



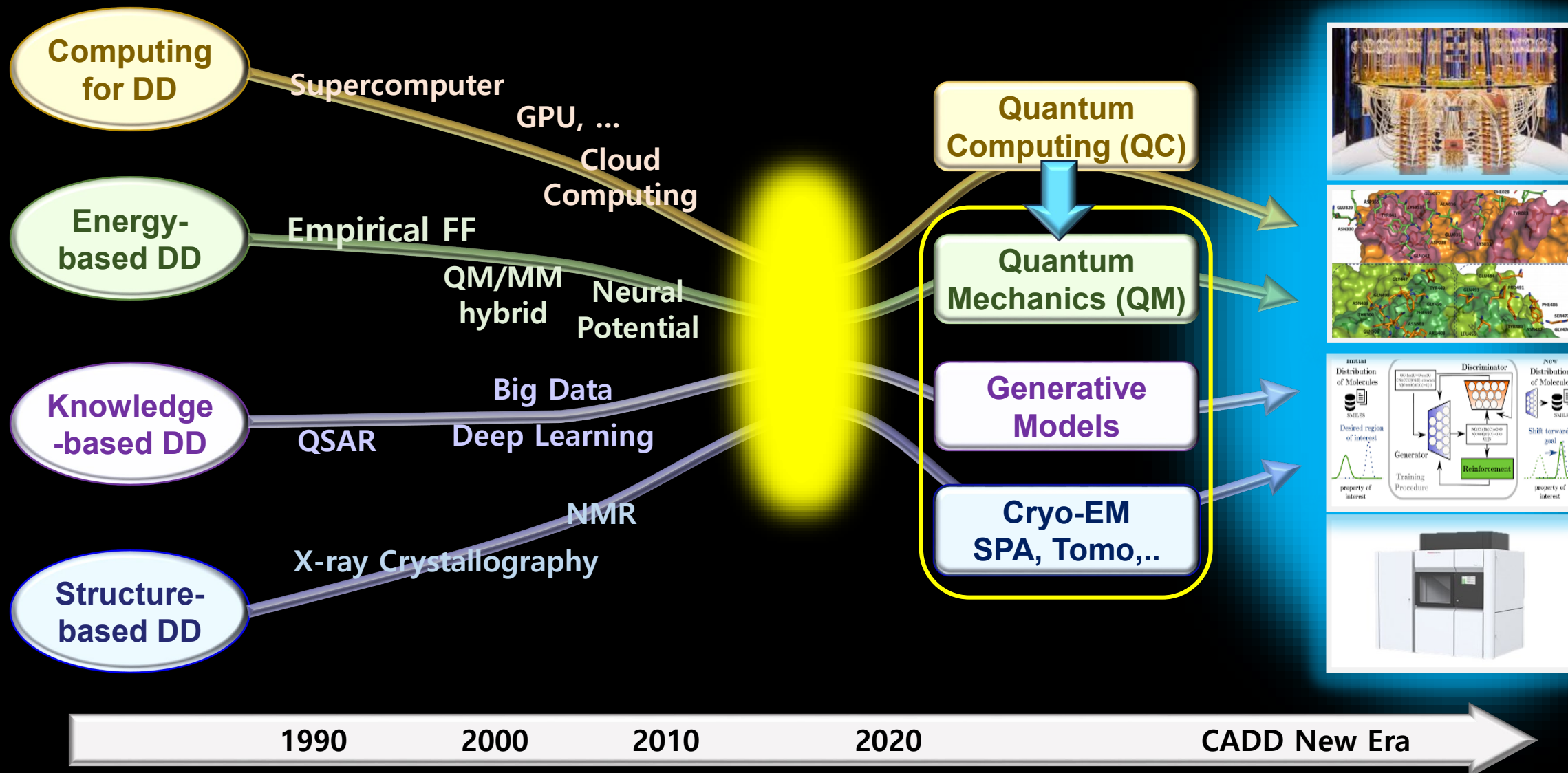
양자컴퓨팅으로 신약탐색의 화학공간을 확장 할 수 있을까?

Can Quantum Computing Expand the Chemical Space for Drug Discovery?

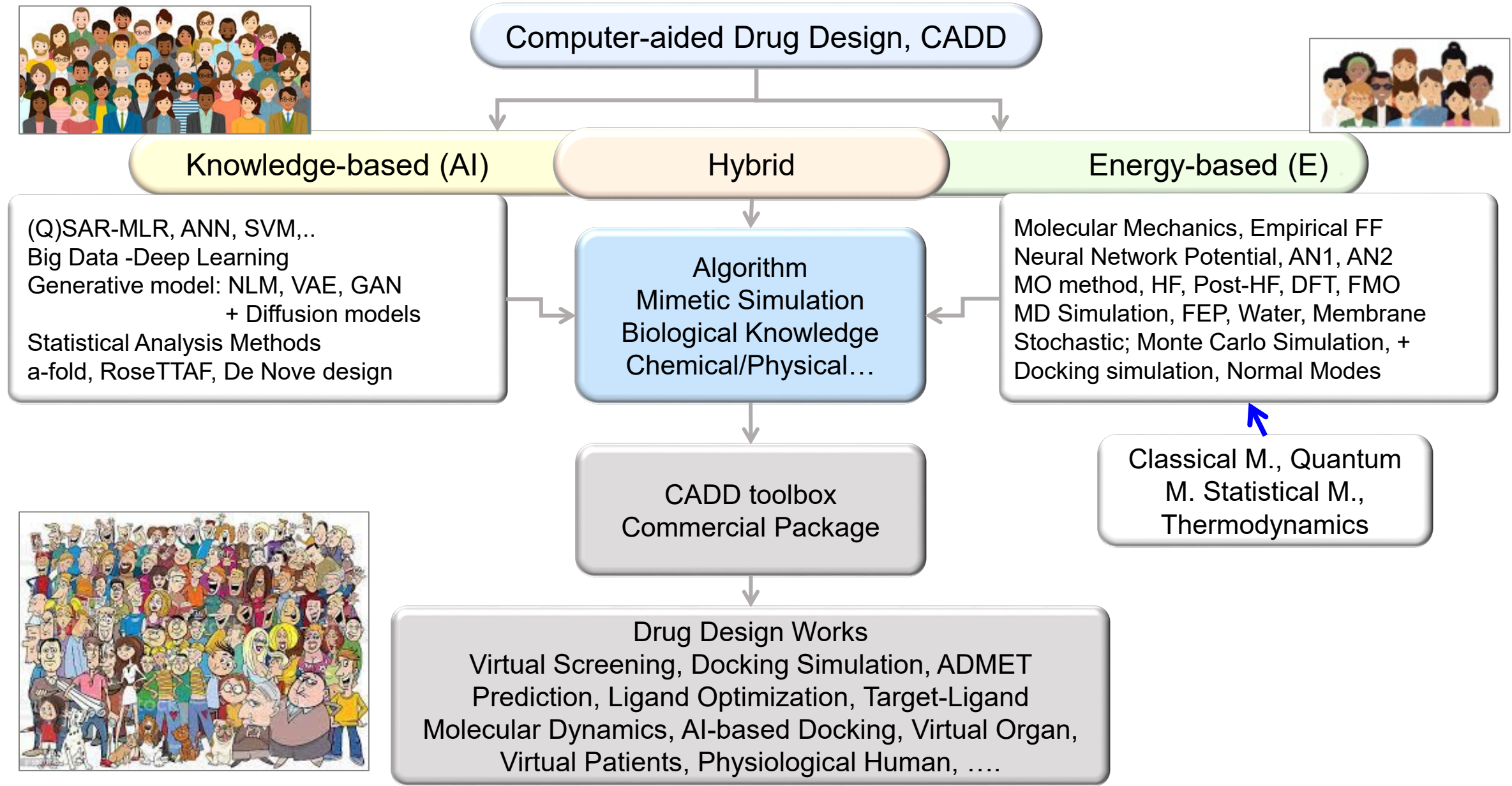
BaobabAiBIO Inc., BMBRC, and Yonsei University

No, Kyoung Tai (노경태)

Evolution of Computer-aided Drug Discovery (CADD) Methods

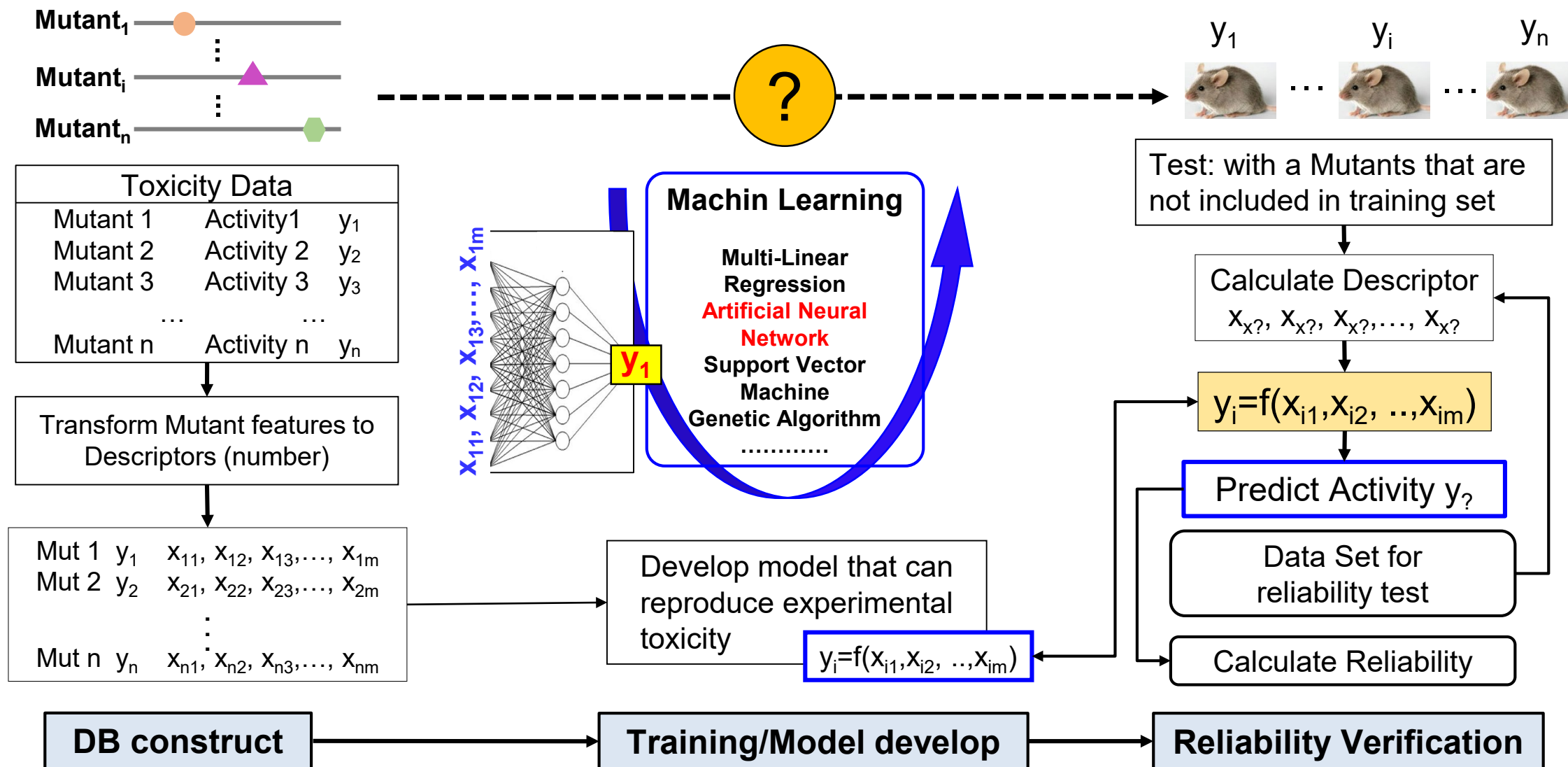


CADD Methods



QSAR, AI Model

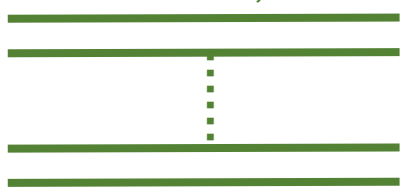
QSAR (Quantitative Structure Activity Relationship)



Reliability of System's Energy in Mechanics-based Drug Design

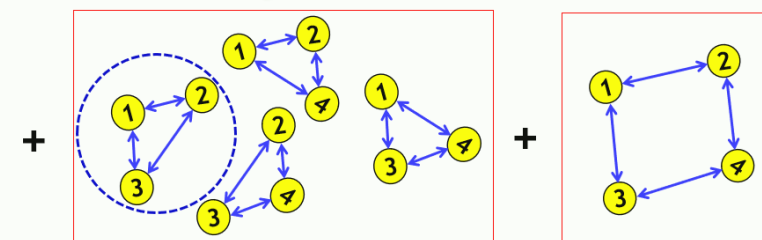
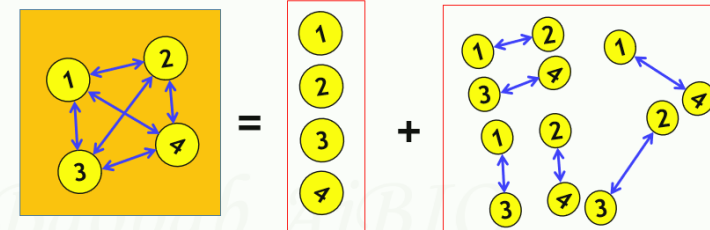
Accuracy in Describing ΔE , $\Delta \Delta E$

ECEPP, Amber
CHARMM, OPLS,...



1970~Now

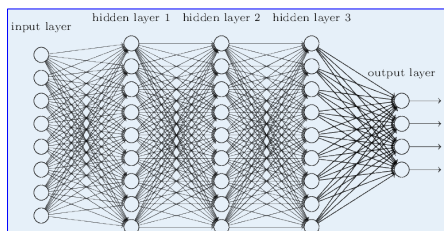
Currently, the most commonly used Force Field assumes "Effective Pair-Potential" and cannot express the "Multibody" effect that actually exists..



Pair potential 형식으로는 계산이 불가능한 Multibody effect, Cooperative Phenomena

GAP

2020~Now



Neural Net Potential (NNP)

$$\nabla^2 \Psi + \frac{8\pi^2 m}{h^2} (E - V) \Psi = 0$$

QM, First Principle
→ Real & Native State

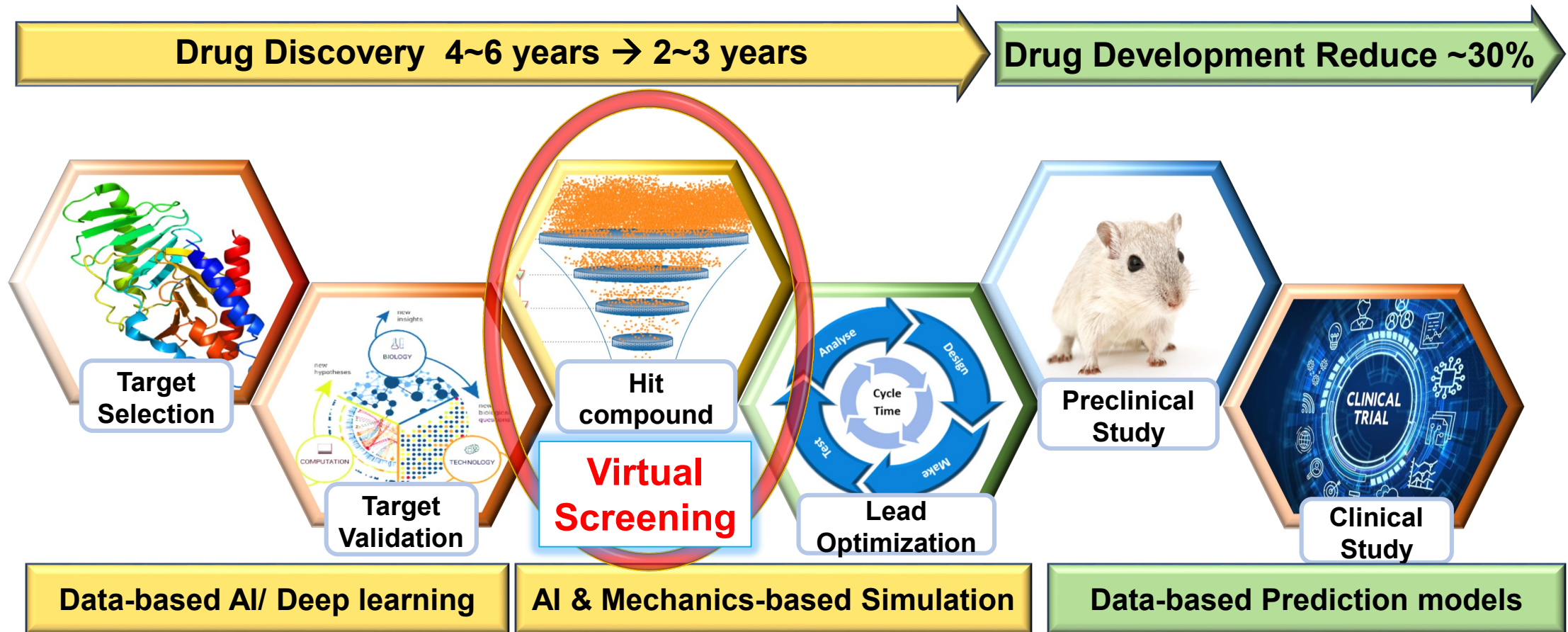
ANIn

HF-MO

Post-HF-MO

- NNPs can perform molecular dynamics with post-HF energy accuracy.
- Calculation of the post-HF level of protein-ligand can be accurately calculated through the Fragment MO (FMO) method.
- As a result, it is possible to design new drugs with high reliability.

Computer-Aided Drug Design: CADD



- **CADD has dramatically reduced the time and cost of new drug development and has become an essential technology in drug discovery & development.**

Quantum Computing in Drug Discovery

Study MOA of Active Ingredient

On a longer time scale, the use of QC is

- Find structure-property relationships using machine learning
- Predict the 3D structure of target protein
- Expected to change the way we find hypotheses

CADD screening

On a **short time scale**, QC could enhance current CADD approaches by increasing the accuracy of modeling to match ligands with target proteins

Efficacy
Evaluation

Requires 5~
20 repetitions
to discover
hits and lead
compounds

Synthesis of
Designed
Compounds

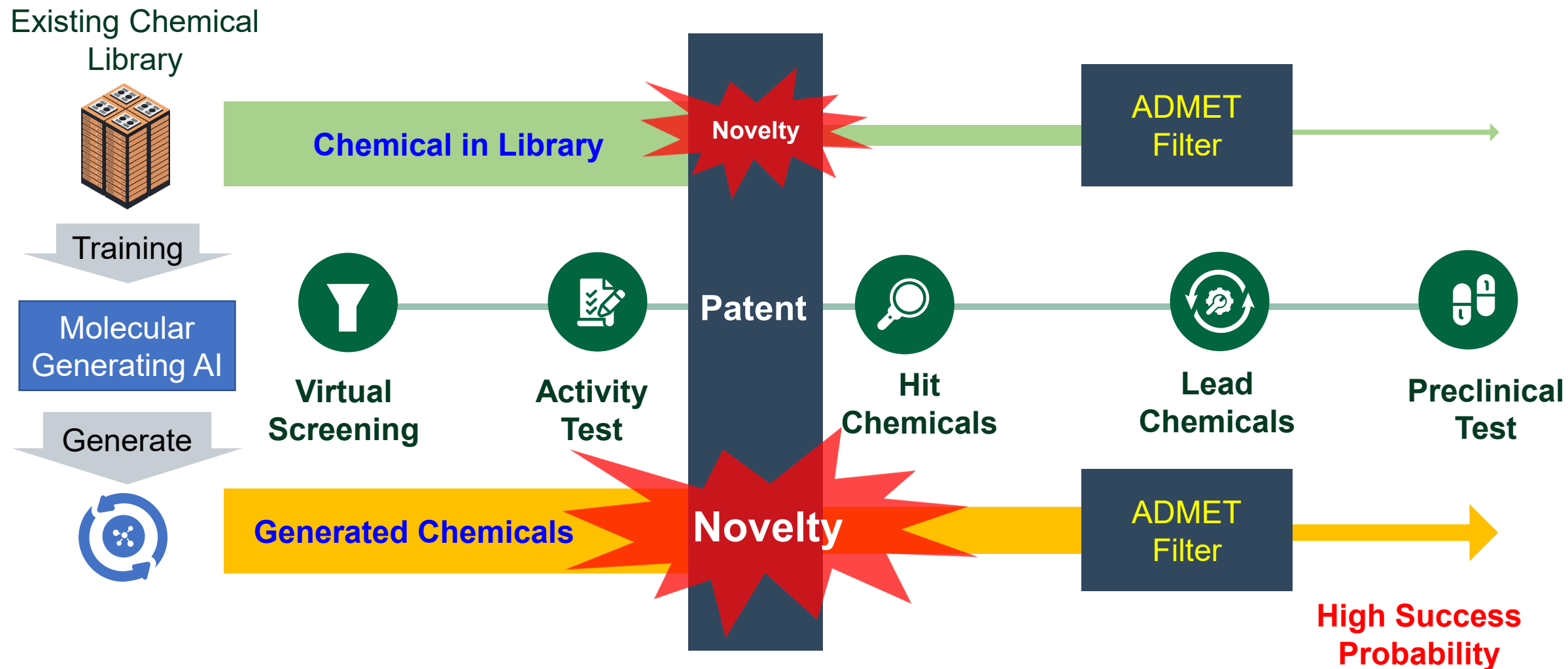
Drug
Property
Evaluation

QC in the New Drug Discovery,

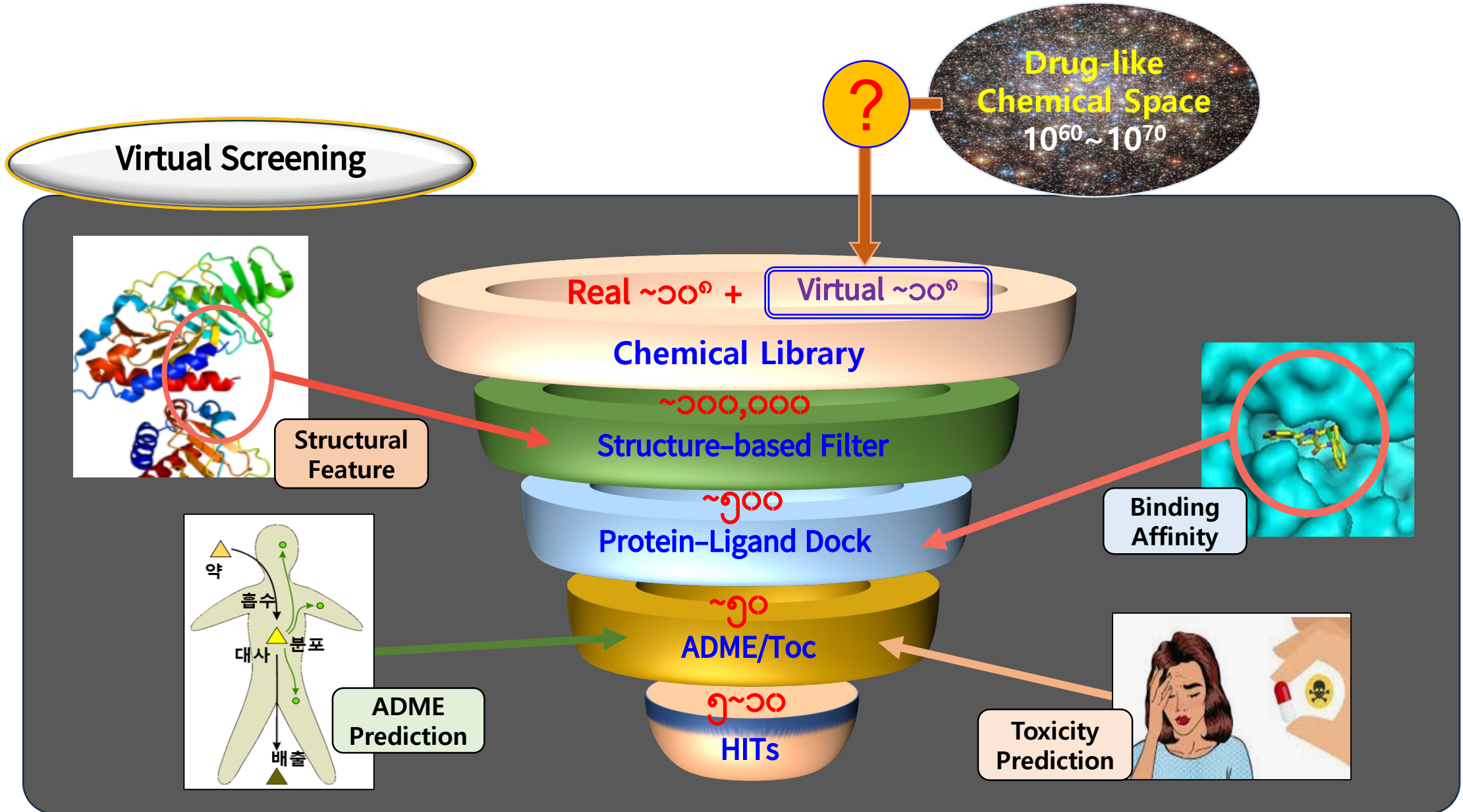
- Reduce the number of cycle repetitions
- Increase the quality of optimized compounds

Impact of Expansion of Chemical Space on Drug Discovery

Increases the probability of securing a material patent by generating compounds with high novelty.

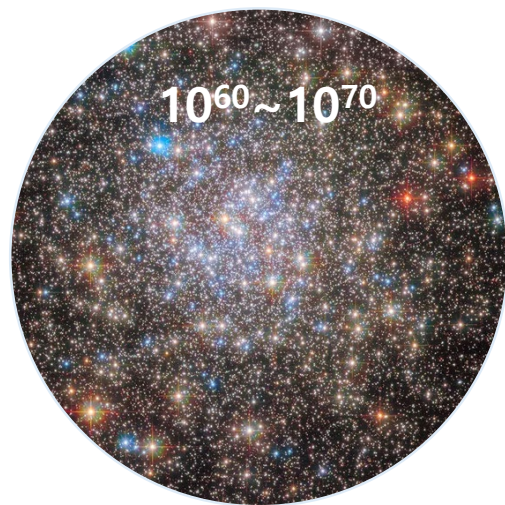
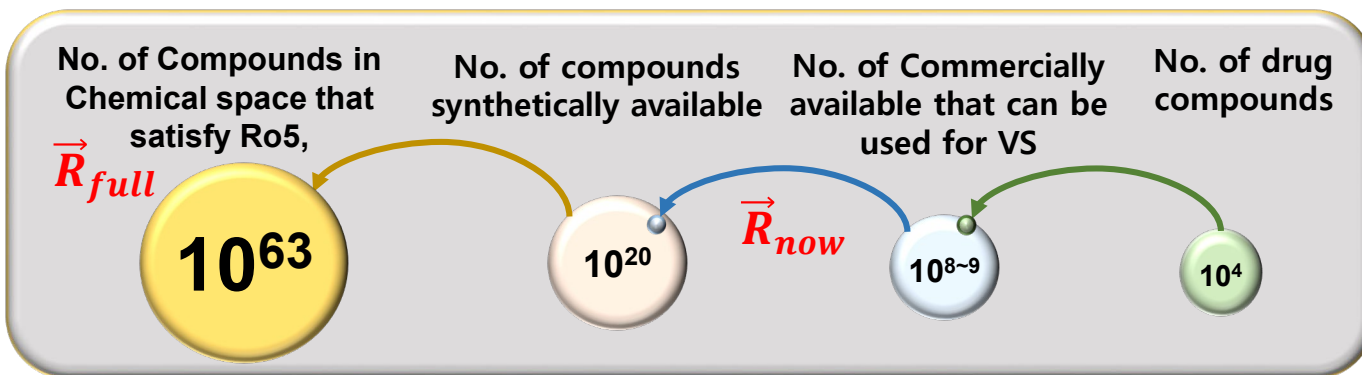
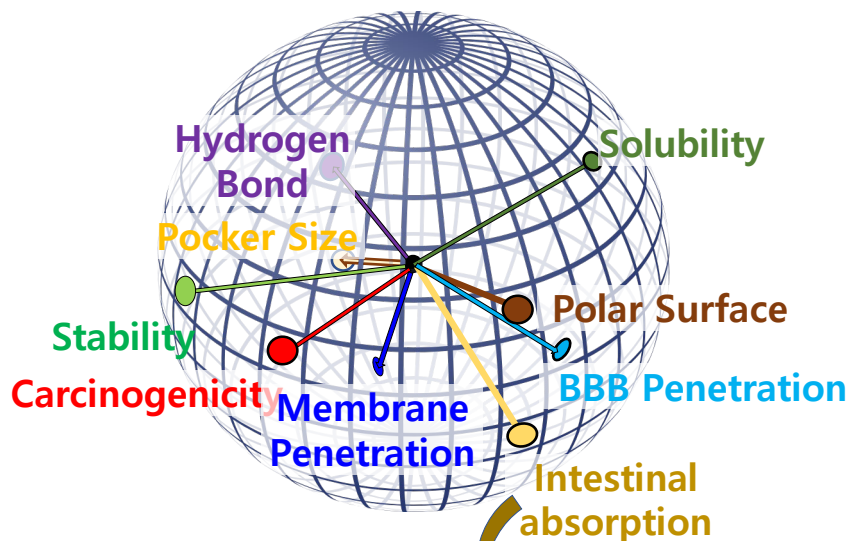


Virtual Screening Strategy in CADD



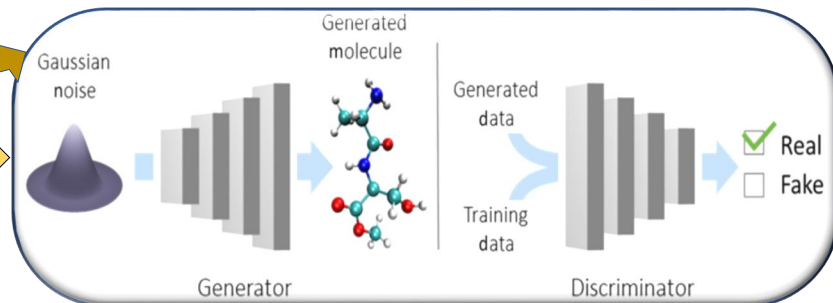
Expand the Chemical Space for Drug Discovery, Generative Model

Latent Space vector



Drug-like Chemical Space

Molecular Generative Model



Crude Filter

$10^{12} \sim 10^{15}$

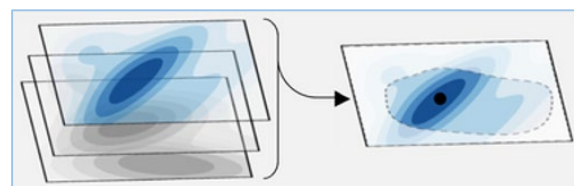
$10^3 \sim 10^5$



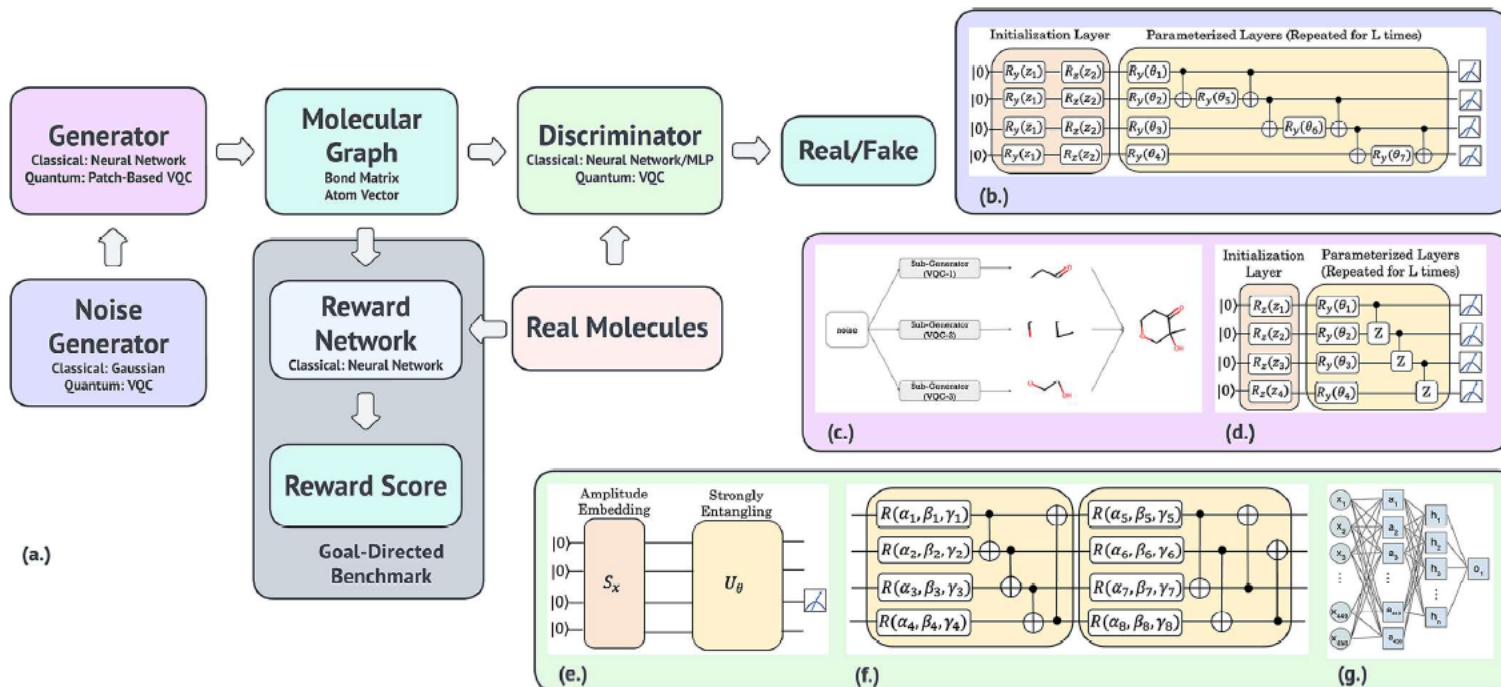
HIT Molecules

3~10

Virtual Screening



Introduce Quantum Algorithm for Molecular Generator (MolGAN)



Latent Space

- Binding condition
- ADMET properties
- Physico-Chemical Prop.
- Restriction-Clinical study
- Iso-type of Target
-

Table 1. Comparing Generated Molecules of QuMolGAN and MolGAN in Drug Properties^a J. Chem. Inf. Model. 2023, 63, 3307

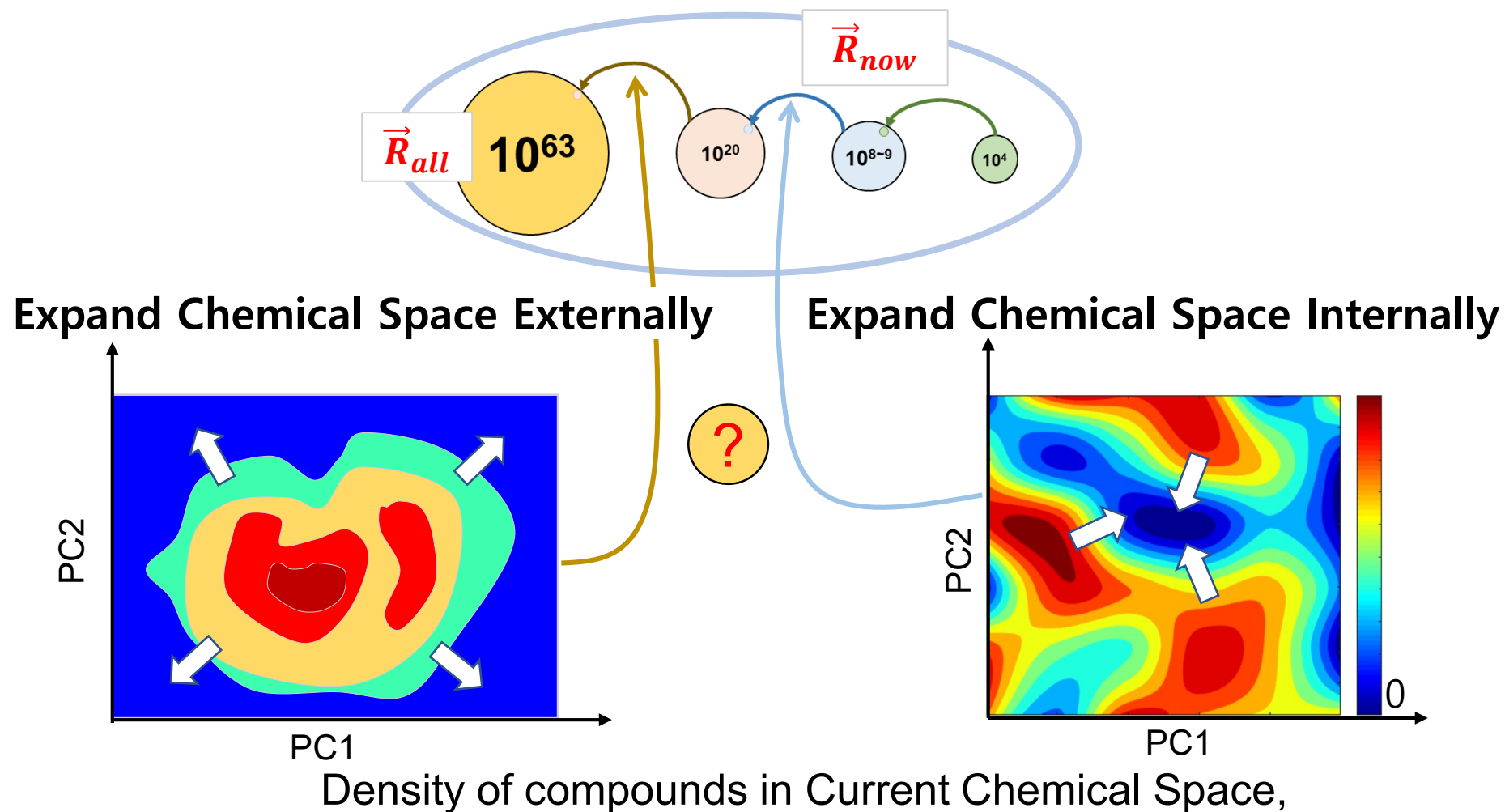
	z_dim = 2			z_dim = 3			z_dim = 4		
	QuMolGAN	MolGAN	p-value	QuMolGAN	MolGAN	p-value	QuMolGAN	MolGAN	p-value
number of molecules ^b	363	657	—	414	2163	—	511	3085	—
QED ↑	0.489	0.475	<0.01	0.489	0.465	<0.01	0.473	0.465	<0.05
solubility ↑	0.343	0.324	<0.05	0.370	0.305	<0.01	0.317	0.298	<0.01
SA ↑	0.367	0.336	<0.05	0.310	0.307	<0.05	0.308	0.296	0.246
KL score (S) ^c ↑	0.653	0.824	—	0.797	0.913	—	0.846	0.957	—

^aBold numbers highlight the better scores in QuMolGAN, compared to the corresponding MolGAN. Note that the QED, Solute, and SA scores in this table are calculated from the valid and *unique* molecules. ^bNumber of valid and unique molecules from 5000 samples. ^cFrom eq 2.

Quantitative Estimate of Druglikeness (QED) Kullback–Leibler (KL) divergence, Synthetic

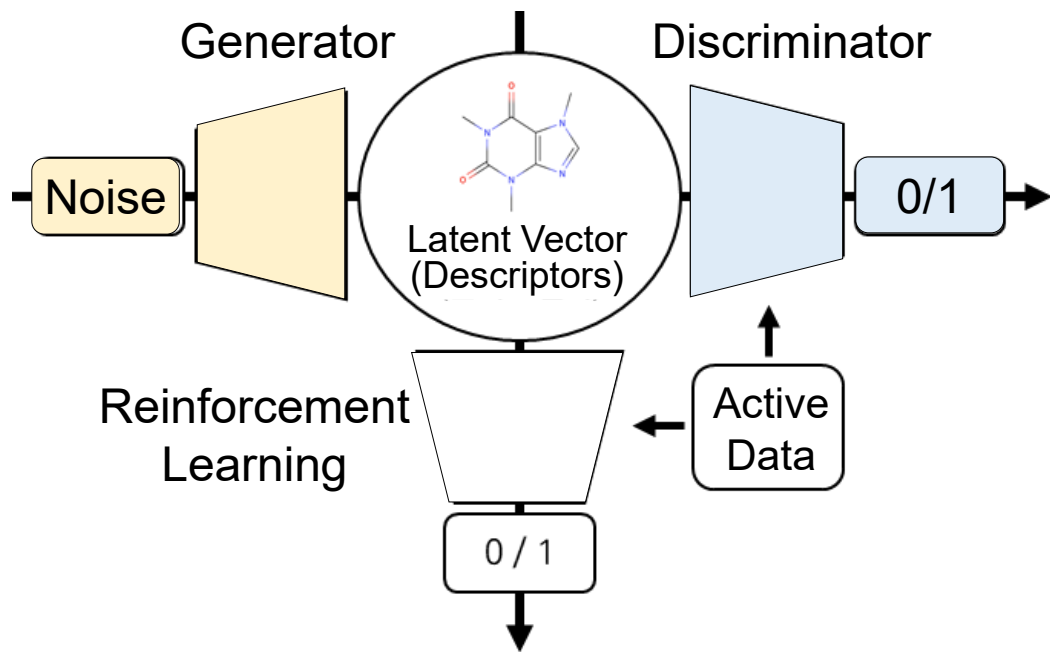
Two Ways of Expanding the Current Chemical Space for CADD

The methods to expand the Chemical Space for CADD may broadly consists of 1) extending the outer boundaries of the current chemical space, externally, and 2) filling the empty spaces within the current chemical space that remain vacant for various reasons, internally.



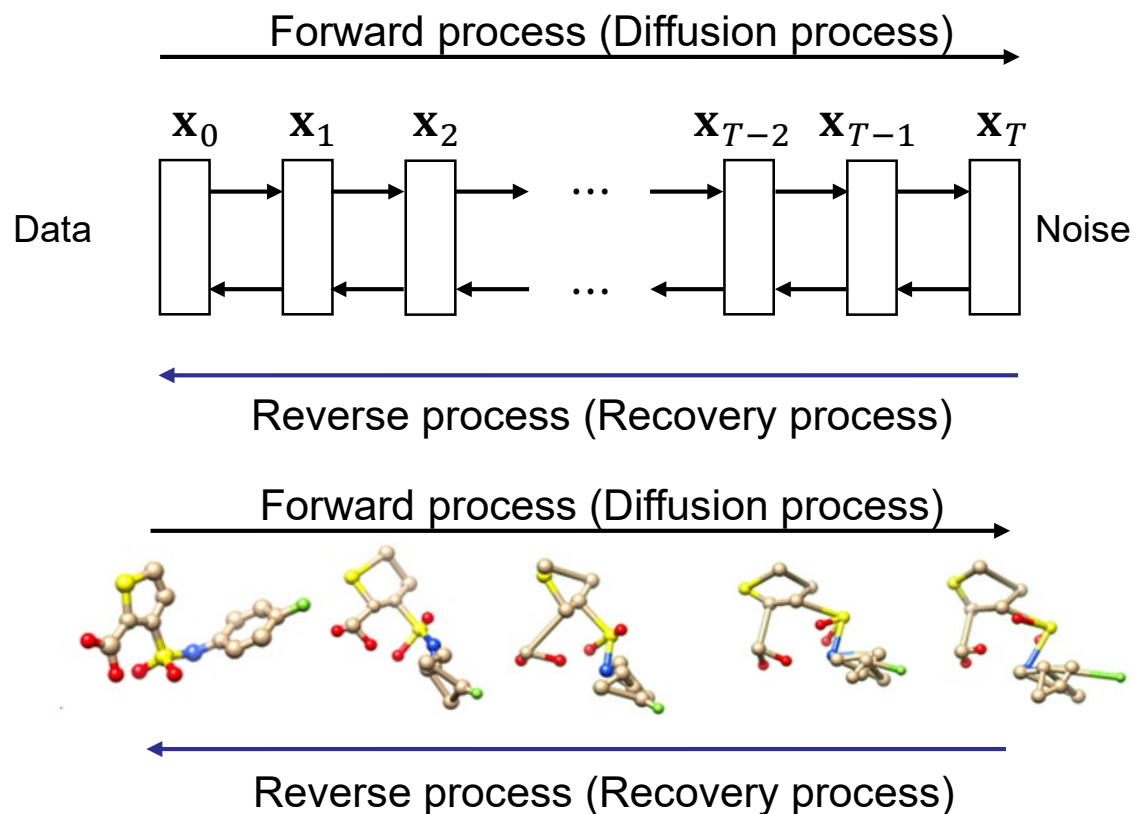
Commonly used Molecular Generative Models

Generative Adversarial Network



The generator trains the discriminator to be unable to distinguish the molecules it creates from real molecules through repeated learning.

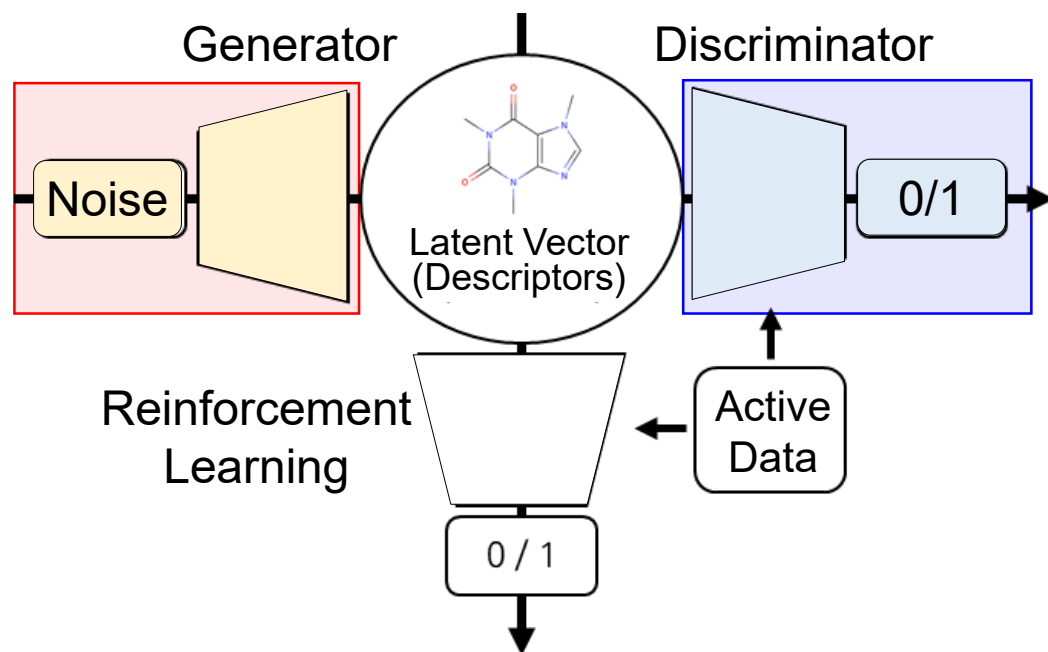
Diffusion Model



Learn how to recover original data from noise and learn how to create molecules.



Applying QC to molecular generation model



Internal Diversity

Feature	Training Data	Classical Reinforce	QC-Noise/ Reinforce
QED	0.461	0.470	0.480
Solubility	0.289	0.310	0.440
syntheability	0.327	0.310	0.660

External Diversity

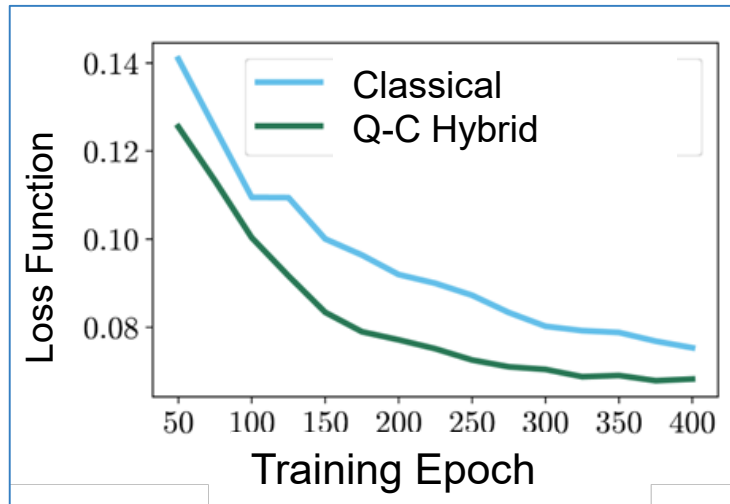
Feature	Training Data	Classical Reinforce	QC-Noise/ Reinforce
QED	0.461	0.520	0.570
Solubility	0.289	0.450	0.440
syntheability	0.327	0.650	0.760

QED: Quantitative Estimation of Drug-Likeness

Quantum Benefit in Classical-Quantum Hybrid Machine Learning - Efficiency

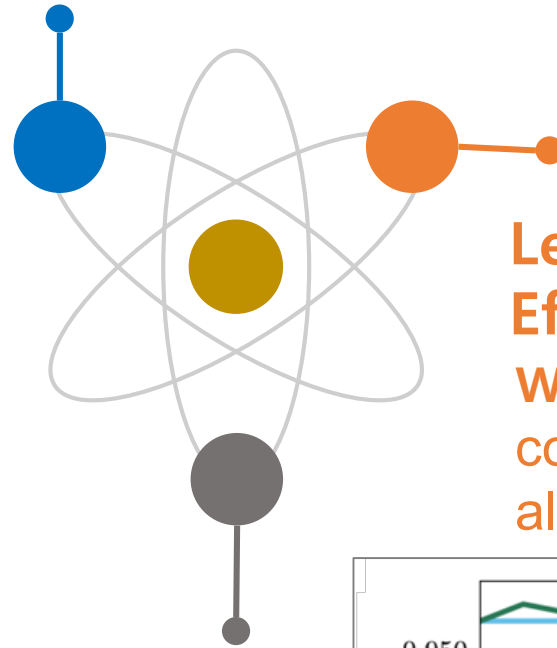
Learning Effectiveness

It shows similar level of performance even using a smaller dataset.



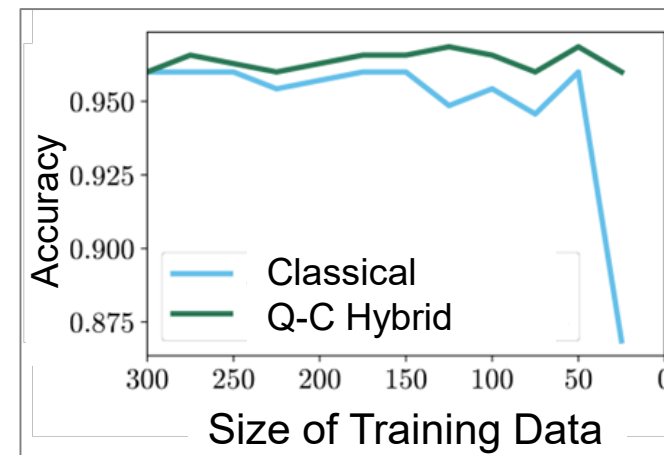
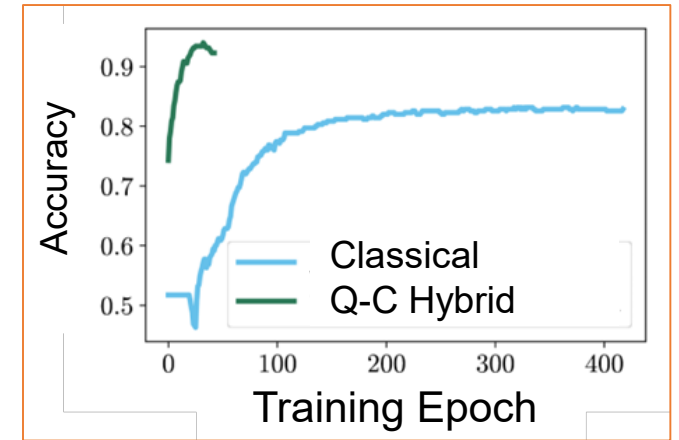
Improved Performance

Shows superiority in the accuracy of prediction model and mean square error

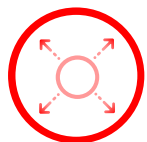


Learning Efficiency

When trained on the same epoch, it converges faster than the classical algorithm.



Efficient Drug Design using Quantum Computing



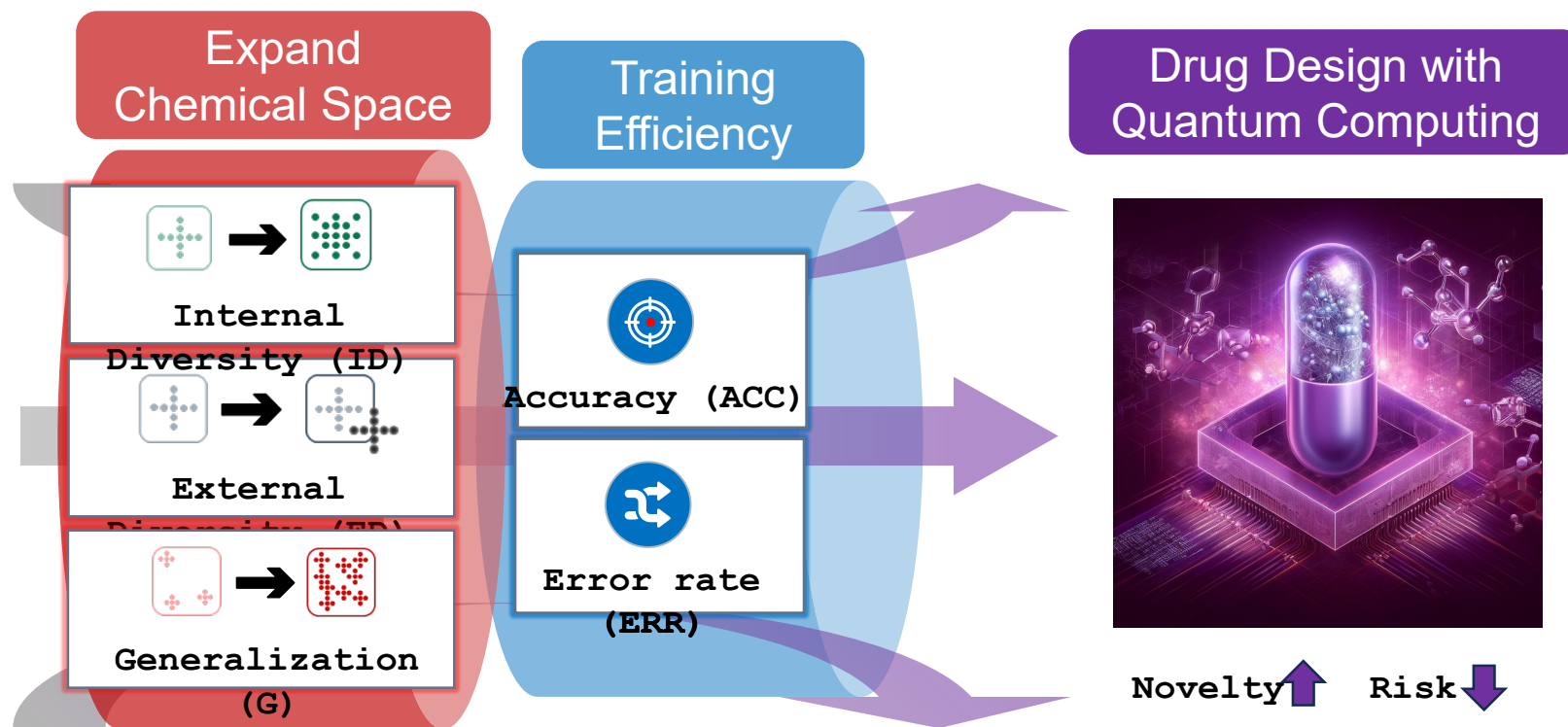
Expanded Chemical Space

- The goal is to pursue innovation through **novel scaffold discovery**.
- Diversity and generalization performance are measures that indicate the possibility of finding **novel scaffolds with desired properties**.



Efficiency of Training

- Effective prediction models are needed for important but sparse data types.
- Accuracy and error rate are measures of the **ability to identify compounds with desired properties**.

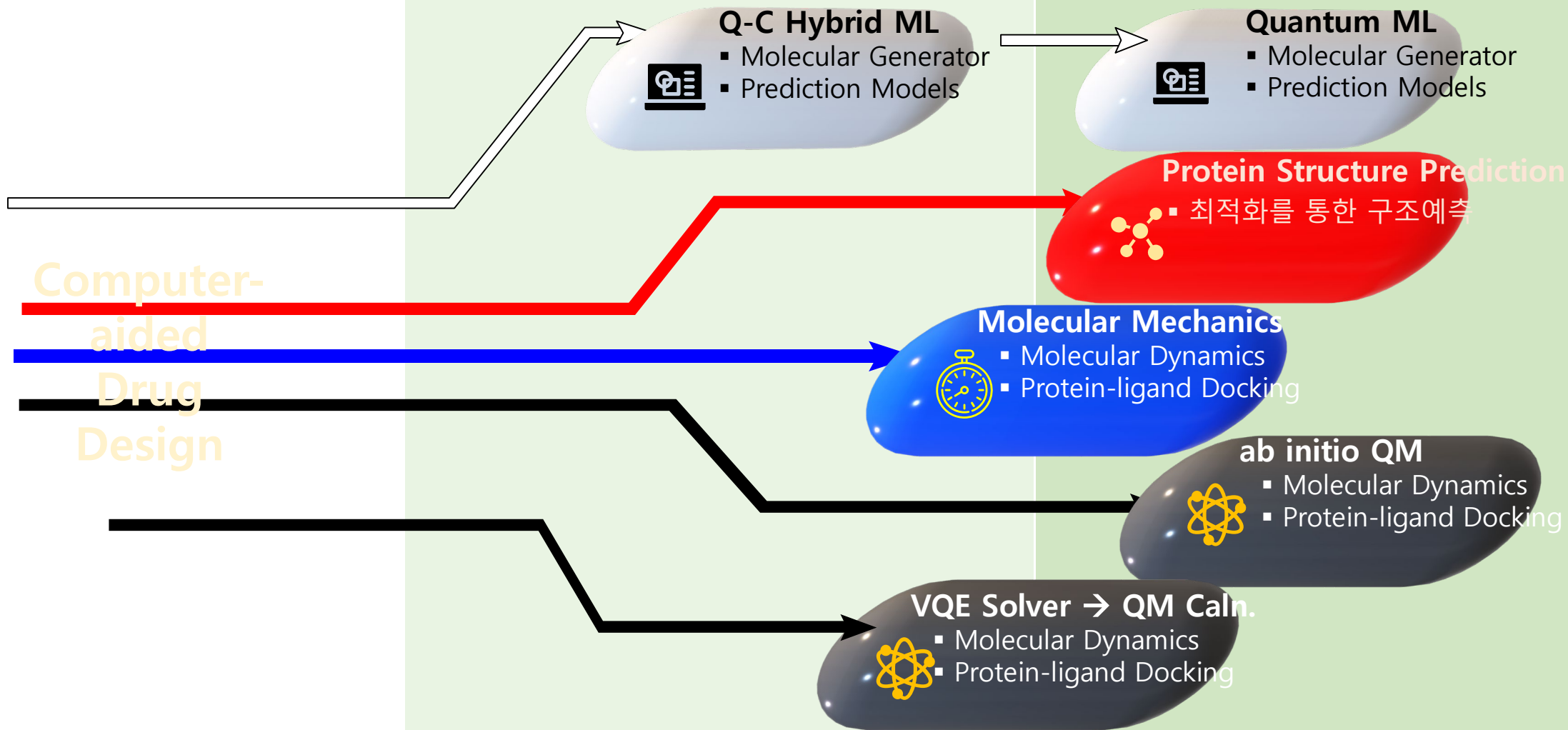


Molecular Simulation at NISQ & FTQC Era

Classical Computing (Now)
(High-Performance Computing)

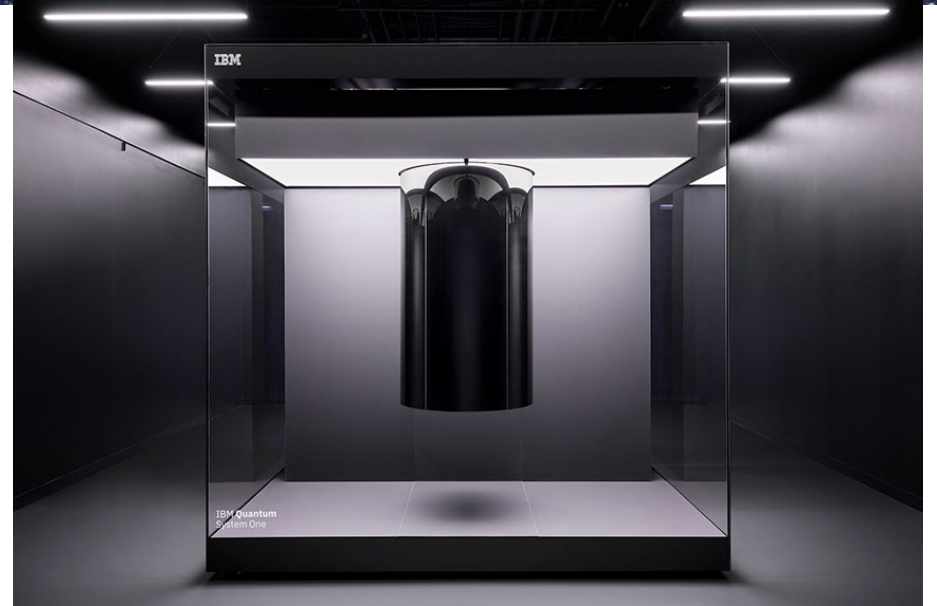
NISQ (Now)
(Noisy Intermediate-Scale Quantum)

FTQC (Future)
(Fault-Tolerant Quantum Computing)



2024년 연세대학교 송도 국제캠퍼스에 양자컴퓨터 설치

- 연세대학교 송도캠퍼스에 IBM 양자컴퓨터를 도입 운영 할 계획으로 본 연구진들은 쉽게 QC 자원을 사용 할 수 있음.
- 연세대와 IBM은 2024년 가동을 목표로 연세대 국제캠퍼스 내 연세사이언스파크(YSP)에 '연세-IBM 쿼텀 컴퓨팅 센터'를 착공.
- 기종은 IBM의 '127큐비트(Qubit) IBM 쿼텀 시스템 원'을 송도 국제캠퍼스에 연내 설치 예정.
- 양자컴퓨터를 송도 바이오클러스터 및 K-bio Lab Hub의 주요 개발 분야인 신약개발 등 바이오 분야 연구에 집중적으로 사용을 지원 할 계획임.





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