019

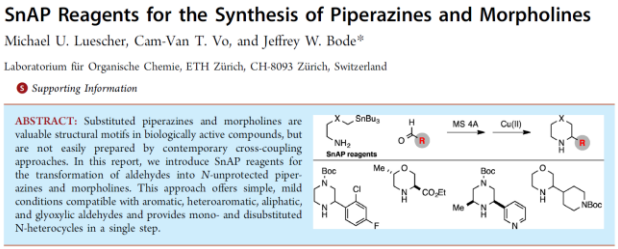
Problem: Design von Synthesewegen!

DNA-kodierte Molekülbibliotheken



Problem: Design von Synthesewegen!

Derzeit: Chemische Intuition - Romantik



SnAP Reagents for the Synthesis of Piperazines and Morpholines

Michael U. Luescher, Cam-Van T. Vo, and Jeffrey W. Bode*

Laboratorium für Organische Chemie, ETH Zürich, CH-8093 Zürich, Switzerland

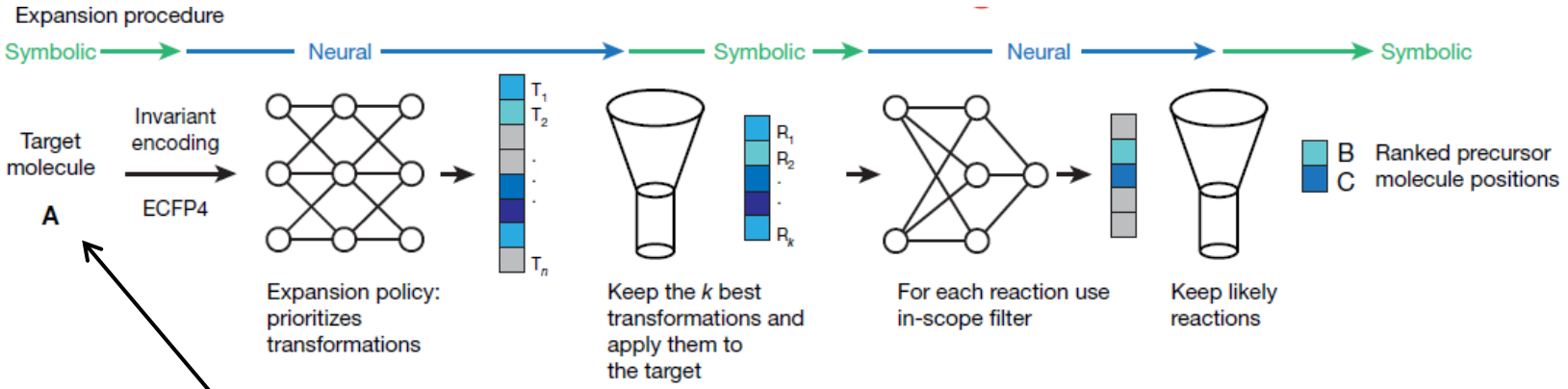
Supporting Information

ABSTRACT: Substituted piperazines and morpholines are valuable structural motifs in biologically active compounds, but are not easily prepared by contemporary cross-coupling approaches. In this report, we introduce SnAP reagents for the transformation of aldehydes into *N*-unprotected piperazines and morpholines. This approach offers simple, mild conditions compatible with aromatic, heteroaromatic, aliphatic, and glyoxylic aldehydes and provides mono- and disubstituted N-heterocycles in a single step.

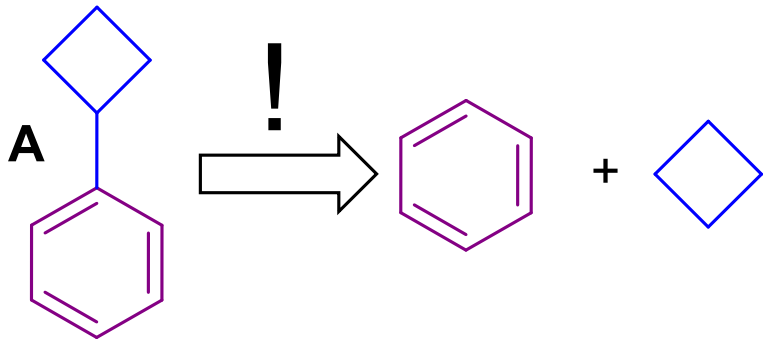
DNA-kodierte Molekülbibliotheken

Planning chemical syntheses with deep neural networks and symbolic AI

Marwin H. S. Segler[1,2], Mike Preuss[3] & Mark P. Waller[4]



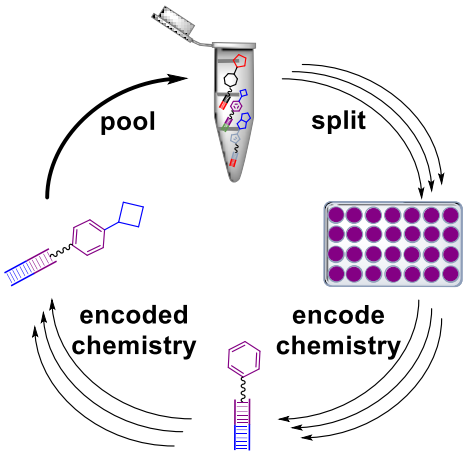
Rationale Syntheseplanung einer Zielstruktur

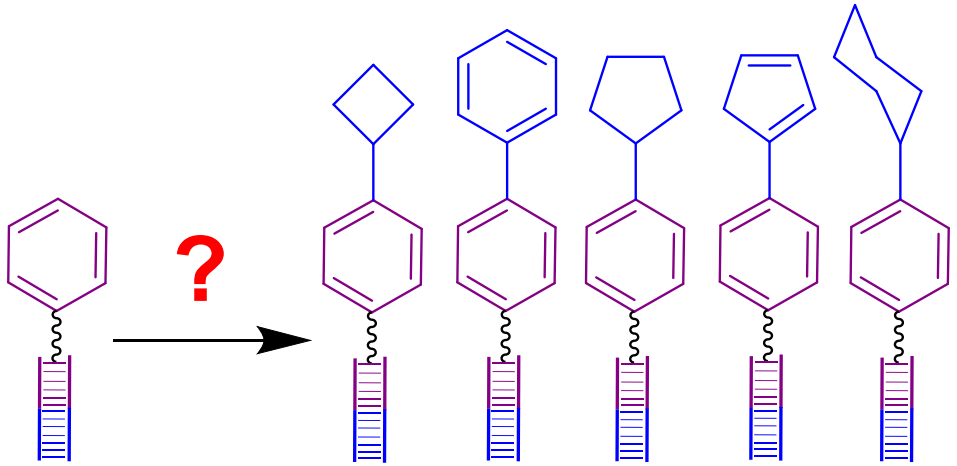


DNA-kodierte Molekülbibliotheken

Problem: Rationales Design von Synthesewegen!

Rationales Design chemischer Diversität





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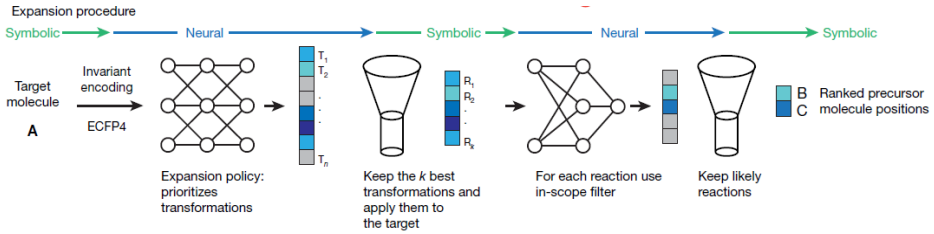
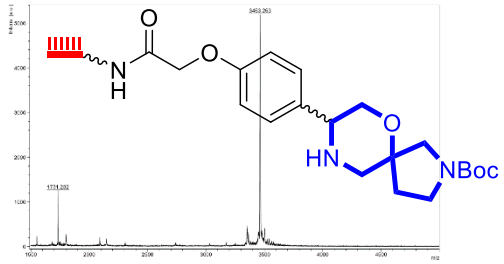
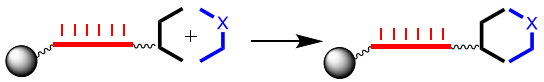


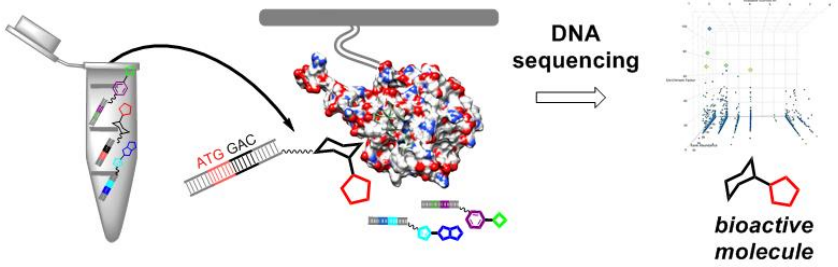
Technologieentwicklung

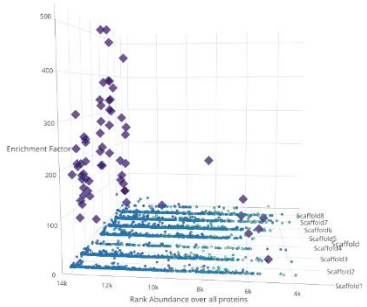




ATGCAG

Chemische Diversität





Molekulare Evolution

technische universität dortmund

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EM images

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Analysis of sequencing data

Ina Dormuth and Lukas Arendt

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Bundesministerium für Bildung und Forschung