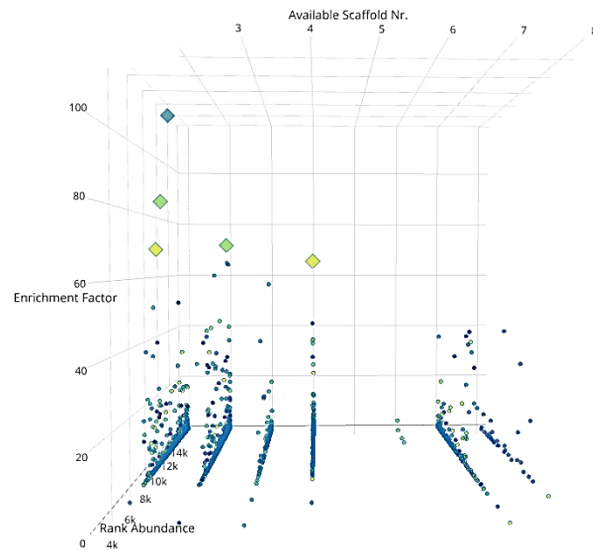
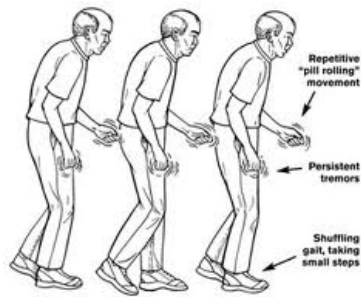


Wirkstoffsuche mit DNA-kodierten Molekülbibliotheken –

von der Roma

zur Ratio

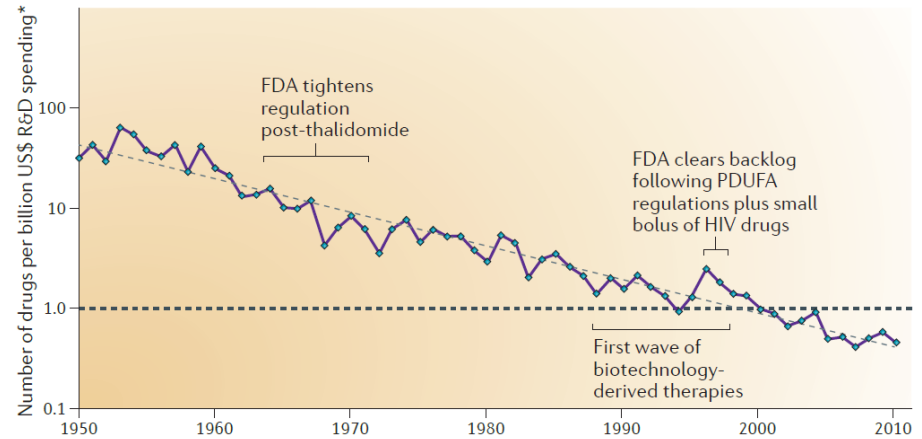




Diagnosing the decline in pharmaceutical R&D efficiency

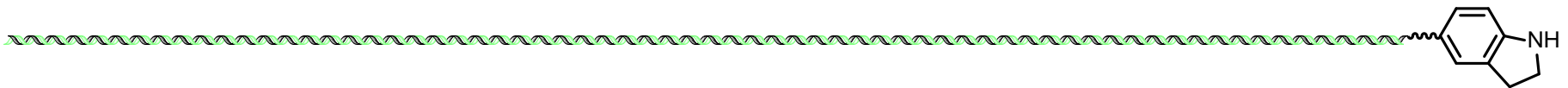
NATURE REVIEWS | DRUG DISCOVERY

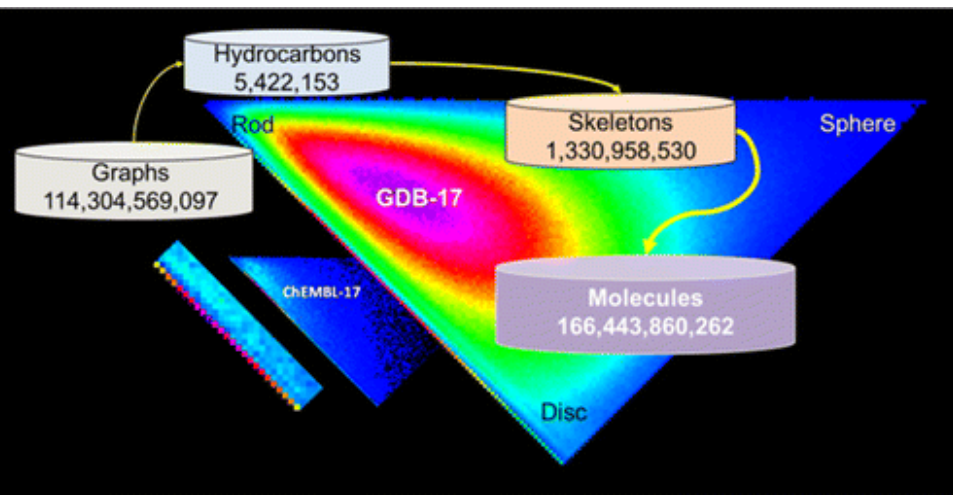
a Overall trend in R&D efficiency (inflation-adjusted)



Entwicklungskosten eines Medikaments: 1,6 Mia \$

**Technologien für die Arzneimittelentwicklung:
gesellschaftlich relevant**

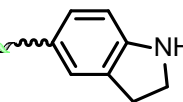




Wirkstoffsuche

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

Abdeckung des chemischen Raums?



DNA-kodierte Molekülbibliotheken



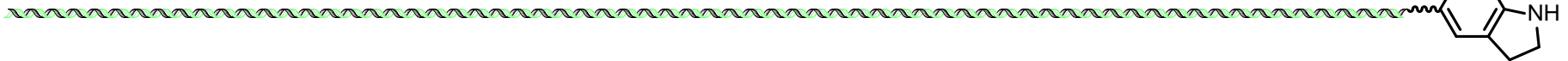
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AGCTACTTCCCAAGGCACATGCACATGCACATGGGGCCCTATTCTTAG-LINK-Gly-Gly-Gly
AGCTACTTCCCAAGGCACATGCACATGACGGTAGGGCCCTATTCTTAG-LINK-Met-Gly-Gly
AGCTACTTCCCAAGGCACATGACGGTACACATGGGGCCCTATTCTTAG-LINK-Gly-Met-Gly
AGCTACTTCCCAAGGCACATGACGGTAACGGTAGGGCCCTATTCTTAG-LINK-Met-Met-Gly
AGCTACTTCCCAAGGACGGTACACATGCACATGGGGCCCTATTCTTAG-LINK-Gly-Gly-Met
AGCTACTTCCCAAGGACGGTACACATGACGGTAGGGCCCTATTCTTAG-LINK-Met-Gly-Met
AGCTACTTCCCAAGGACGGTAACGGTACACATGGGGCCCTATTCTTAG-LINK-Gly-Met-Met
AGCTACTTCCCAAGGACGGTAACGGTAACGGTAGGGCCCTATTCTTAG-LINK-Met-Met-Met
    
```

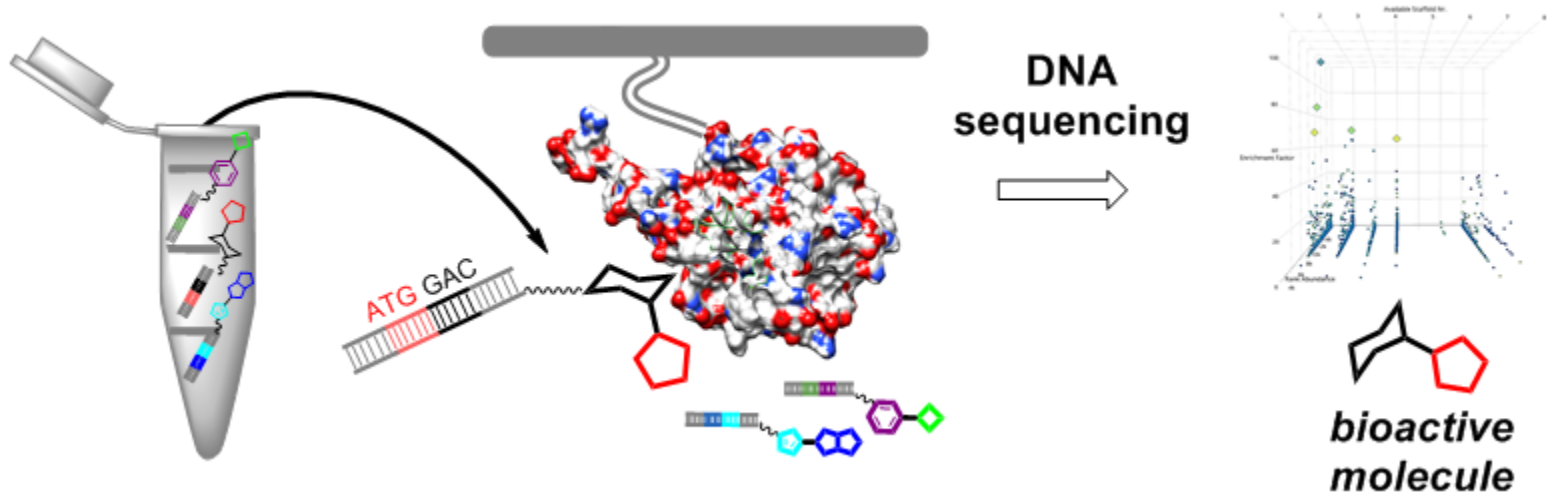
Phänotyp-Genotyp-Kopplung

DNA-Encoded Libraries, „DELs“

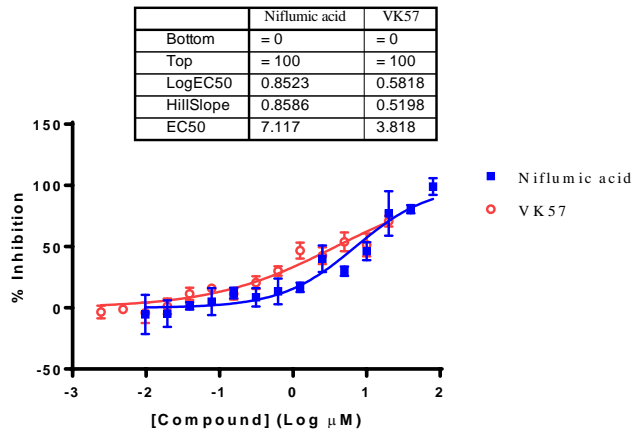
Skalierung von Screeningbibliotheken



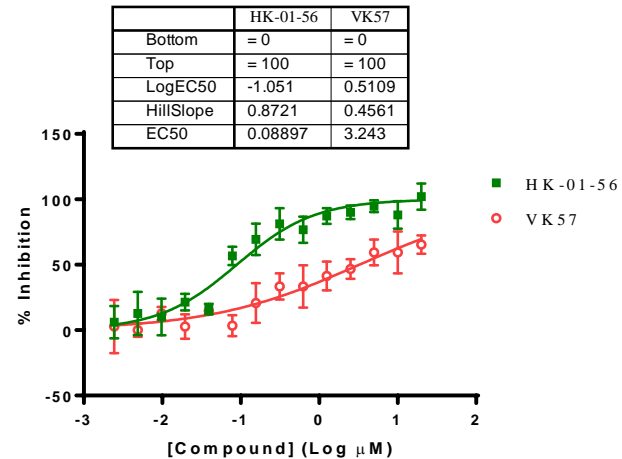
DNA-kodierte Molekülbibliotheken



Competitive Binding to TEAD Central Pocket

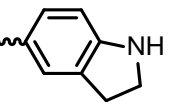


Inhibition of YAP Binding to TEAD

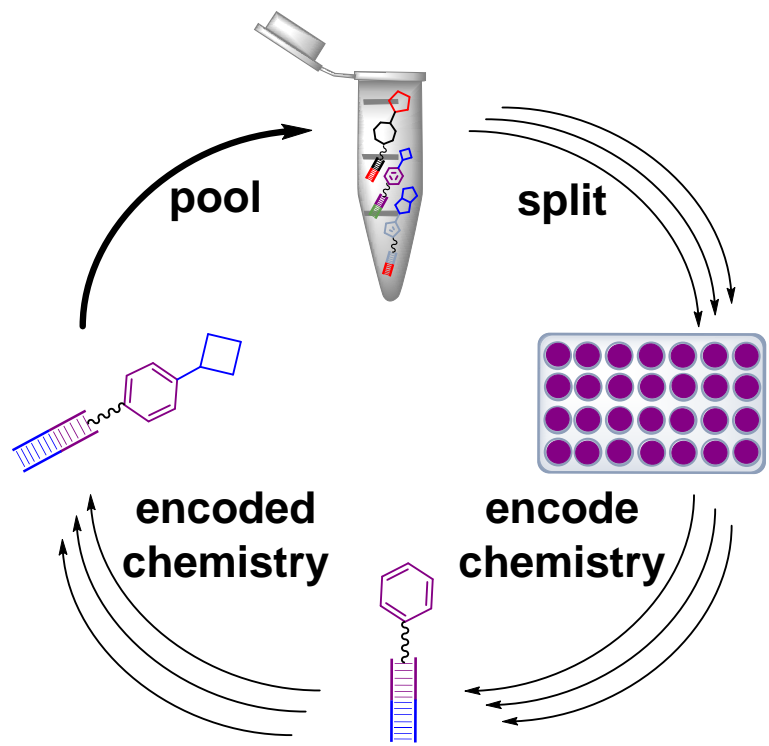


8.000 Moleküle – 20 mio Datenpunkte – Wirkstoffkandidaten

mit Profs. Rahmenführer and Fried (Department of Statistics, TU Dortmund)



DNA-kodierte Molekülbibliotheken

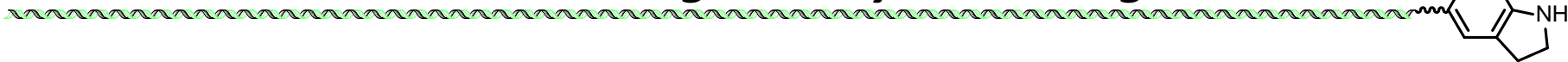


Synthese von DELs: Kombinatorik

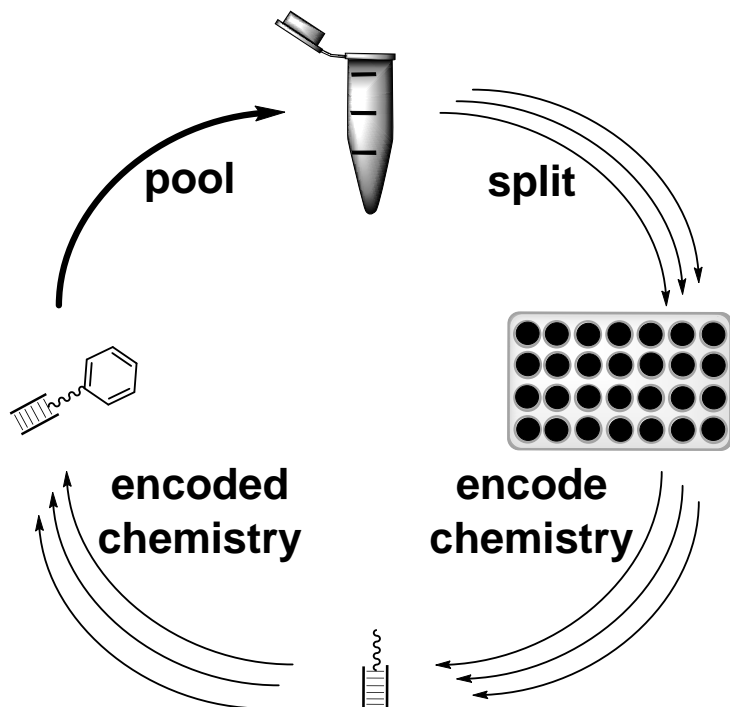
Chemoresistentes Genom: *Chem. Sci.* **2017**

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

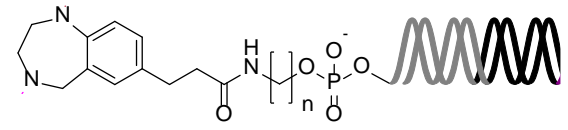
Problem: Design von Synthesewegen!



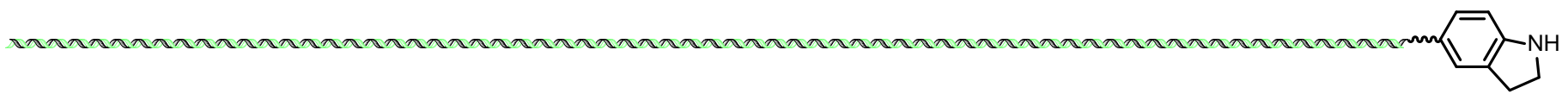
Synthese von DELs: Kombinatorik
Chemoresistentes Genom: *Chem. Sci.* **2017**
Mizellare Katalyse: *J. Am. Chem. Soc.* **2019**
Problem: Design von Synthesewegen!

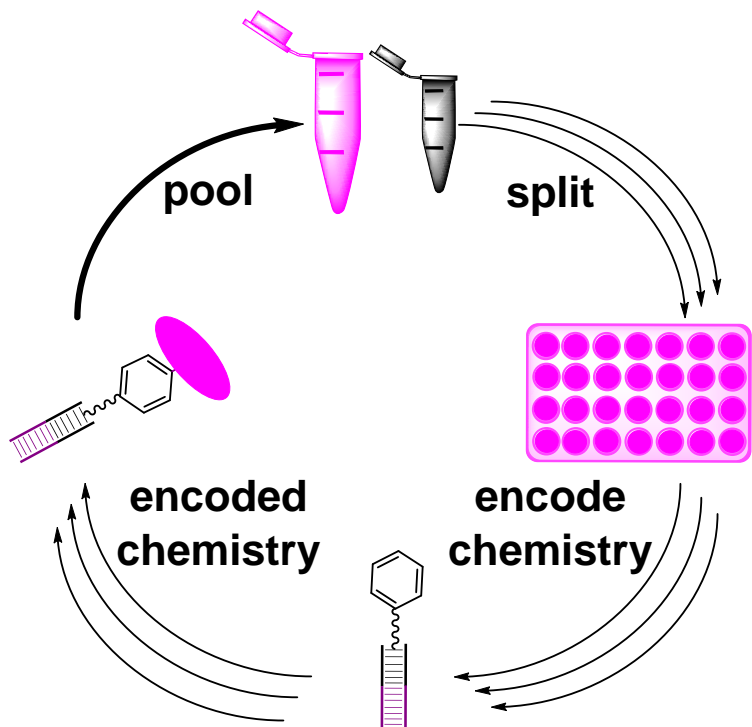


split and pool
combinatorial chemistry

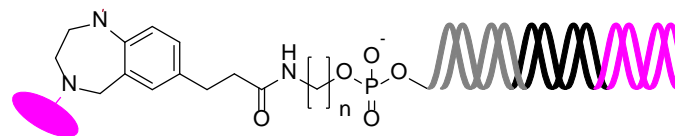


encoded library

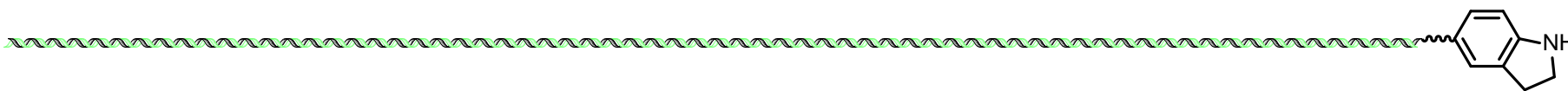


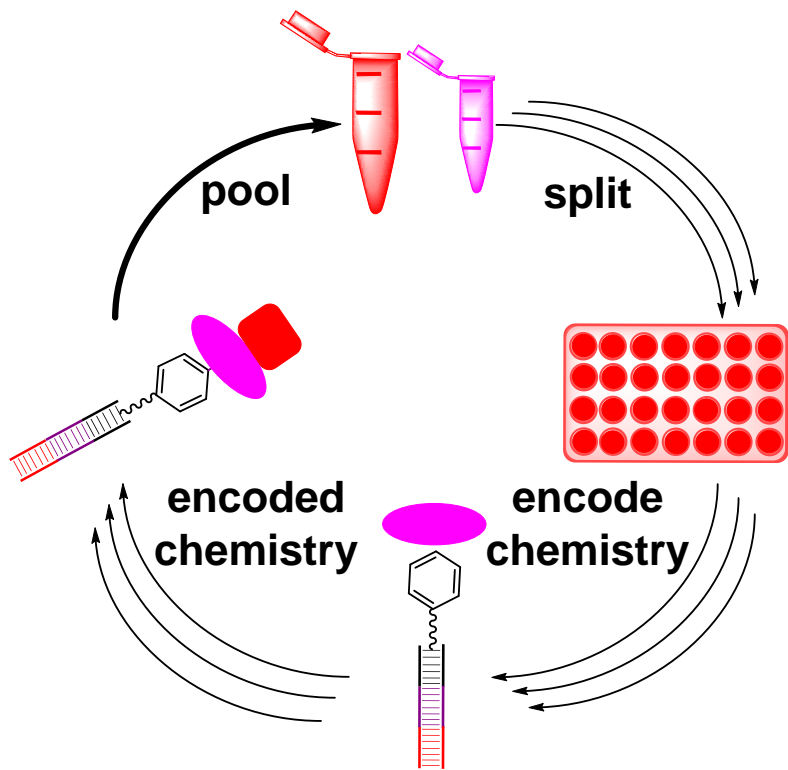


split and pool
combinatorial chemistry

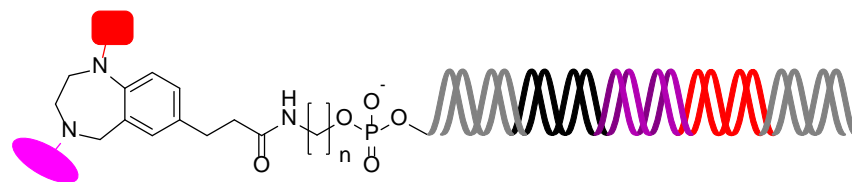


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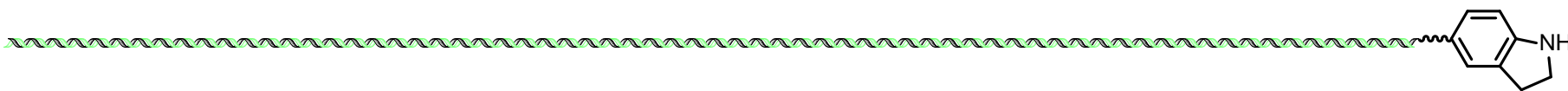


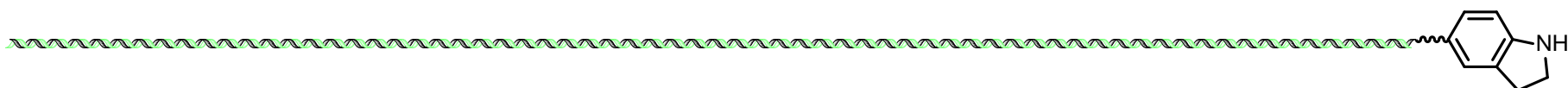
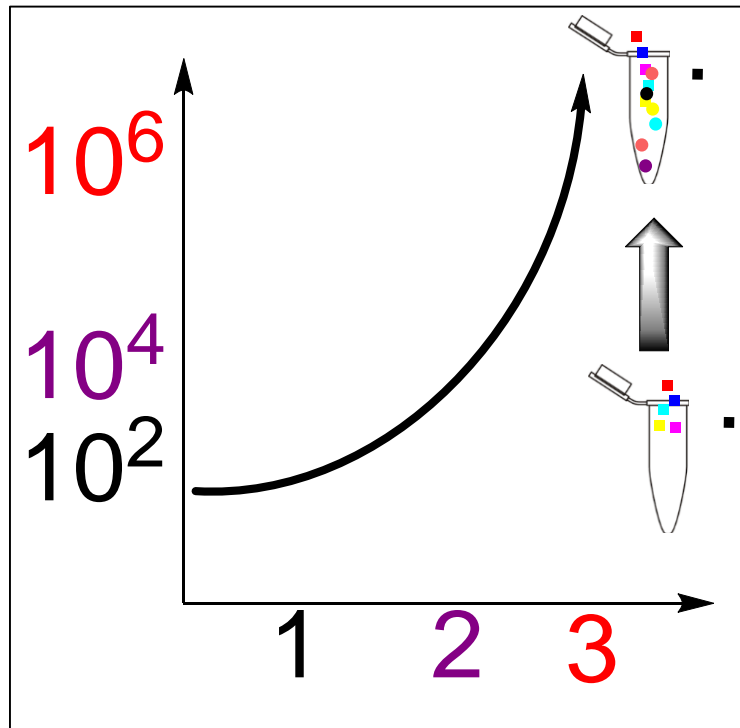
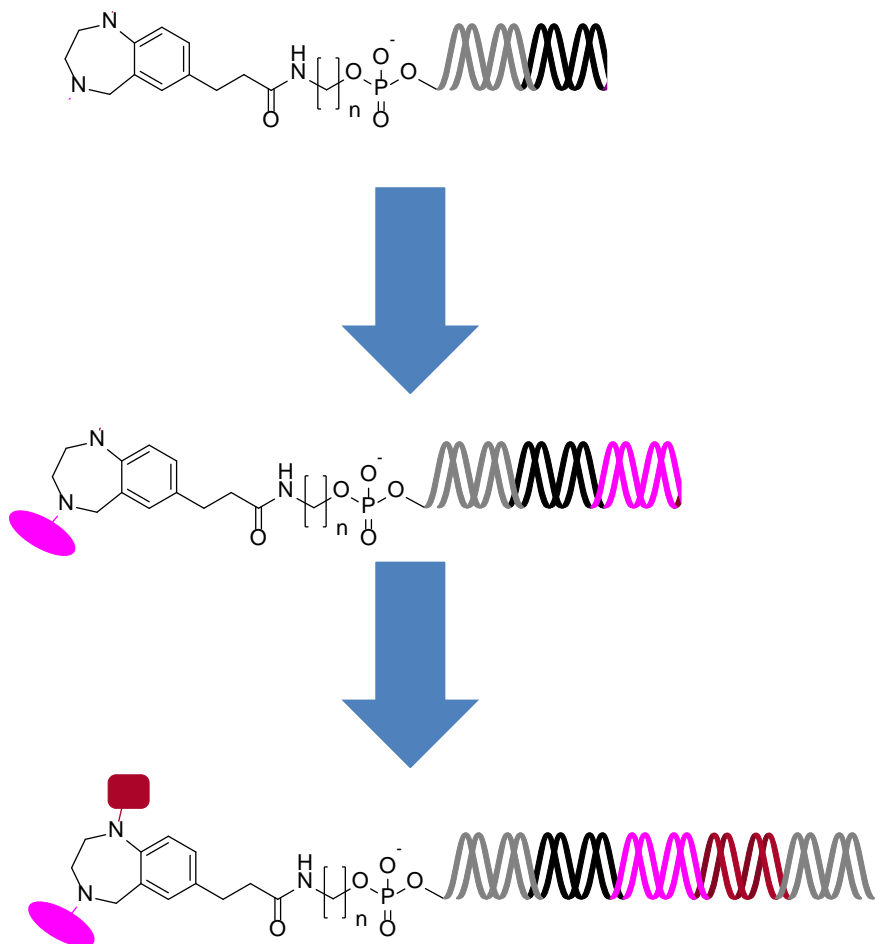


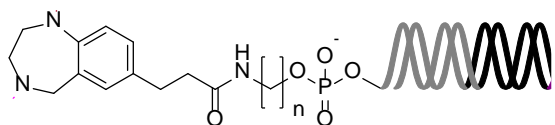
split and pool
combinatorial chemistry



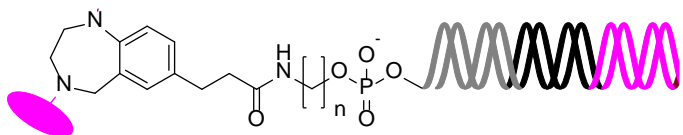
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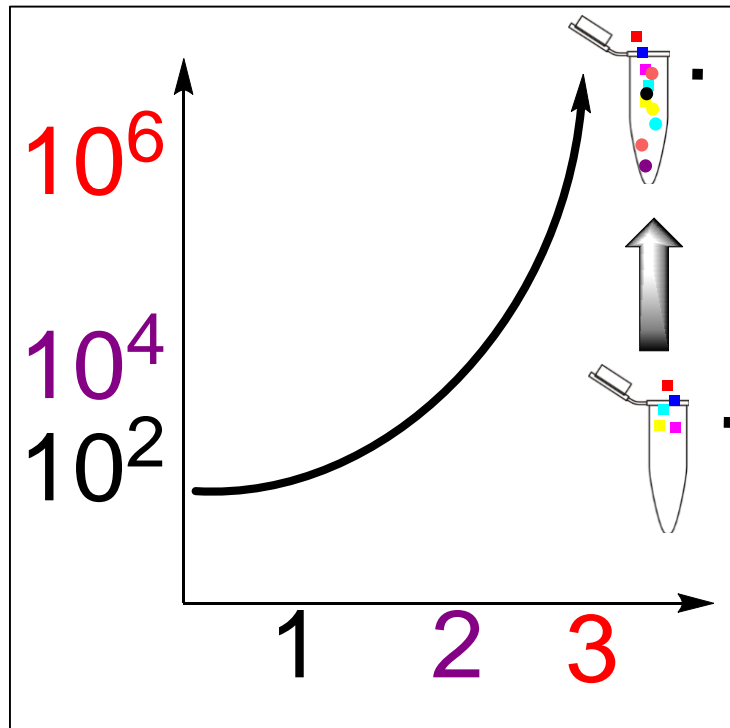
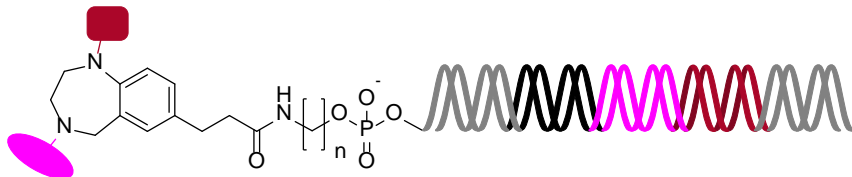




Chemische Intuition



Chemische Intuition



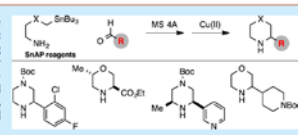
SnAP Reagents for the Synthesis of Piperazines and Morpholines

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

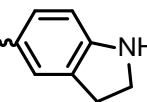
Laboratorium für Organische Chemie, ETH Zürich, CH-8093 Zürich, Switzerland

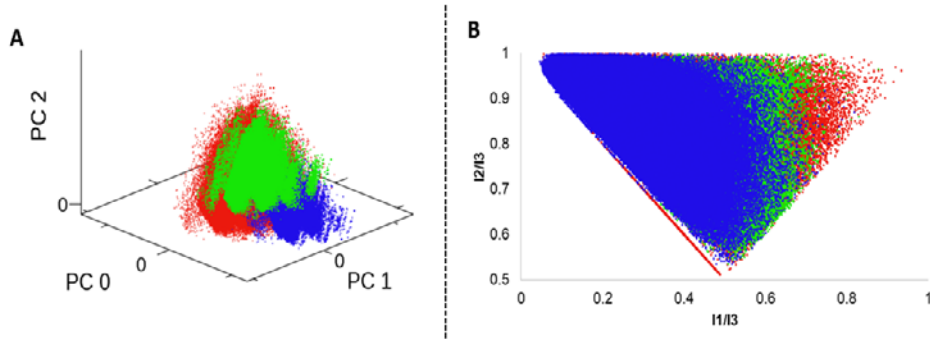
Supporting Information

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.



Derzeit: Design von DELs durch chemische Intuition

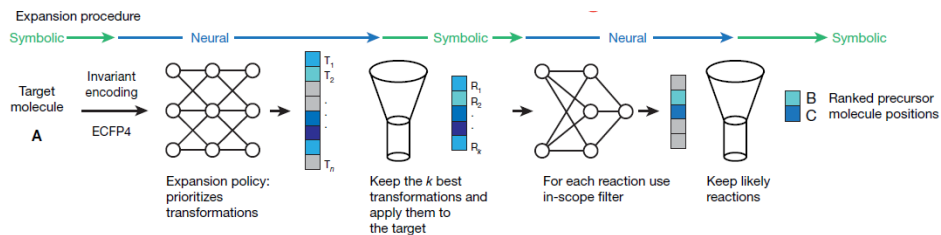




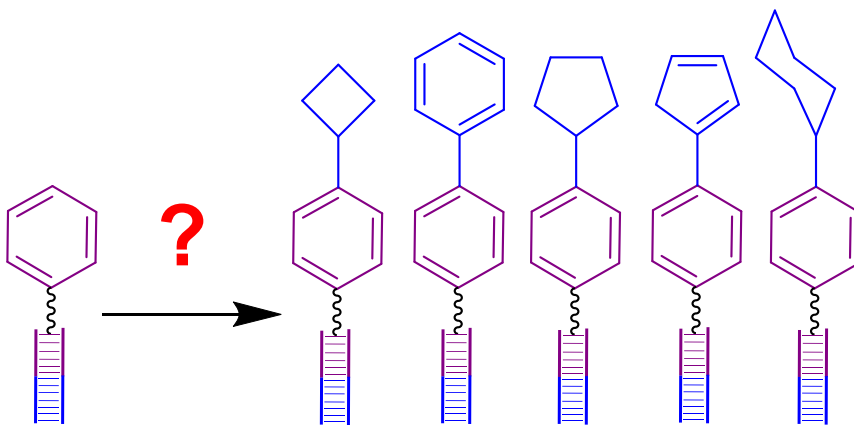
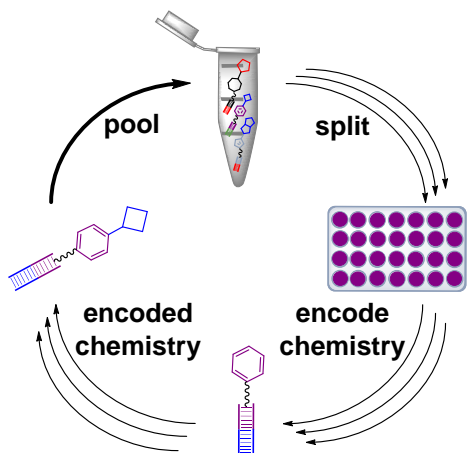
post-hoc-Analyse von Molekülbibliotheken
rationale Auswahl von Ausgangsprodukten

Planning chemical syntheses with deep neural networks and symbolic AI

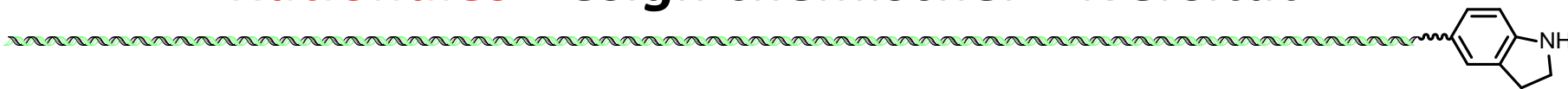
Marwin H. S. Segler^{1,2}, Mike Preuss³ & Mark P. Waller⁴

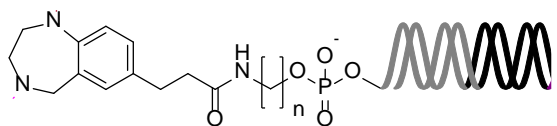


Retrosynthese von Molekülen

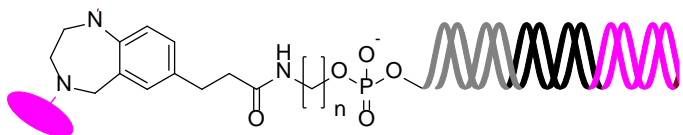


Problem: Rationales Design von Synthesewegen!
Rationales Design chemischer Diversität

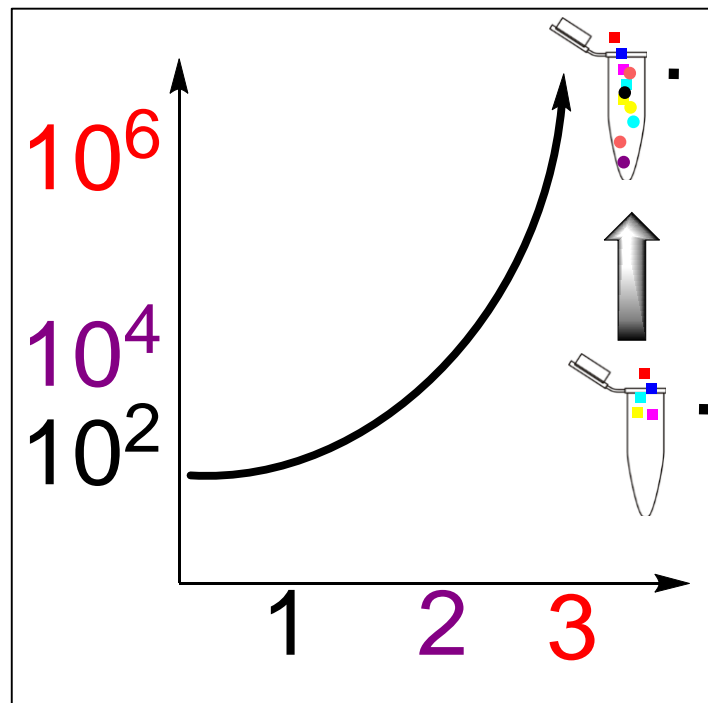
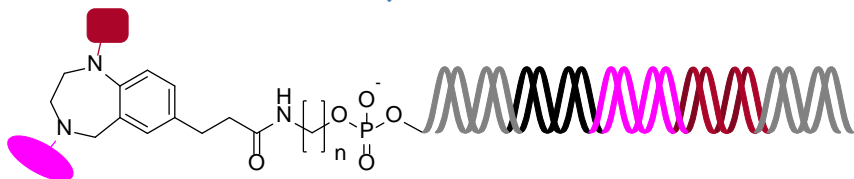




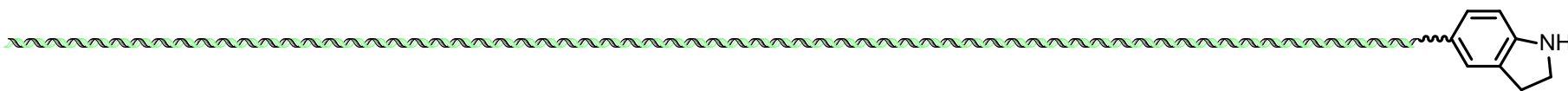
Chemie 1
Chemie 2
Chemie 3

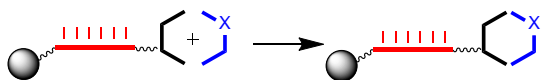
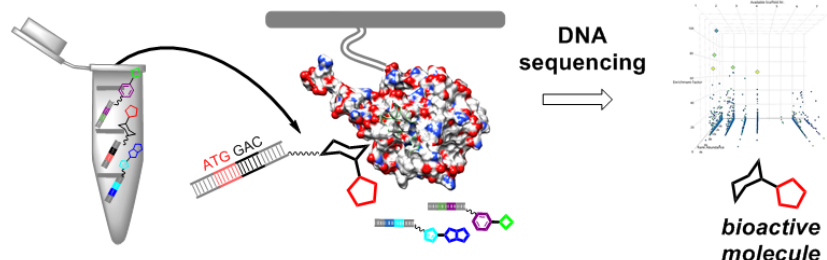
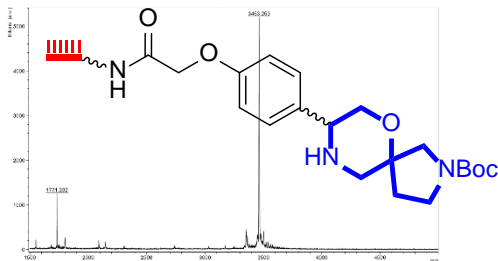


Chemie 1
Chemie 2
Chemie 3



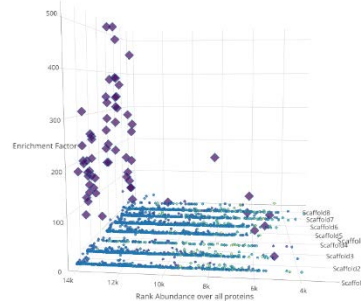
Design chemischer Diversität durch Synthesewege?



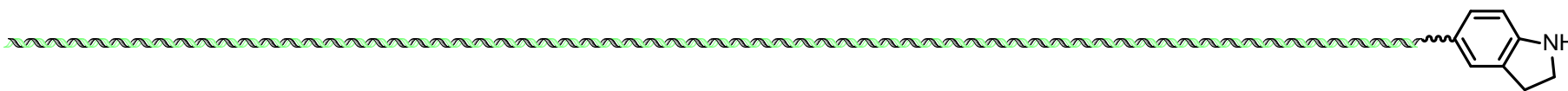


ATGCAG

Chemische Diversität



molekulare Evolution





The DNA-Team

- Silvia Chines
- Katharina Götte
- Mateja Klika Škopić
- Verena Kunig
- Marco Potowski

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- Prof. Herbert Waldmann

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- Prof. Ralf Weberskirch, TUDo
- Prof. Jeffrey Bode
- Prof. Alexander Dömling



EM images

- Sabrina Pospich
- Prof. Stefan Raunser, MPI Dortmund

Analysis of sequencing data

- Ina Dormuth and Lukas Arendt
- Prof. Jörg Rahnenführer, TUDo
- Prof. Roland Fried, TUDo



Boehringer Ingelheim Stiftung



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