Artificial Intelligence for Antibiotic Discovery

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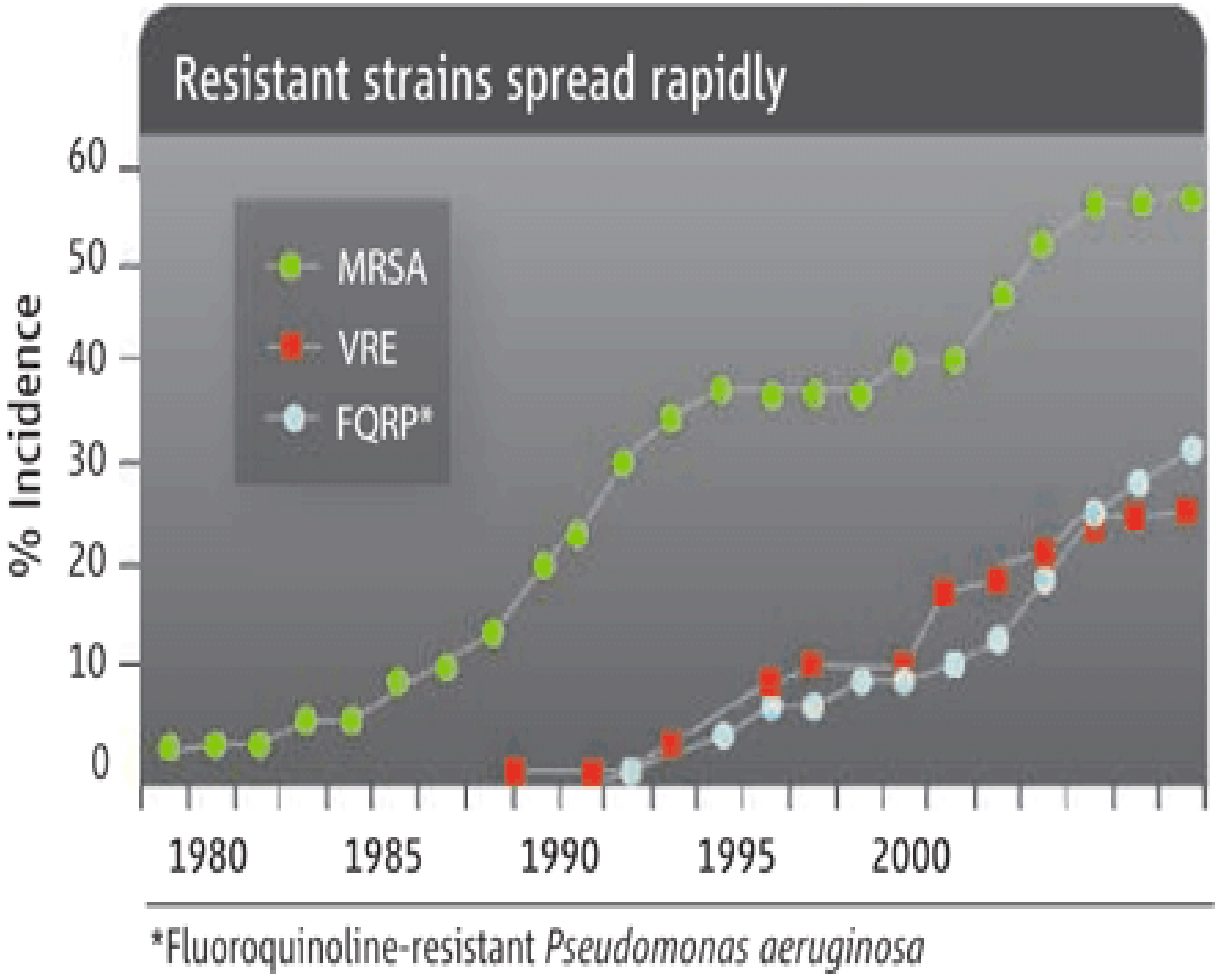
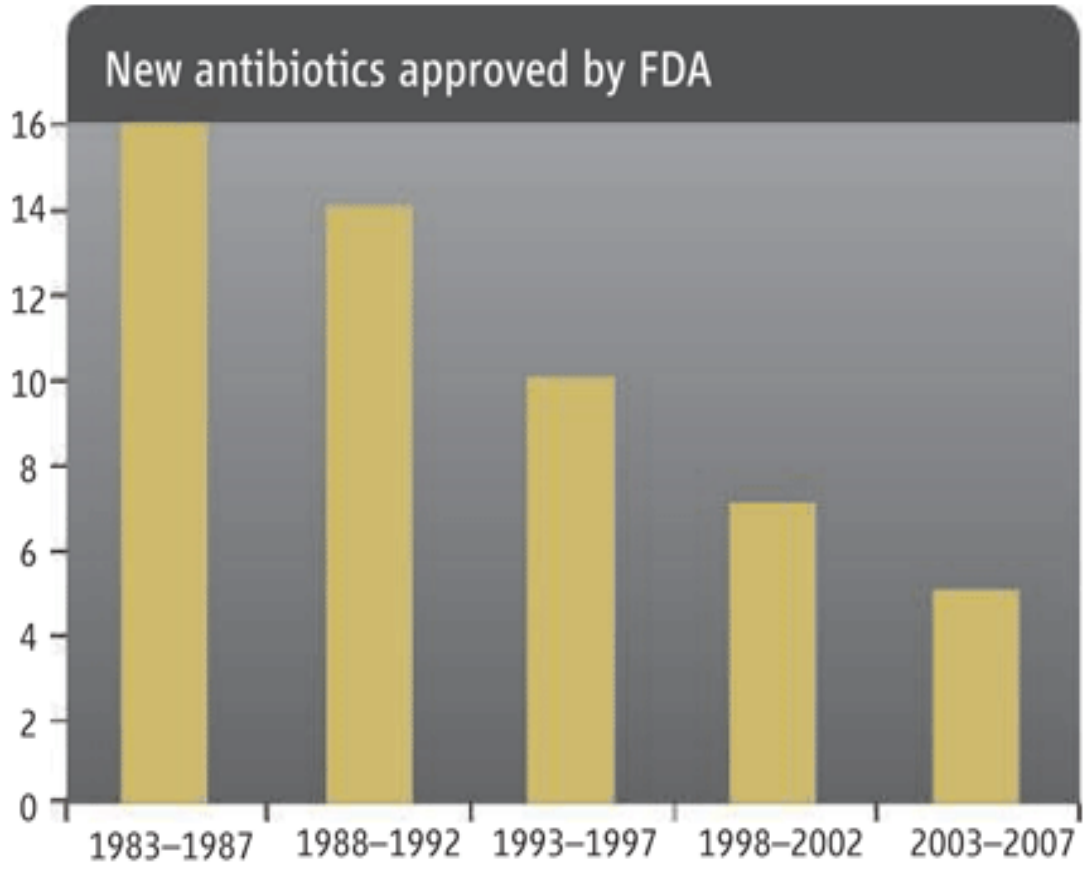
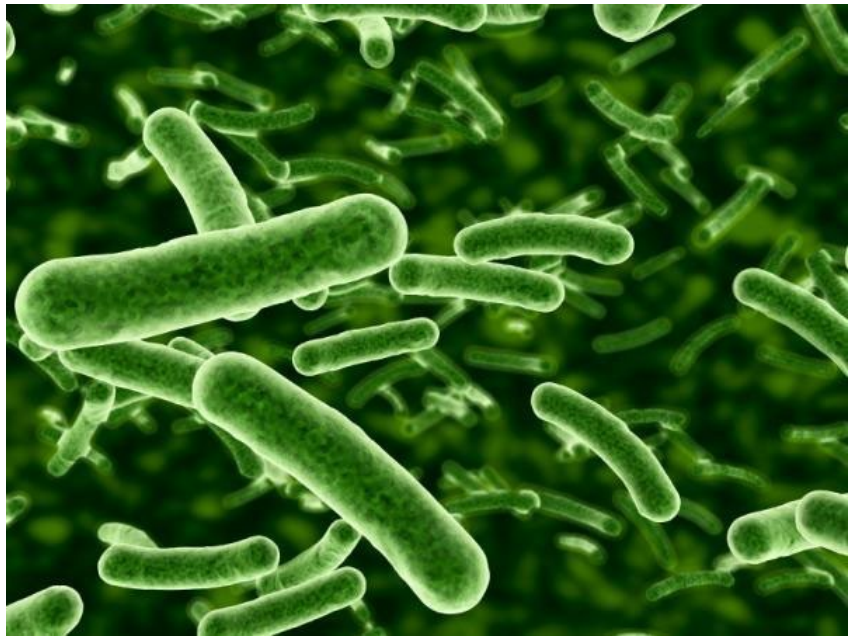
More Resistance, Fewer New Antibiotics

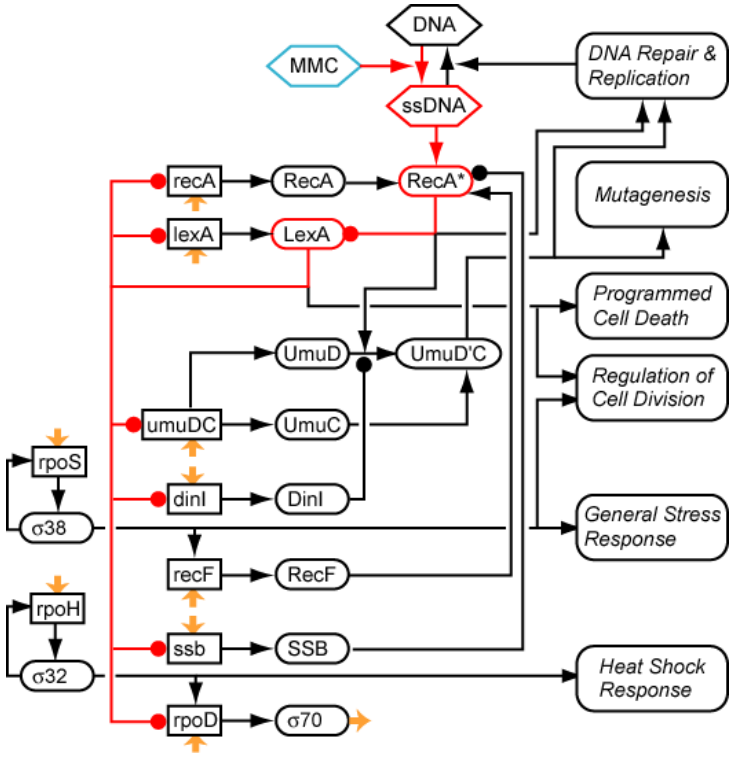




Taubes, Science, 2008

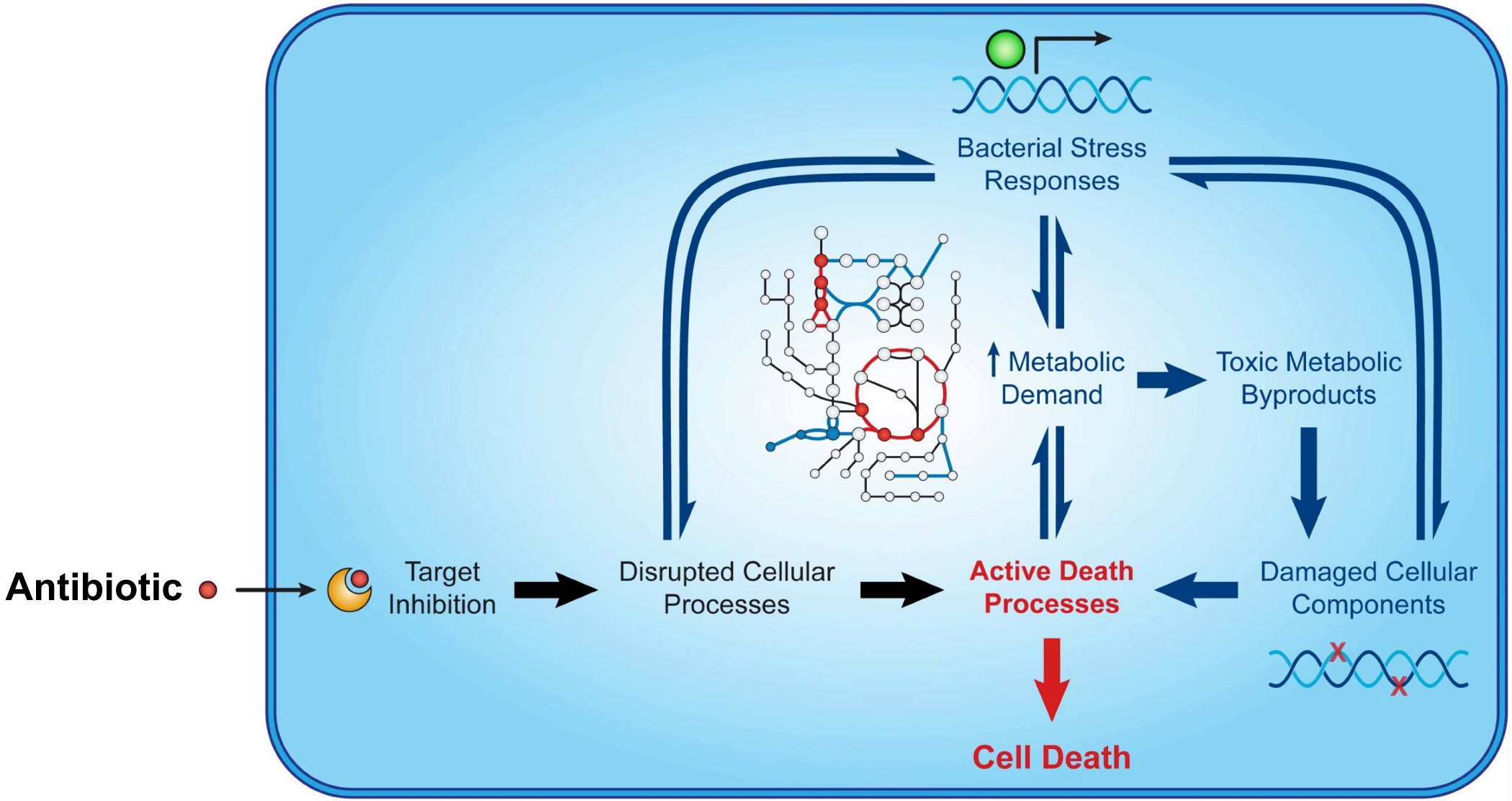
Machine Learning and Antimicrobial Research





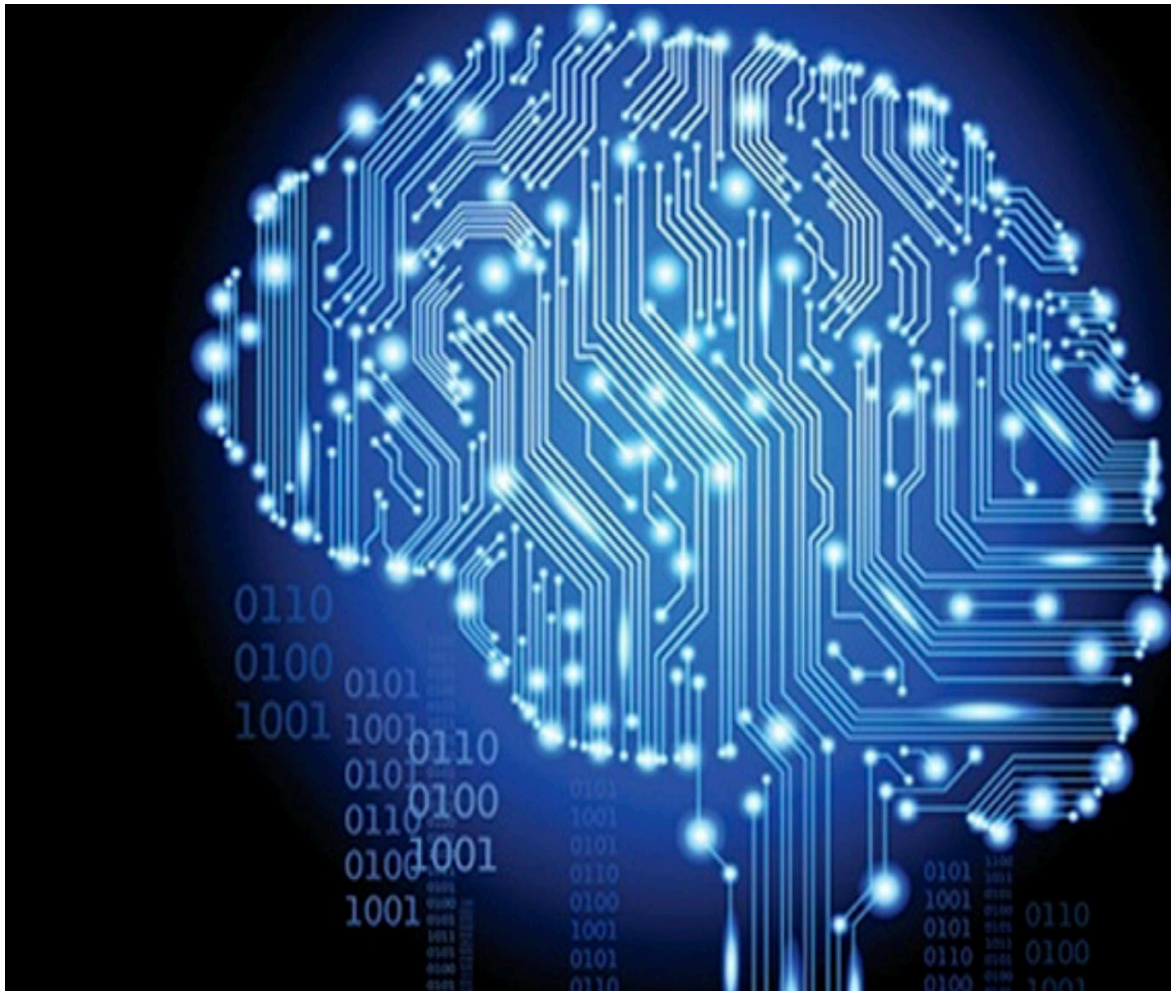
TS Gardner et al., Science, 2003
D di Bernardo et al. Nature Biotechnology 2005

How Antibiotics Kill Bacteria: An Expanded View



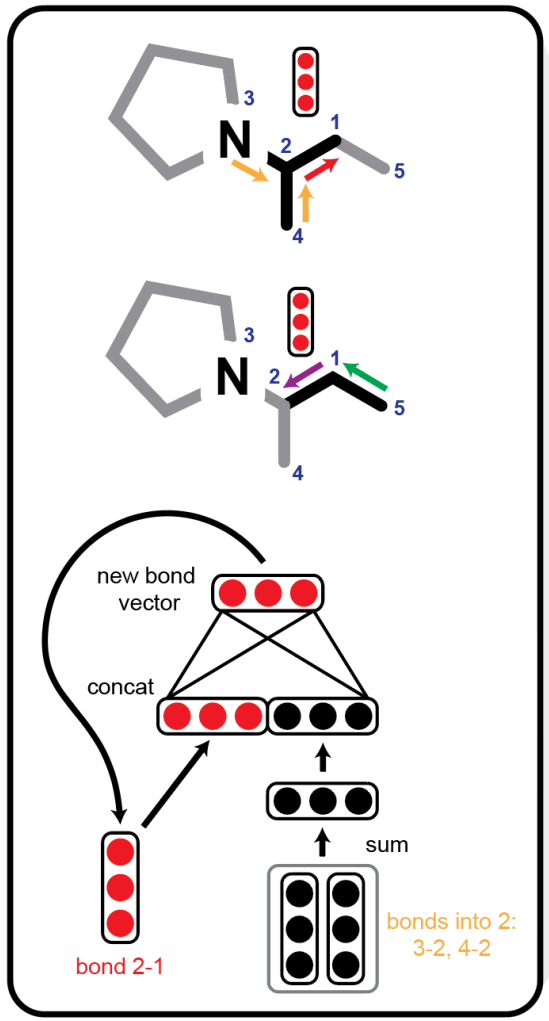
M Kohanski et al., Cell, 2007; D Dwyer et al., PNAS 2014

Deep Learning & Big Data: Biotech & Medicine



Deep Learning Approach to Antibiotic Discovery

Directed message passing neural network

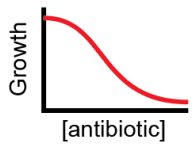


Large scale predictions (upper limit 10^8 +)

Training set (10^4 molecules)

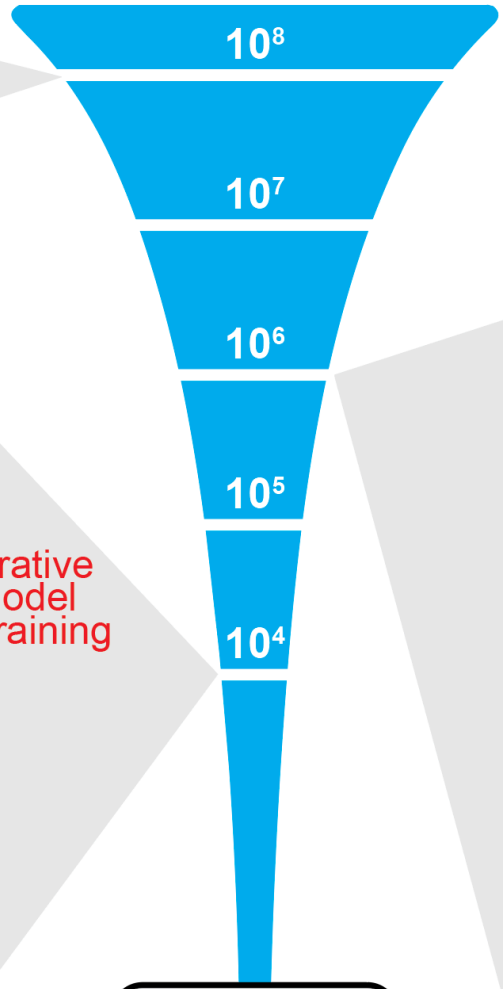
Machine learning

Small scale predictions & molecule validation



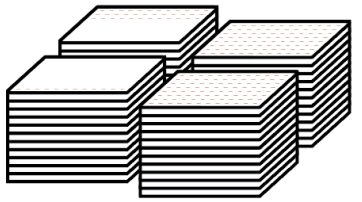
Iterative model re-training

Chemical landscape



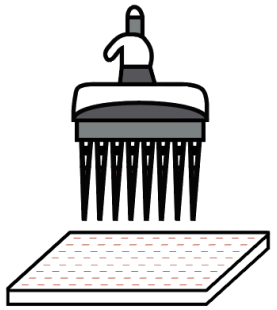
Lead identification & optimization

Conventional antibiotic screening

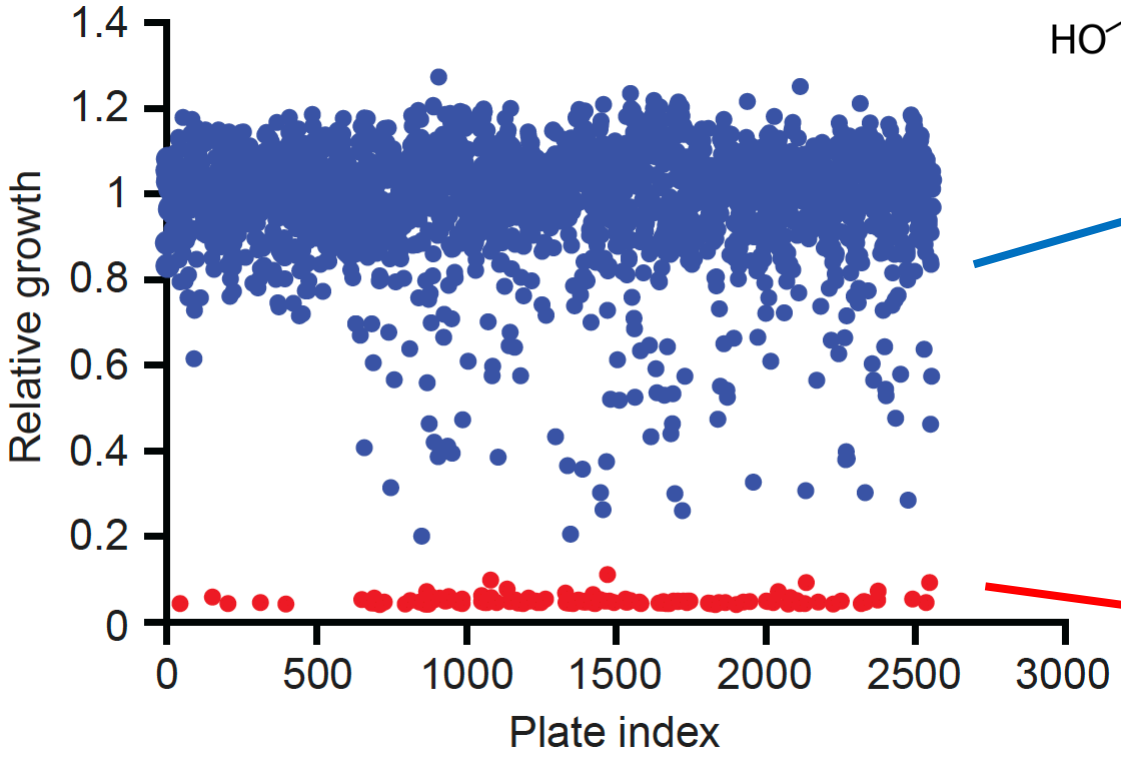


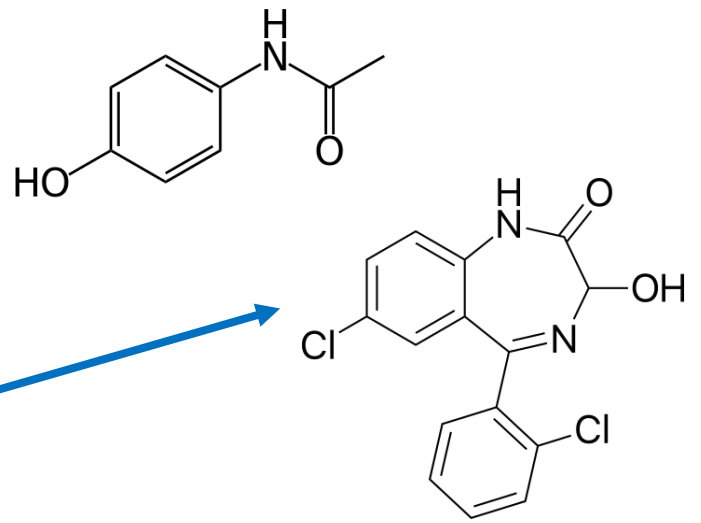
Chemical screening (upper limit 10^5 - 10^6)

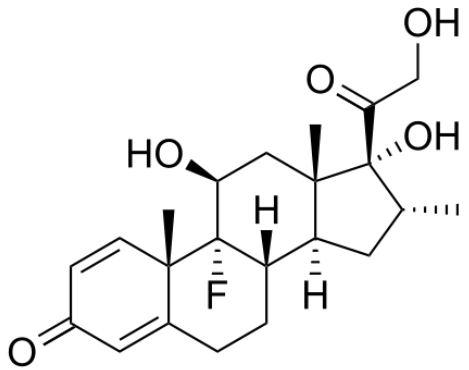
Hit validation (1 - 3% hit rate)



Training Data Set: Growth Inhibition against *E. coli*







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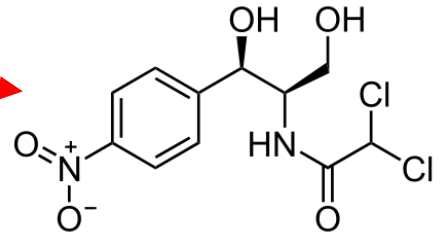

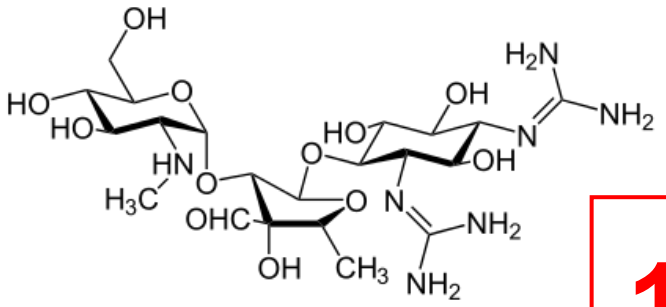

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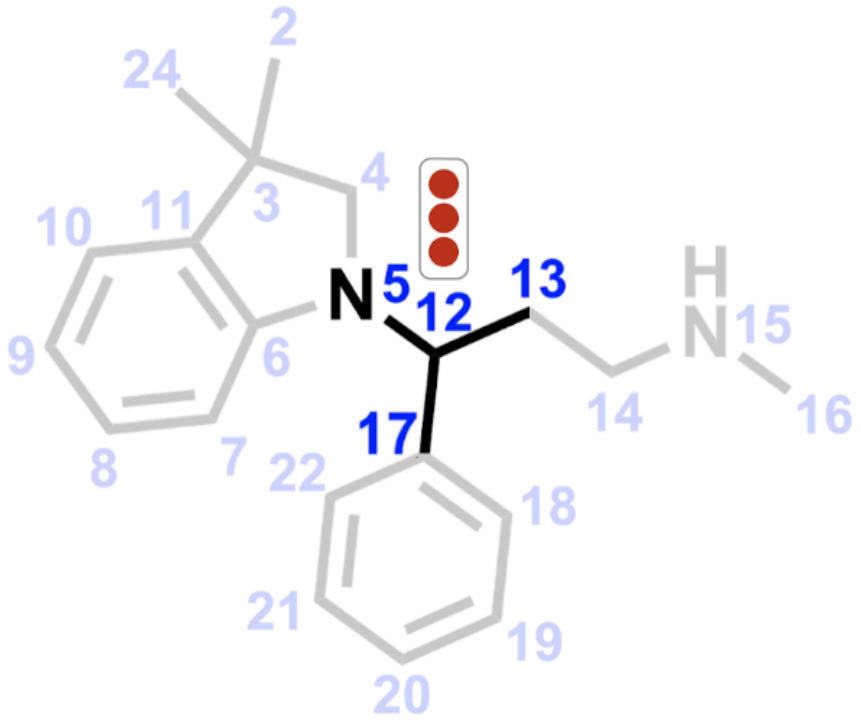
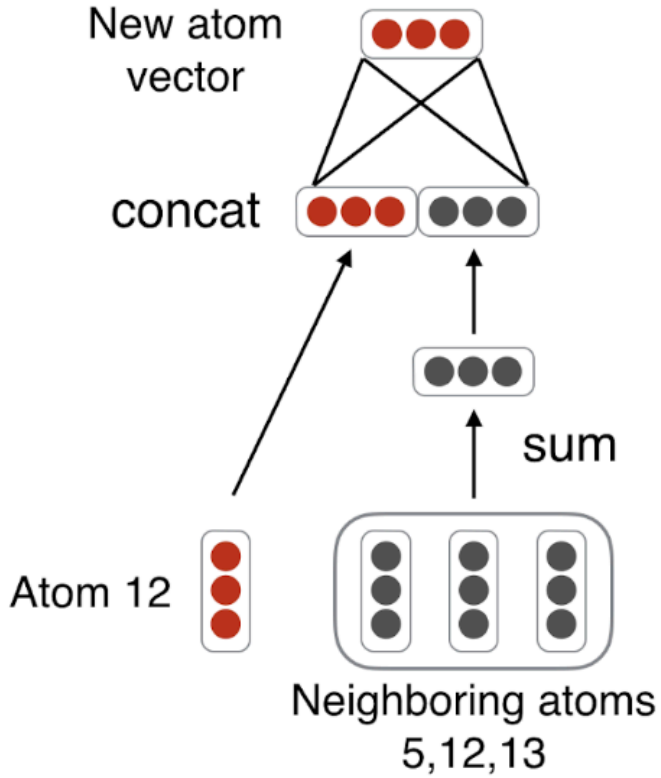
J Stokes et al., Cell, 2020

Deep Neural Network for Molecular Property Prediction

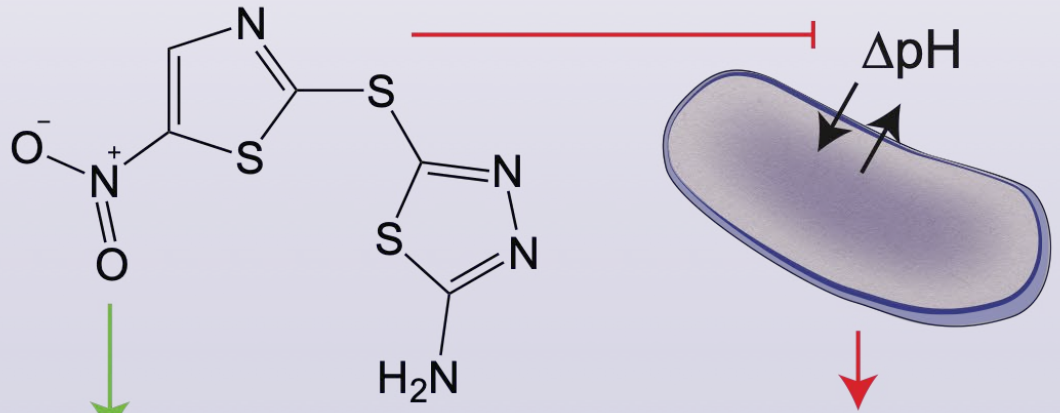




Message Passing Neural Network: train on a dataset containing molecules along with known property values for each molecule

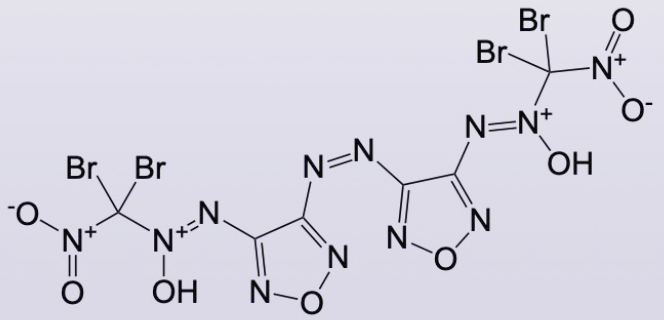
Deep Learning Approach to Antibiotic Discovery

Drug Repurposing Hub
HALICIN

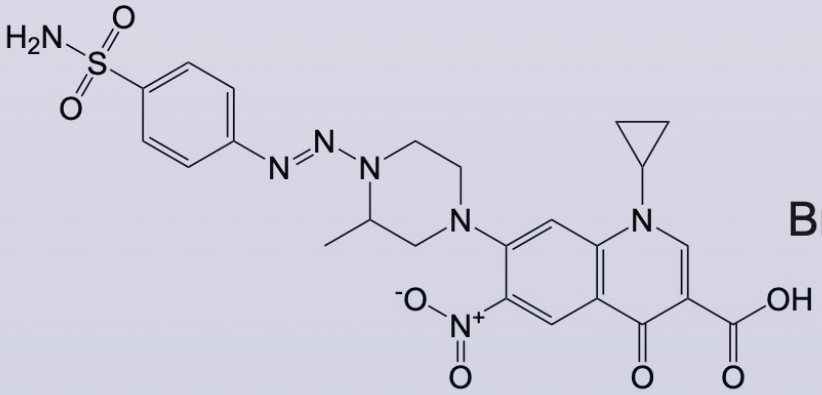


Acinetobacter baumannii
Clostridioides difficile

ZINC15 Database



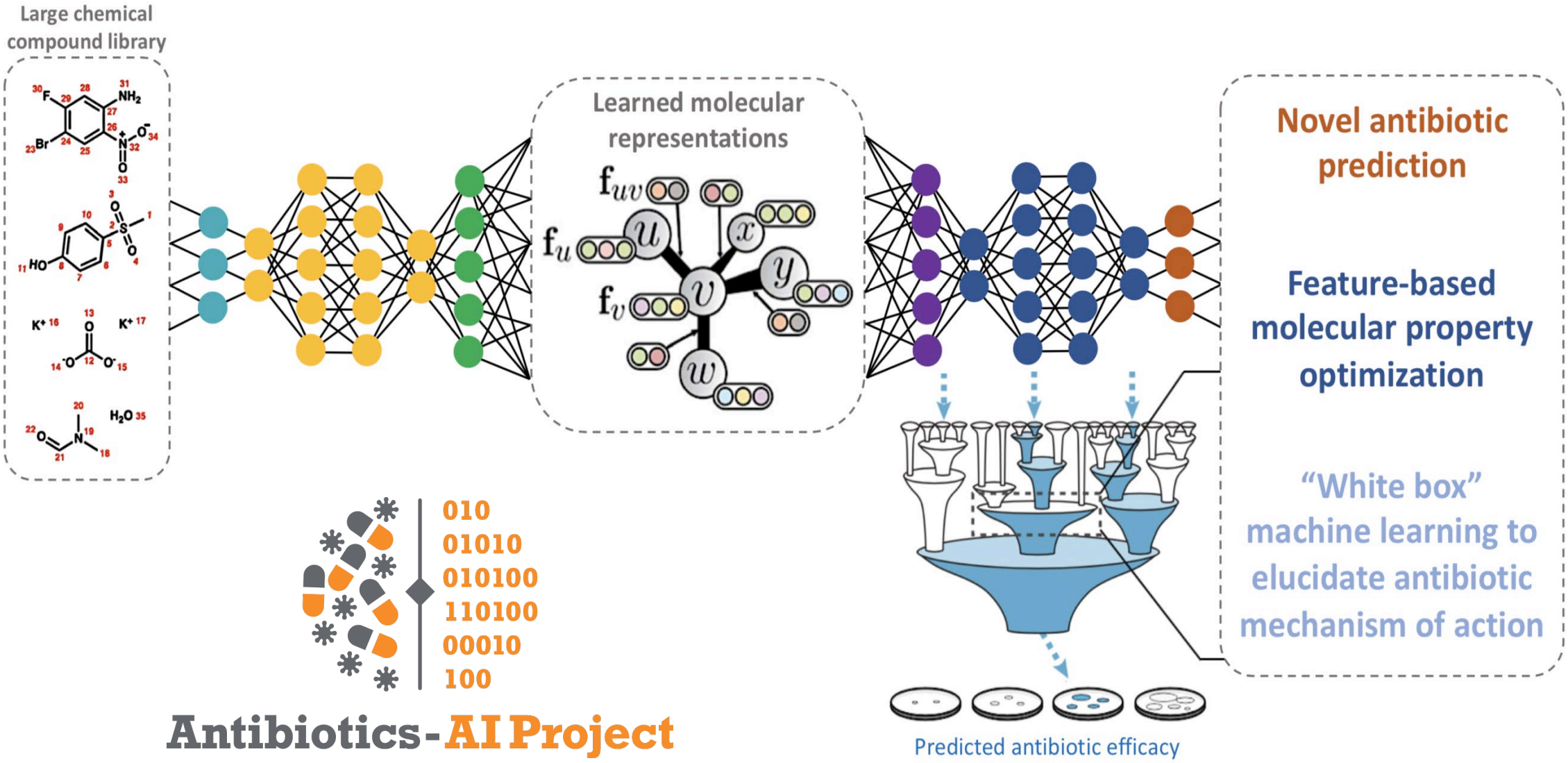
Rapidly bactericidal
Broad-spectrum



Low MIC
Broad-spectrum

J Stokes et al., Cell, 2020

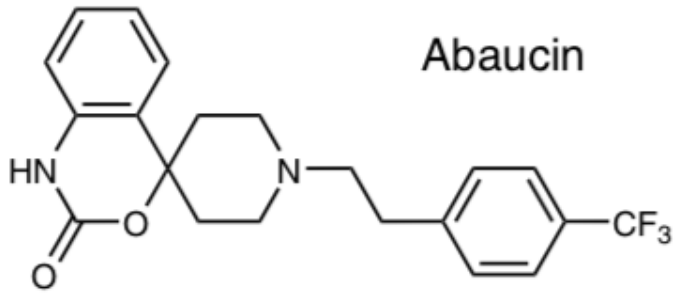
AI-Based Discovery and Design of Novel Antibiotics



AI-Based Discovery of Abaucin

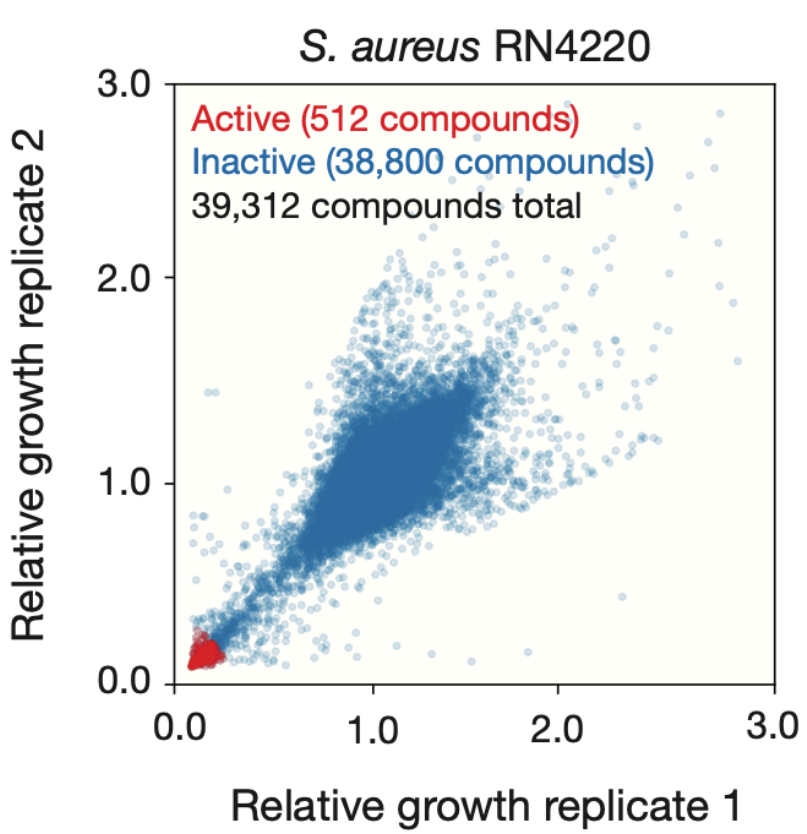
BBC

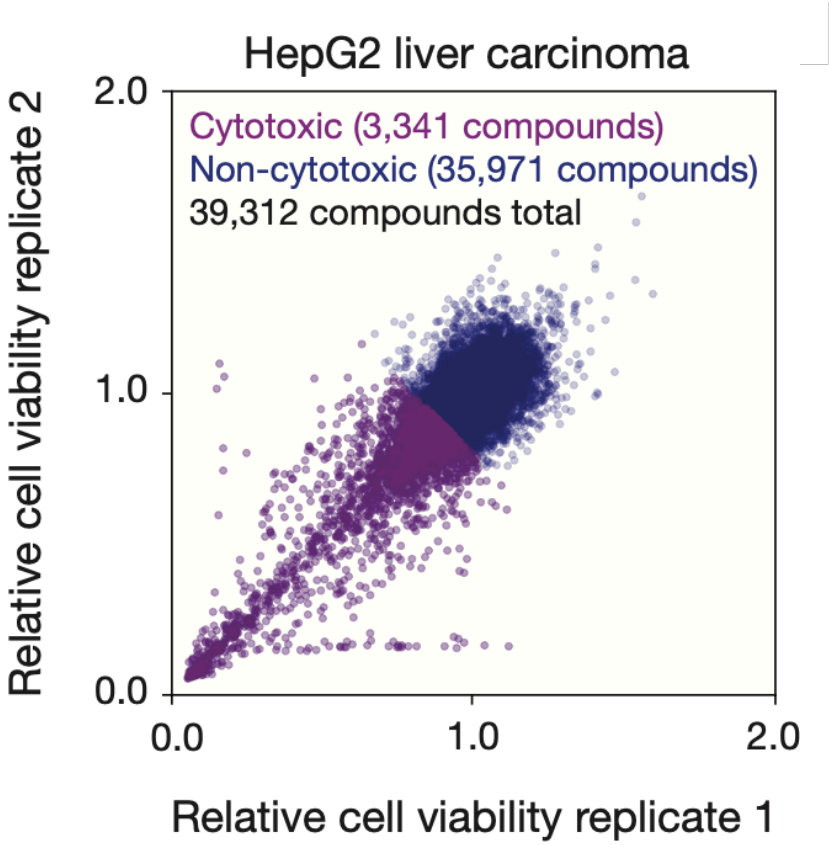
CNN

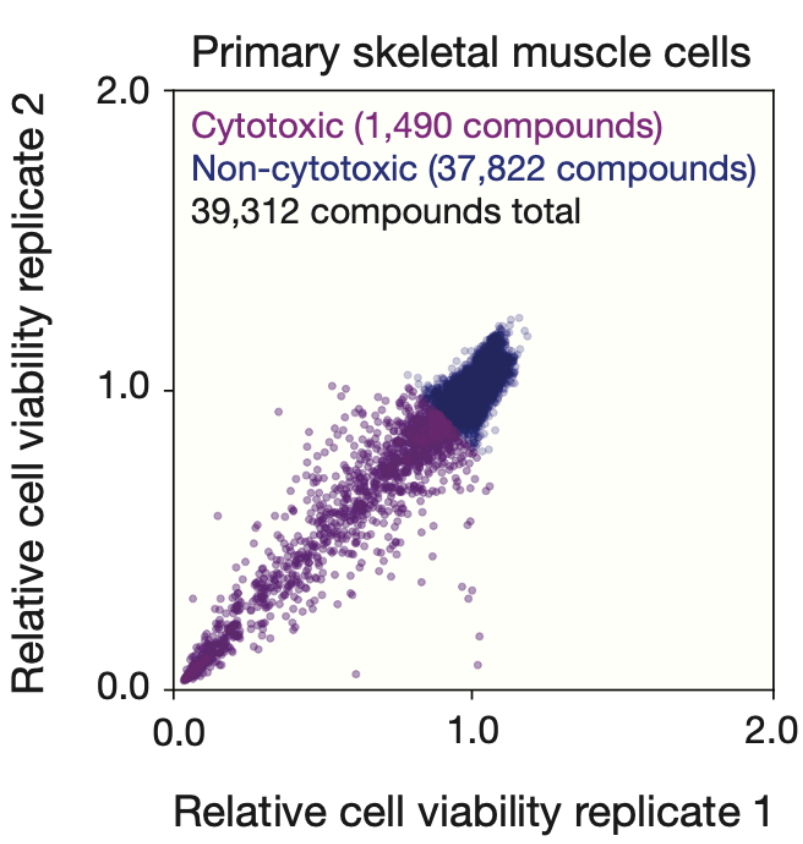


G Liu et al., Nature Chemical Biology, 2023

Deep Learning for Antimicrobial Activity and Cytotoxicity

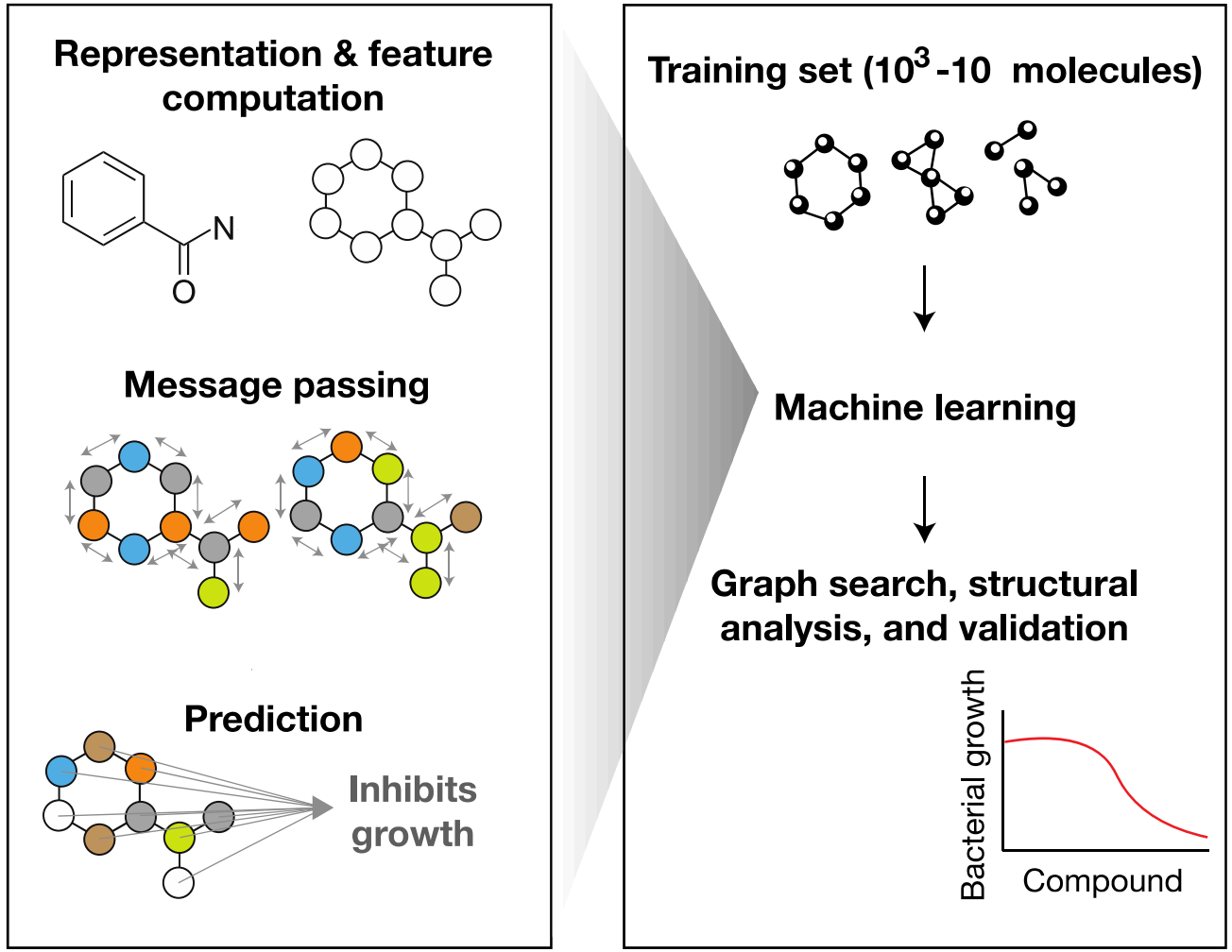






F Wong et al., Nature, 2023

Explainable DL for Structural Classes of Antimicrobials

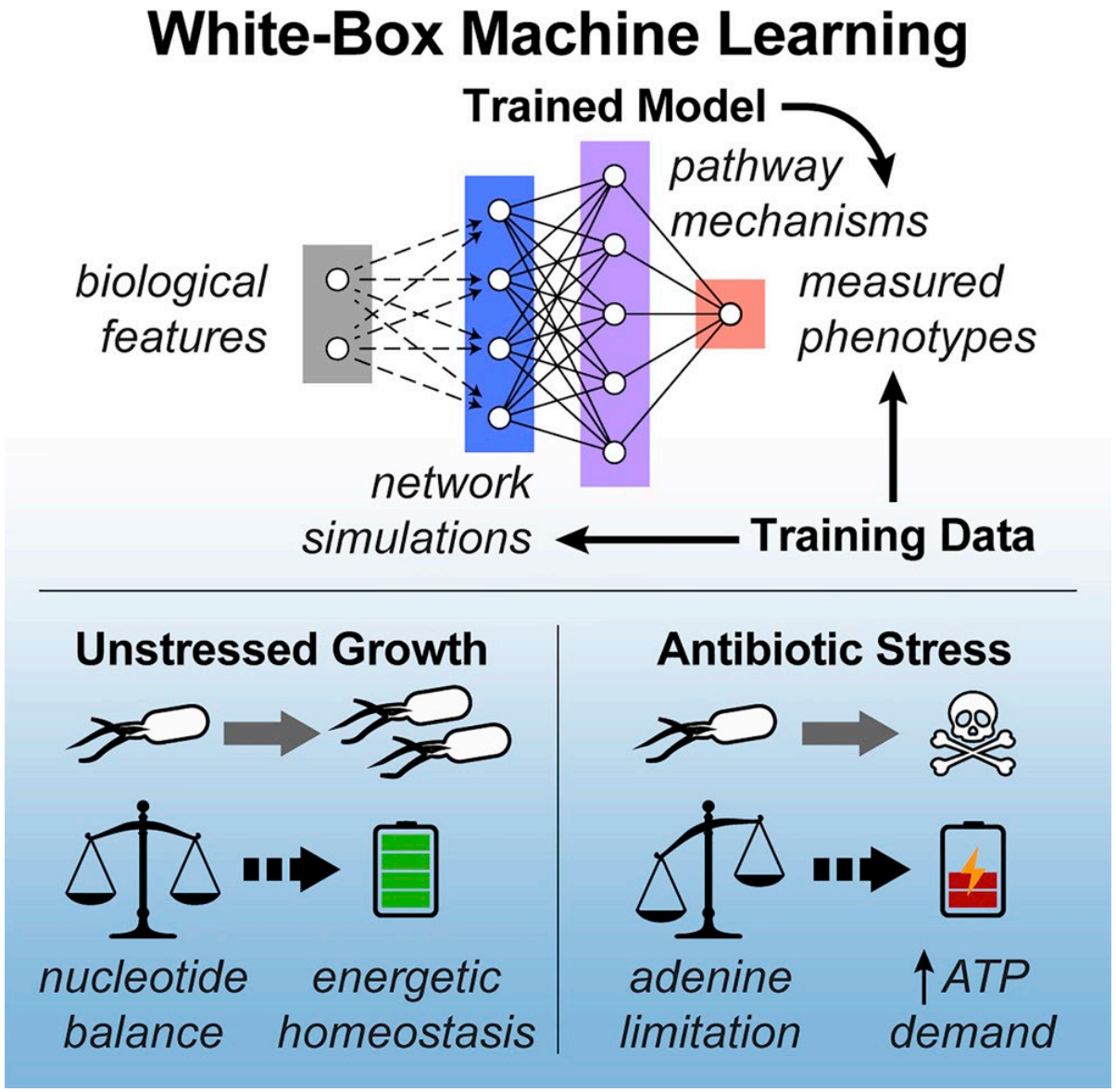


Chemical landscape

$>10^9$	Upper limit of deep neural network predictions
$\sim10^8$	Number of molecules in large compound database
$\sim10^3$	Number of strong predicted hits
$\sim10^2$	Number of test molecules screened

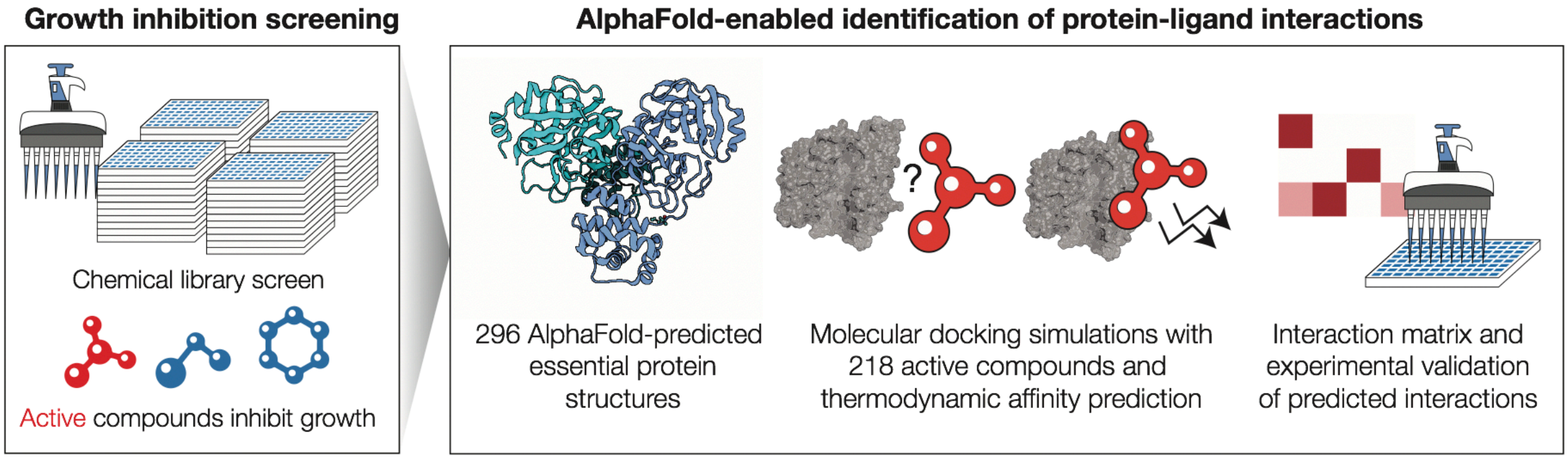
F Wong et al., Nature, 2023

White-Box Machine Learning: Identifying Antibiotic MoA



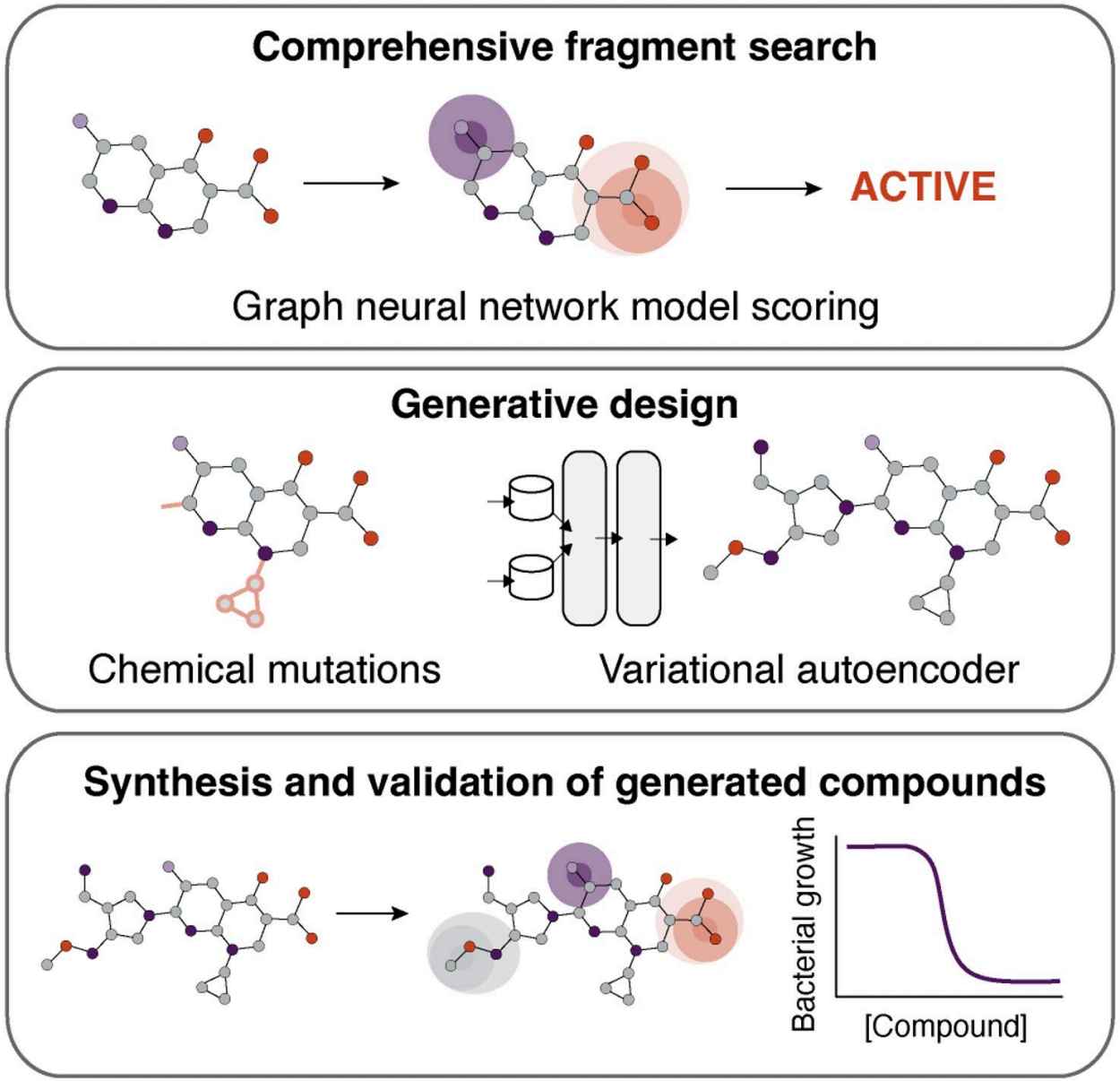
J Yang et al., Cell, 2019

ANTIBIOTICS-AI PROJECT: LEVERAGING ALPHAFOLD



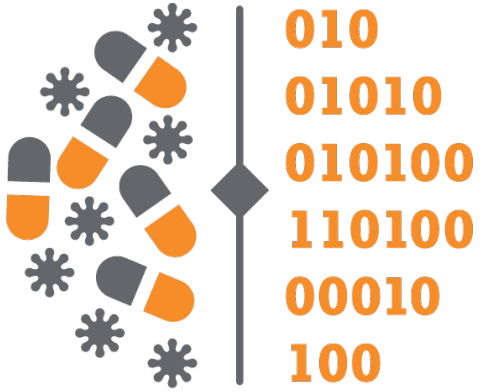
F Wong et al., Molecular Systems Biology, 2022

GENERATIVE AI FOR *DE NOVO* ANTIBIOTIC DESIGN



Antibiotics-AI Project and Phare Bio

THE AUDACIOUS PROJECT



Antibiotics-AI Project

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