WECOMPUT

计算驱动创新药物研发

Computation-Driven Drug Discovery Innovation

北京中大唯信科技有限公司
唯信知药(上海)科技有限公司
Wecomput Technology Co., Ltd.

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About Wecomput

Wecomput Group

2020

SEQUOIA CAPITAL 红杉资本 | CHINA

Jun 2021

NVIDIA INCEPTION PROGRAM

Jul 2021

WECOMPUT

20+ 研发人员

30+ 软著专利

50+ 算法模型

200+ SCI论文

300+ 客户

6K+ 公众号订阅

Beijing Office

Shanghai Office

Guangzhou Office

北京：北京市海淀区上地信息路甲28号科实大厦D座504

上海：上海市浦东新区张江人工智能岛14号楼303

广州：广州市天河区珠江西路5号广州国际金融中心（西塔）807-809

代表客户与合作伙伴

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企业

NVIDIA	大冢制药 Otsuka	先声药业 Simcere
SPH 上海医药 SHANGHAI PHARMA	国药集团 SINOPHARM	華潤三九 CR SANJIU
轩竹医药 XuanZhu Pharma	艾力斯	安必奇生物 Abace Biotechnology
SYNVIDA 循曜生物	SCIWIND 先为达生物	普利制药 POLY HAINAN POLY PHARM.
CHEMXAI	K2	Top mRNA company To be disclosed

研究机构

中国科学院上海药物研究所 SIMM	中国医学科学院 北京协和医学院 药物研究所 Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College	中国科学院武汉病毒研究所 WUHAN INSTITUTE OF VIROLOGY, CAS
CDC 中国疾病预防控制中心 CHINESE CENTER FOR DISEASE CONTROL AND PREVENTION	CSIJRI CHINA-SINGAPORE INTERNATIONAL JOINT RESEARCH INSTITUTE 中新国际联合研究院	ICCAS 中国科学院化学研究所 INSTITUTE OF CHEMISTRY CHINESE ACADEMY OF SCIENCES
中国科学院理化技术研究所 Technical Institute of Physics and Chemistry,CAS	国药集团 SINOPHARM 中国生物研究院 NATIONAL VACCINE & SERUM INSTITUTE	IMPLAD 药用植物研究所

1951 | IBMS | CAAS

医院

上海交通大学医学院附属瑞金医院	复旦大学附属中山医院 ZHONGSHAN HOSPITAL	上海交通大学医学院附属仁济医院
四川大学华西医院 WEST CHINA HOSPITAL SICHUAN UNIVERSITY	中南大学湘雅医院 XIANGYA HOSPITAL CENTRAL SOUTH UNIVERSITY	上海交通大学医学院附属第九人民医院
首都医科大学附属北京天坛医院 BEIJING TIANTAN HOSPITAL, CAPITAL MEDICAL UNIVERSITY	华中科技大学同济医学院附属同济医院	上海中醫藥大學附屬龍華醫院 LongHua Hospital Shanghai University of Traditional Chinese Medicine
山东大学齐鲁医院 QILU HOSPITAL OF SHANDONG UNIVERSITY	中国医学科学院肿瘤医院 CANCER HOSPITAL CHINESE ACADEMY OF MEDICAL SCIENCES	解放军西部战区总医院
南方医院 NANFANG HOSPITAL 南方医科大学第一临床医学院	SYSUCC SINCE 1964 中山大學附属肿瘤医院 SUN YAT-SEN UNIVERSITY CANCER CENTER	解放军南部战区总医院

高校

北京大学 PEKING UNIVERSITY	清华大学 Tsinghua University	上海交通大学 Shanghai Jiao Tong University
香港大學 THE UNIVERSITY OF HONG KONG	THE UNIVERSITY OF CALIFORNIA, DAVIS	復旦大學 FUDAN UNIVERSITY
浙江大學 ZHEJIANG UNIVERSITY	武汉大学 WUHAN UNIVERSITY	空軍軍醫大學 The Fourth Military Medical University
中国药科大学 CHINA PHARMACEUTICAL UNIVERSITY	中山大學 SUN YAT-SEN UNIVERSITY	南京大學 NANJING UNIVERSITY
北京中医药大学 BEIJING UNIVERSITY OF CHINESE MEDICINE	中国海洋大学 OCEAN UNIVERSITY OF CHINA	中国农业大学 China Agricultural University

Vision

实验数据、算力、算法、预测模型呈指数级增长

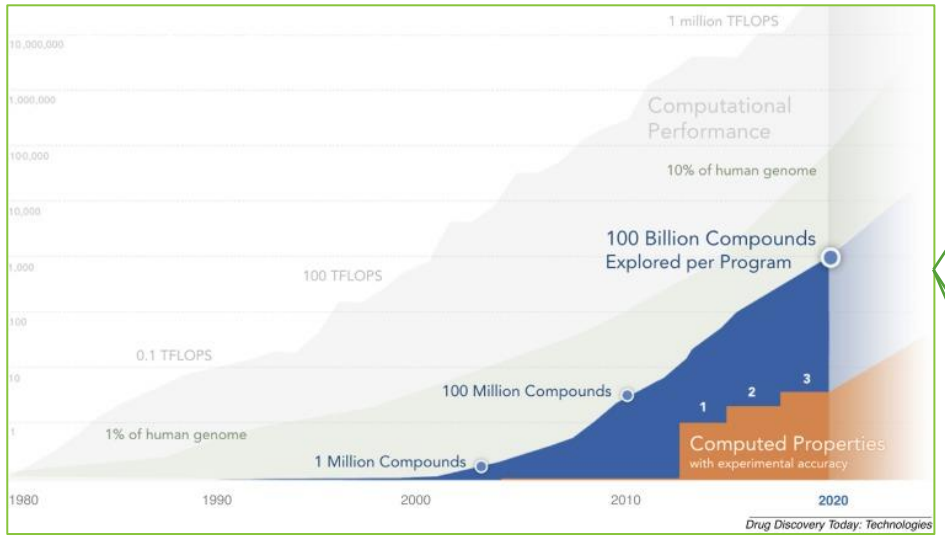

Fig. 1. Here we depict that computational resources, number of experimentally determined protein structures, ability to programmatically enumerate synthetically feasible compounds, and the number of endpoints which can be prospectively predicted with an accuracy approaching wet-lab experiments have all been increasing at an approximately exponential rate. This suggests that computational methods, especially structure-based computational methods, can now be applied to accelerate drug discovery efforts at an unprecedented scale.

1、用AI计算替代部分湿实验环节，降低药物研发成本、缩短周期

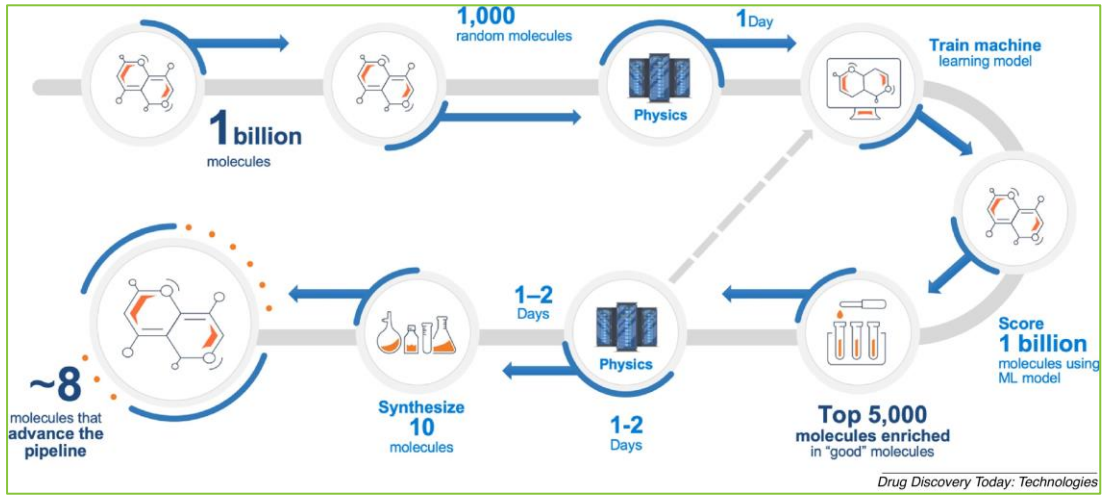

Fig. 3. Active-learning workflow to profile large sets of molecules through physics-based free energy calculations combined with machine learning.

2、积累和学习药物研发中的湿实验数据，促进计算方法迭代进化

3、计算与实验有机结合、干湿闭环，drug the undruggable

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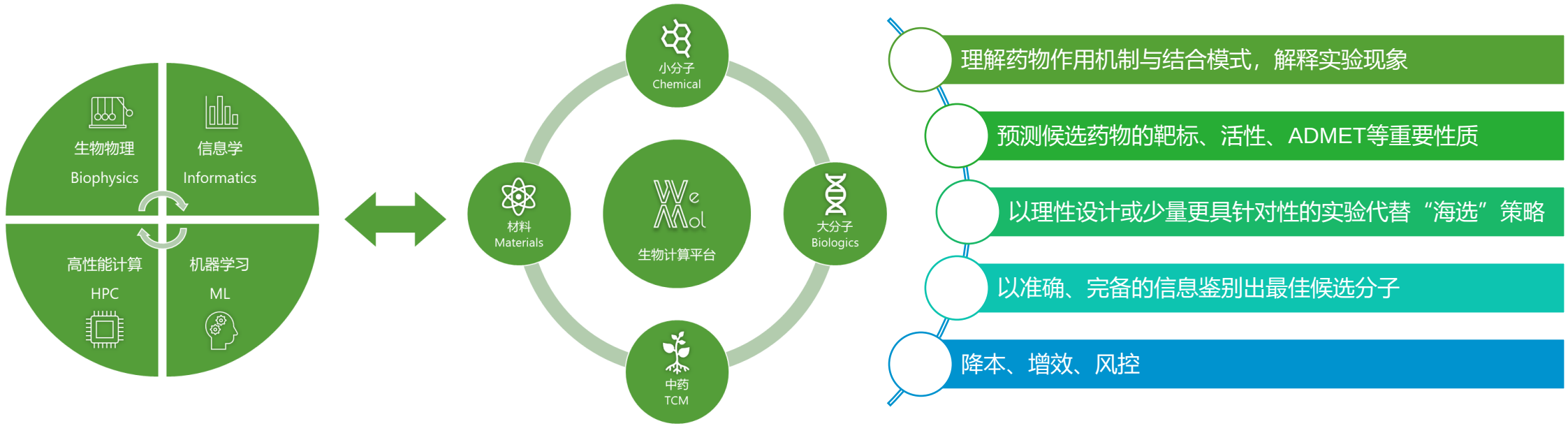
Computational Technology

Technology Overview



Wecomput 专利算法 ALPHA (Algorithms for Pharmaceutical Industry) - 赋能药物发现全流程

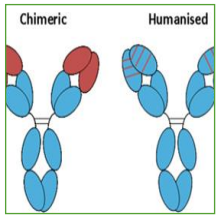
Target Identification	Target Validation	Hit Identification	Lead Optimization	Preclinical tests	Clinical trials
• Bioinformatics • Target fishing • Reverse screening • Neoantigen prediction	• Druggability prediction • Tool compound design • Protein structure prediction	• Library design • De novo design • Virtual screen • Scaffold hopping • Antigen design • Epitope prediction	• (Q)SAR • Structure-based optimization • Molecule generation • Free energy calculation • Developability prediction • Virtual affinity maturation	• ADMET prediction • Metabolic site prediction • Metabolite prediction • Physiologically-based phamacokinetic (PBPK) simulations	• Off-target prediction • Side-effect prediction • Drug combination prediction • Immunogenicity prediction

Featured Platforms

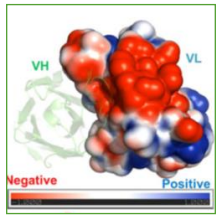
Protein Design Platform

- Approved/ Clinical Antibody Database
- Approved/ Clinical Protein Database
- Human Protein Structure Database
- Antibody Structure Database
- Observed Antibody Space
- (Non-) Cleavable Linker Database
- Functional Element Database
- Multi-Specific Format Database

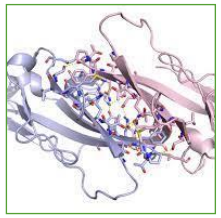
Antibody Design



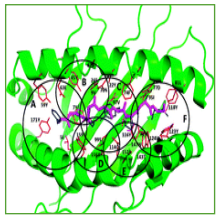
Developability Profiling



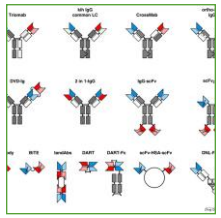
Virtual Affinity Maturation



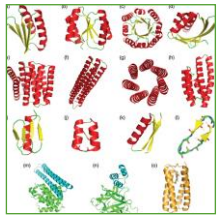
Immunogenicity Prediction



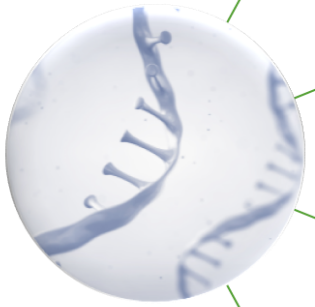
Multi-specific Format Design



De novo Design



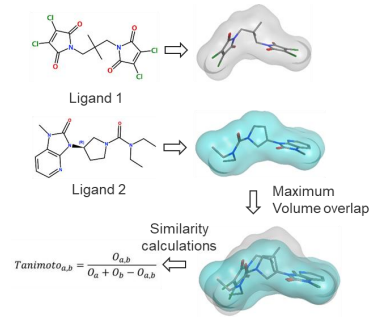
mRNA Design Platform



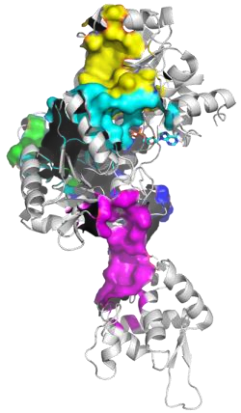
- mRNA序列设计
  - 翻译效率
  - 降解速率
  - 免疫原性
  - 体外转录产量
- LNP 递送系统设计
  - 装载效率
  - 递送效率
  - 靶向能力
  - 可专利性
- mRNA 调控剂设计
  - 可控释放
  - 可控终止
- 新抗原设计 Neoantigen

Small Molecule Design Platform

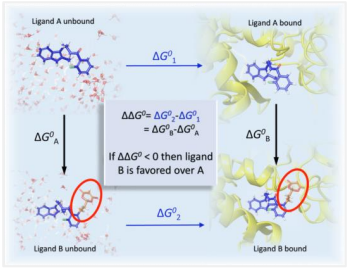
- Purchasable Compound Database
- Synthetic Accessible Compound Database
- Structure-Target-Activity/Toxicity Database
- Conformation Database



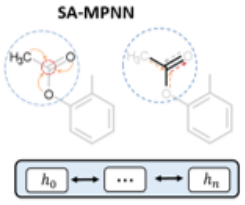
Ultra-High-Throughput Virtual Screening



Allosteric Binding Site Prediction



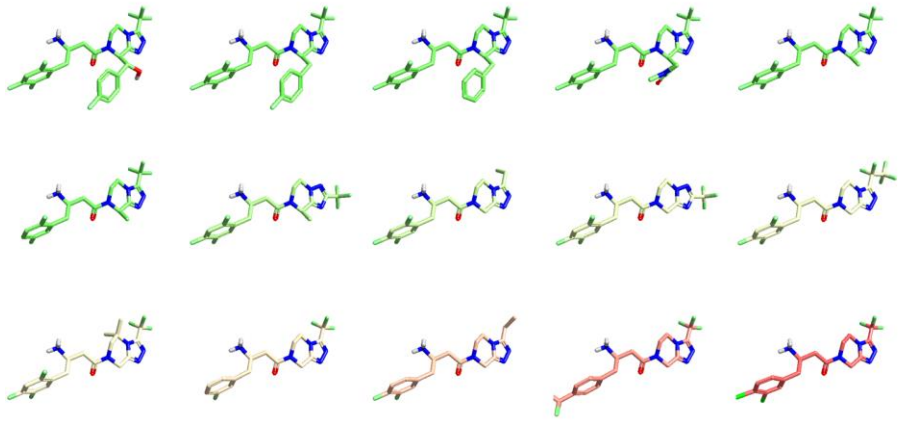
(Relative) Binding Free Energy Prediction



Molecule Generation
ADMET Prediction

AlphaConf – 药物三维构象生成

相比二维结构，药物的三维构象与活性更相关，
准确预测、快速生成、高效存储是痛点



Algorithm	Force Field	RMSD			
		Maximum ensemble size 50		Maximum ensemble size 250	
		Mean	Median	Mean	Median
ConfGenX	OPLS3	**0.63**	0.52	**0.54**	**0.44**
cxcalc	Dreiding	0.87	0.77	0.73	0.61
iCon	MMFF94s	0.72	0.53	0.59	0.47
MOE	MMFF94s	0.75	0.54	0.62	0.50
OMEGA	MMFF94s _NoEstat	0.67	**0.51**	0.57	0.46
RDKit DG	UFF	0.77	0.64	0.63	0.52
AlphaConf	UFF	0.64	0.54	**0.54**	0.46

Storage space for 10M molecules				
	Max allowed conformations per molecule			
File Format	100	250	500	1000
AC (AlphaConf)	7.2 GB	11 GB	17 GB	24 GB
SDF	2.7 TB	6.6 TB	14 TB	22 TB
Ratio	375	600	820	920

AlphaConf高通量三维构象生成算法

- **精度明显优于同类开源算法**，且更好地支持复杂结构
- 高效率的三维构象搜寻技术，**速度远超同类算法**
- 独特构象压缩技术，比主流商业软件的**存储空间降低数百倍**，适用于超大规模三维构象库的构建和超高通量虚拟筛选

J. Chem. Inf. Model. 2017, 57, 11, 2719–2728
X. Yan, J. Li, et al. manuscript, 2021

AlphaShape – 药物三维结构/药效团匹配

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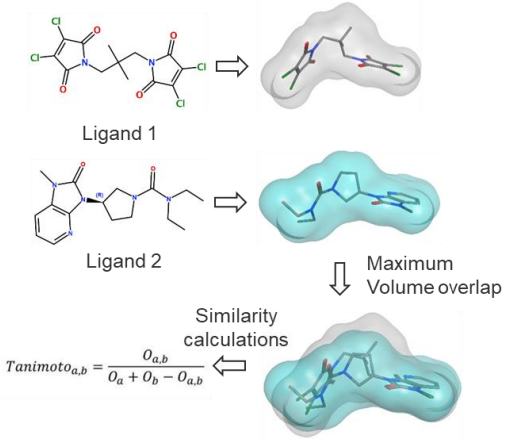
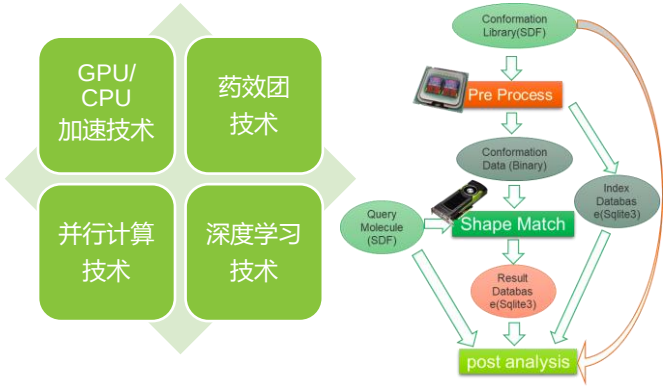
基于高斯函数的形状匹配原理



融合多种HPC和AI技术



超高通量，筛选速度远超实验筛选

264万 overlay/second/GPU*

5600万 compound/day/GPU*

30分钟 筛完160万化合物

(2.38亿三维构象/50个查询构象)

已被合作药企用于虚拟筛选并成功发现hit

* GPU: NVIDIA Tesla V100

精度大幅超过主流商业软件

AUC (Avg.)	Schrodinger / ROCS		AlphaS		
	Shape	Pharmacophore	Shape	Pharmacophore	S+P+DNN
DUD	0.716	0.823	0.750	0.847	0.930
DUD-E	0.663 / 0.696		-	-	0.837

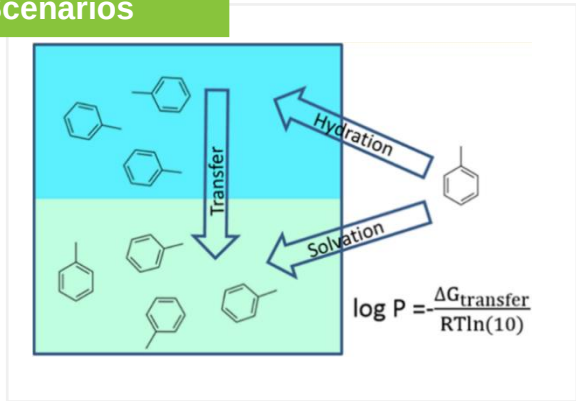
作为底层算法引擎 支持多重应用场景

- 高通量虚拟筛选
- 分子设计突破专利
- 药物重定向老药新用
- 毒副作用位点预测

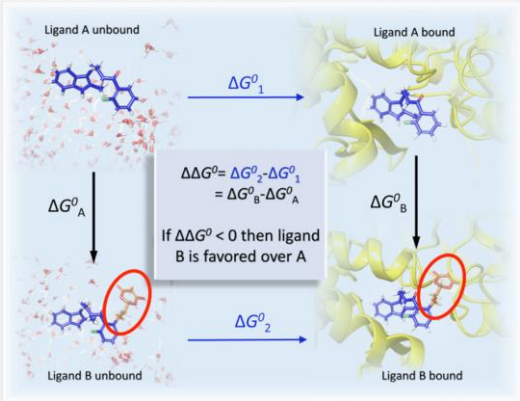
X. Yan, J. Li, et al.. J. Chem. Inf. Model., 2013, 53(8), 1967–1978.
X. Yan, J. Li, et al., J. Comput. Chem., 2014, 35(15), 1122-1130.
M. Xia, X. Yan, J. Li, et al. manuscript, 2021

AlphaFEP – 药物相对结合自由能计算

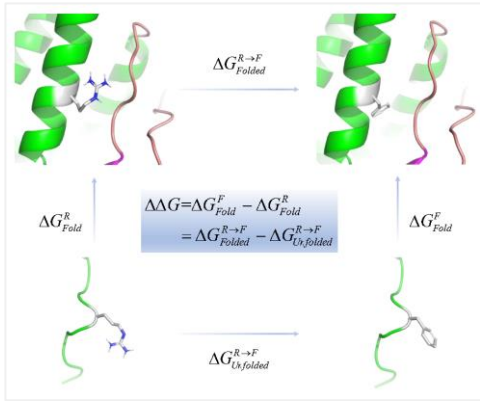
Scenarios



药物性质预测（logP）



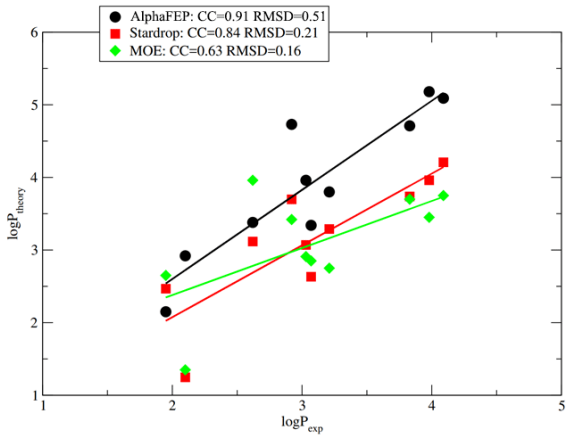
突变亲和力预测、稳定性改造



先导化合物优化

LogP benchmark

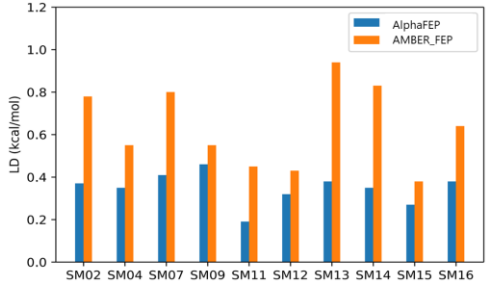
计算类药分子的logP值



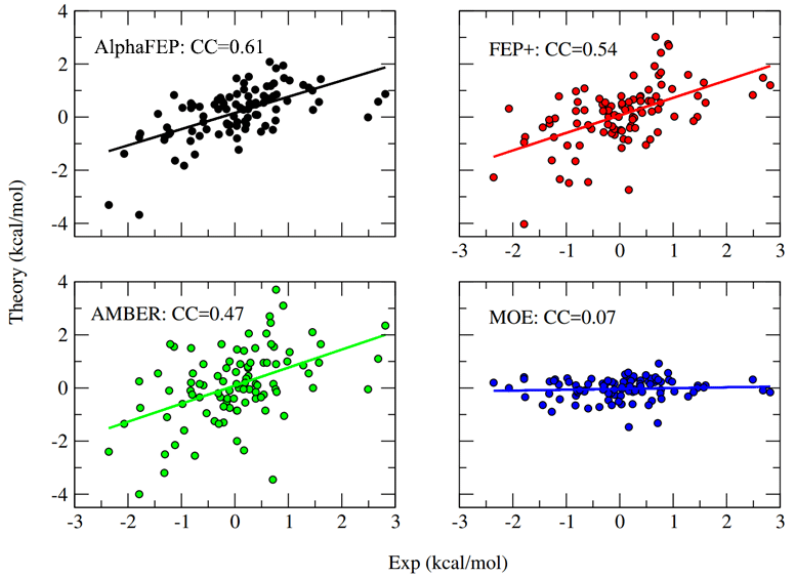
精度优于主流商业软件

* SAMPL6：国际著名计算化学挑战赛

ΔΔG benchmark



显著提高了计算的精度和可重复性
优于同类商业或学术软件

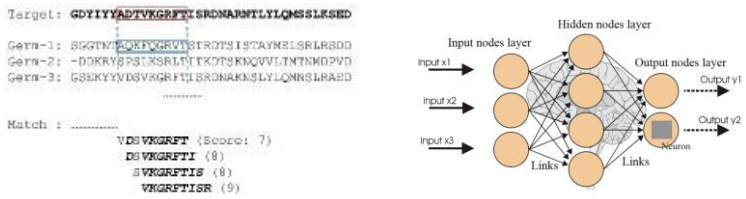


ΔΔG data source: SI of Wang et al. JACS 2015, 137, 2695

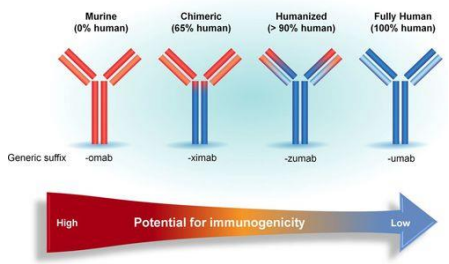
AlphaMHC – 药物免疫原性预测

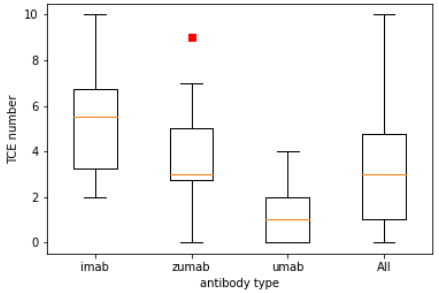
- 相当数量的大分子项目因为免疫原性折戟，体外湿实验手段成本高、周期久且无法准确预测免疫原性的临床表现，AlphaMHC可以**准确预测临床结果**，可以有效地跟体外实验手段结合评价免疫原性风险。
- 还可以预测肿瘤新生抗原（neoantigen）用于疫苗。

AlphaMHC



Benchmarks 1
Approved Abs (n=91)
correctly classified





Benchmarks 3: immunogenicity events of clinical studies correctly predicted (6/7)

Drug Name	Company	Type	Note	ADA rate	Immunogenicity (ground truth)	Predicted Risk (T cell epitopes)	Prediction Accuracy
Alemtuzumab	Bayer	Anti-CD52 Ab	First humanized Ab	85%	High	High (7)	True Positive
Atezolizumab (Tecentriq)	Roche	Anti-PD-L1 Ab		40%	High	High (5)	True Positive
Bococizumab	Pfizer	Anti-PCSK9 Ab	Discontinued	48%	High	Medium (3)	False Negative
Infliximab	Janssen	Anti-TNF-α Ab		28%	High	High (4)	True Positive
Ixekizumab	Novartis	Anti-IL-17A Ab	MAPPs assay identified 5-7 TCE*	18%	High	High (5)	True Positive
Vatreptacog alfa	Novo Nordisk	FactorVIIa analog	Discontinued	11%	High	High (6)	True Positive
NovoSeven	Novo Nordisk	FactorVIIa		0	Low	Low (0)	True Negative

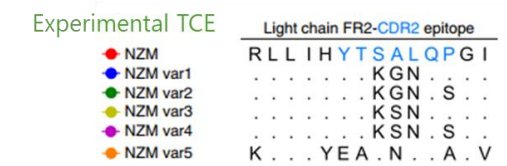
Benchmarks 2
Literature T cell epitope
precisely recognized

Letter | Published: 09 September 2019

A single T cell epitope drives the neutralizing anti-drug antibody response to natalizumab in multiple sclerosis patients

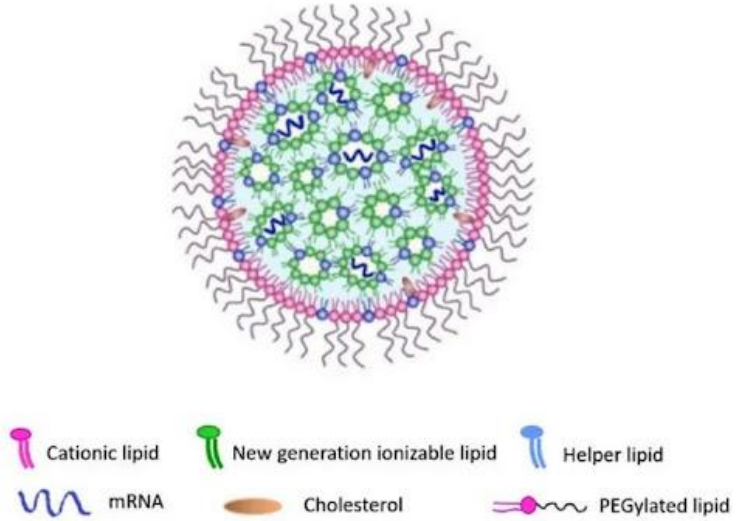
Antonino Cassotta, Vincent Mikol, Thomas Bertrand, Stéphanie Pouzieux, Josiane Le Parc, Paul Ferrari, Jacques Dumas, Michael Auer, Florian Deisenhammer, Matteo Gastaldi, Diego Franciotta, Chiara Silacci-Fregni, Blanca Fernandez Rodriguez, Isabella Giacchetto-Sasselli, Mathilde Foglierini, David Jarrossay, Roger Geiger, Federica Sallusto, Antonio Lanzavecchia & Luca Piccoli

Nature Medicine **25**, 1402–1407(2019) | Cite this article

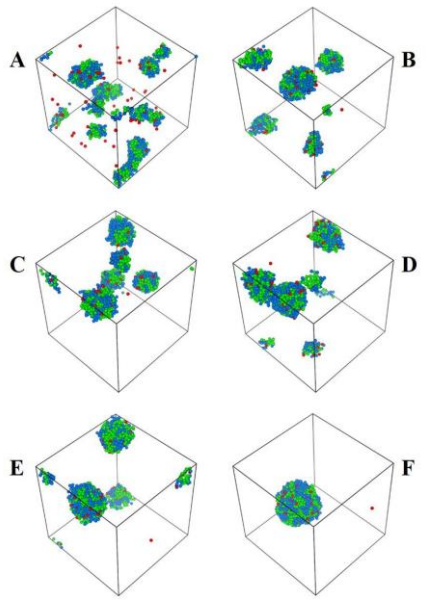
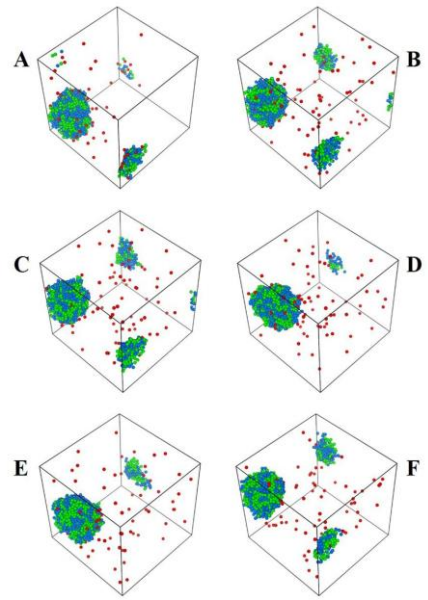


LNP递送系统模拟

- 支持LNP、LPX、LPP及新型脂质体分子的结构设计与模拟
- 动态模拟RNA/LNP自组装、释放等全过程
- 多种精度的分子动力学模拟，成熟的力场参数
- 用于设计、筛选自主知识产权的递送系统



药物载入与释放模拟

中性水环境下， 药物分子自发载入纳米材料	生理环境下， 药物分子从纳米材料中自发释放
	

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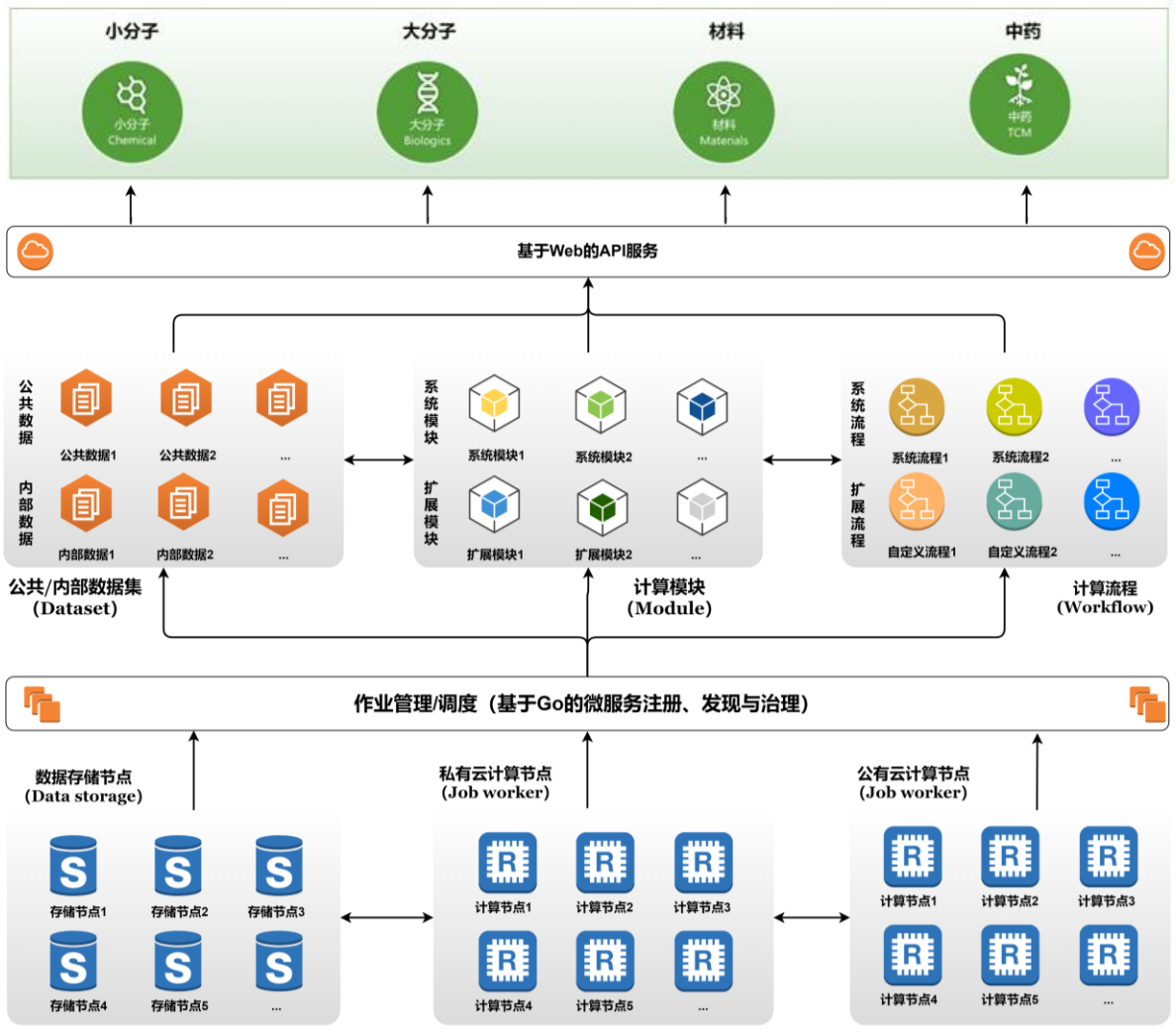
WECOMPUT

Software

WeMol –分子数字化智能计算平台



应用层
计算驱动药物创新场景

数据算法层
数据管理与计算一体化
计算流程化

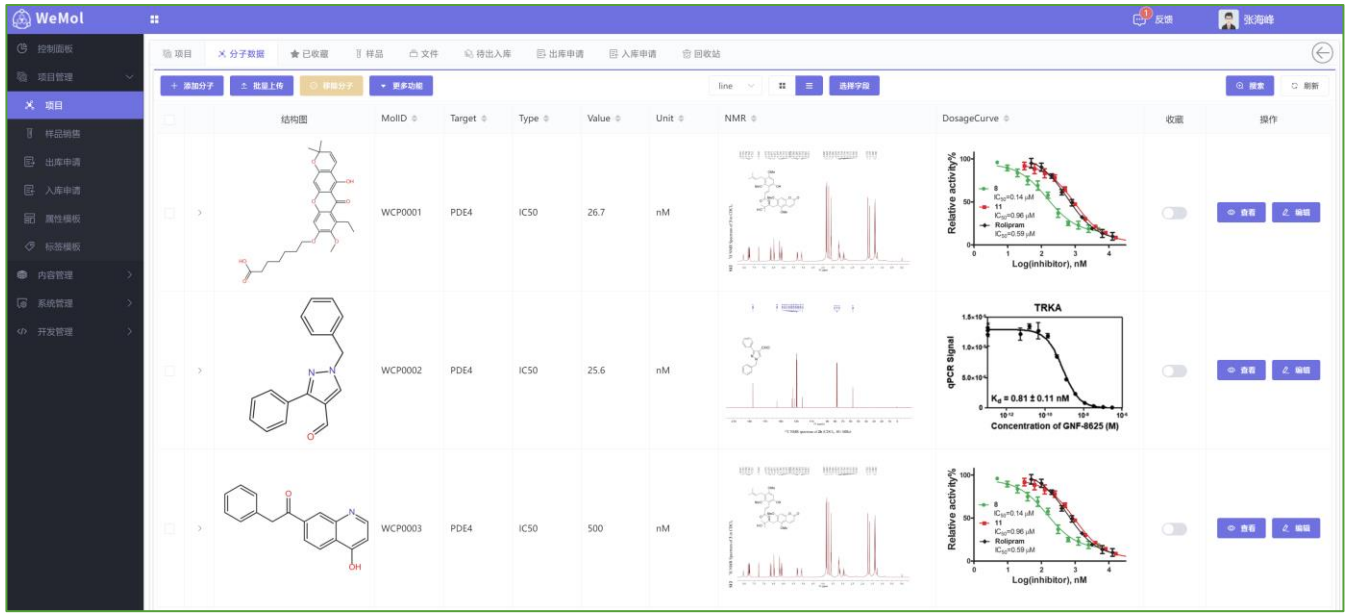
算力层
公有云/私有云混合

免疫原性预测，抗体人源化，
mRNA序列设计，ADMET性质预测，虚拟筛选，
FEP计算，分子生成，靶点预测，量子化学计算等

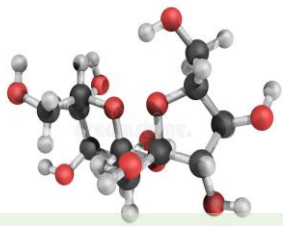
最新前沿AI算法快速部署
自主开发工具快速接入计算流程
公共、内部数据与计算工具无缝衔接

支持公有云、私有云混合
闲散机器调用、不受操作系统限制
不同硬件计算资源轻松维护

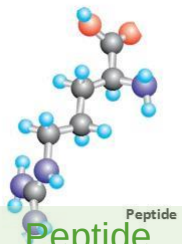
WeMol – 数字化模块



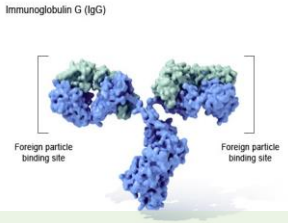
- 实验数据存储与管理
- 出入库流程管理
- 数据类型灵活定制
- 湿实验人员友好
- 在线分享、协作
- 智能汇总分析，辅助决策
- 精细的权限管理



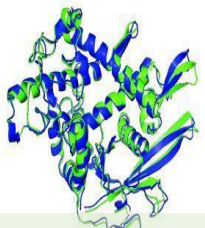
Chemical



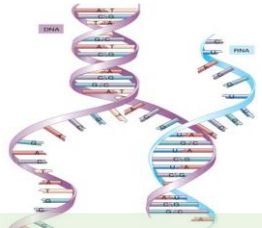
Peptide



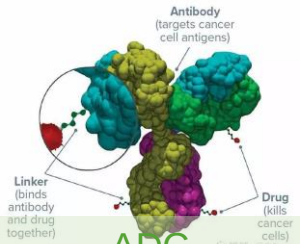
Antibody



Protein



Nucleic Acid

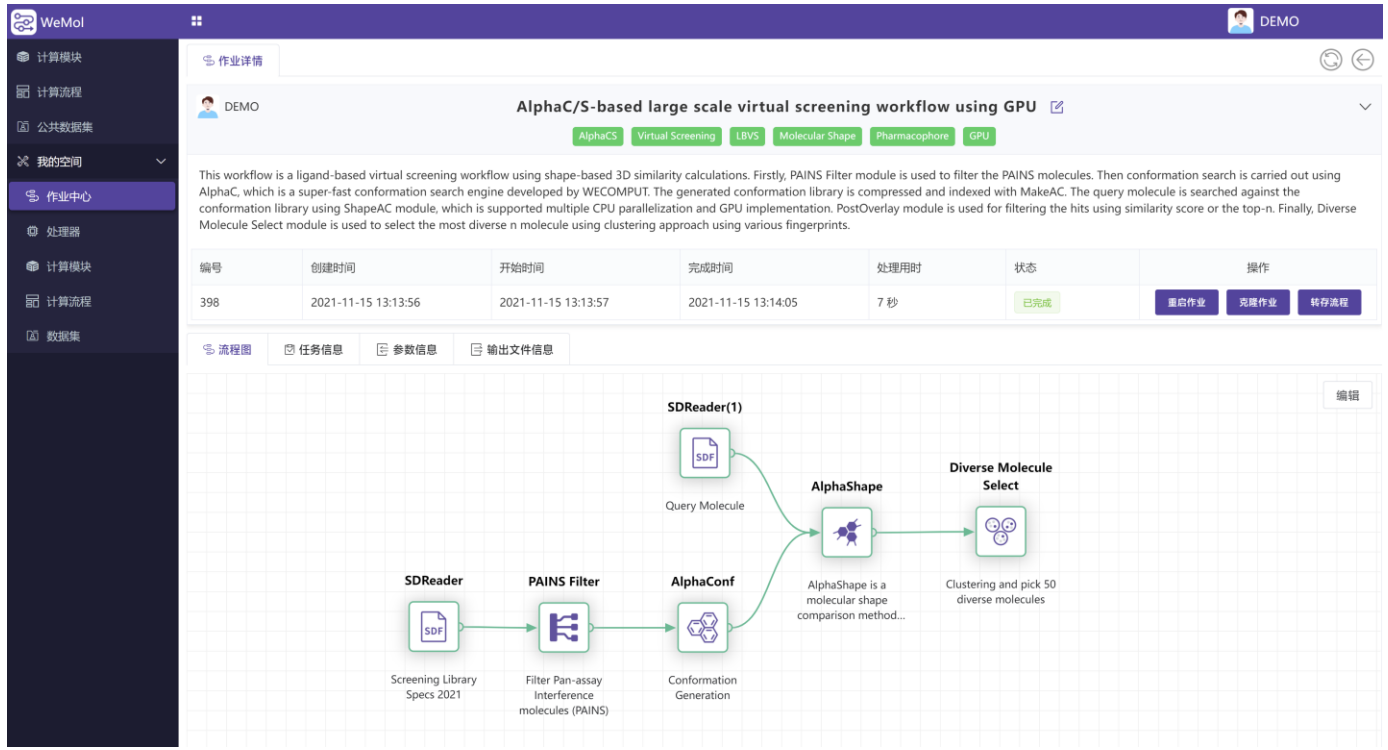


ADC

TCM

WeMol – 智能计算模块

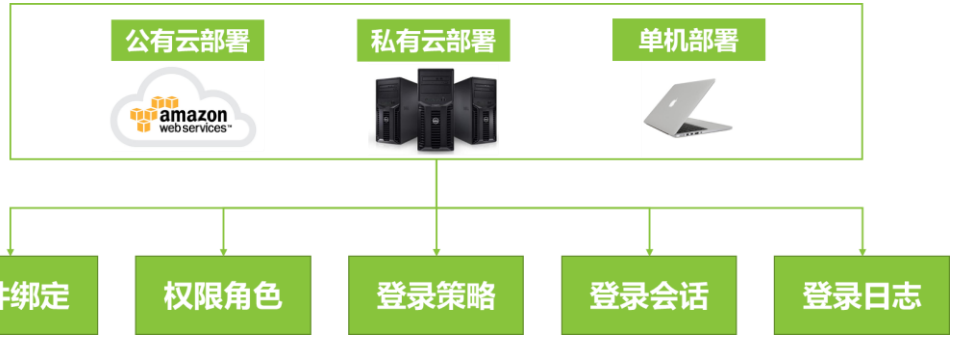
- Connect 流式架构灵活定制
- Compute 算力弹性扩展
- Learn AI深度学习
- Deploy 多端部署
- Develop 低代码开发
- Interact 简明直观
- Access 精细的权限管理

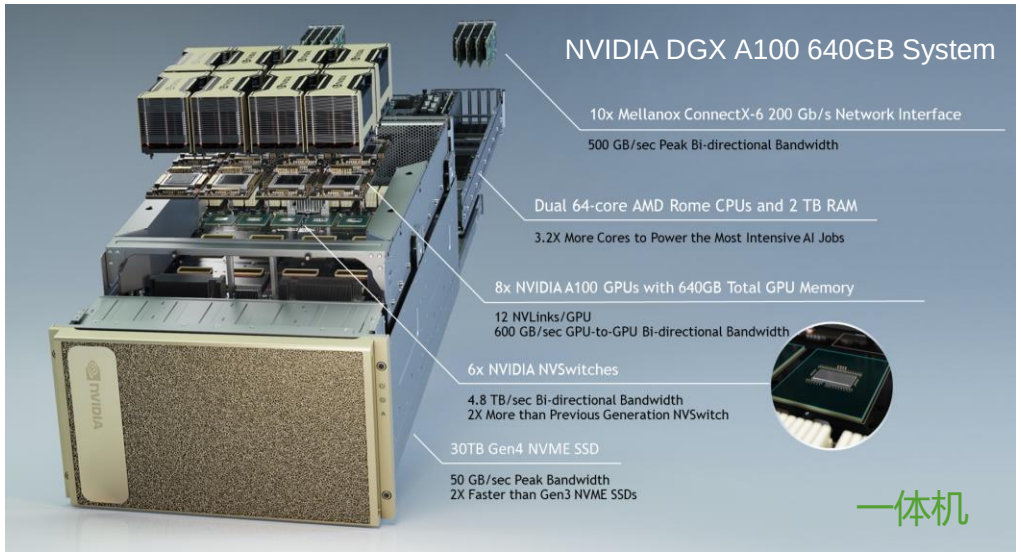


More are coming...

软硬件一体解决方案

灵活的、跨平台、分布式部署方式



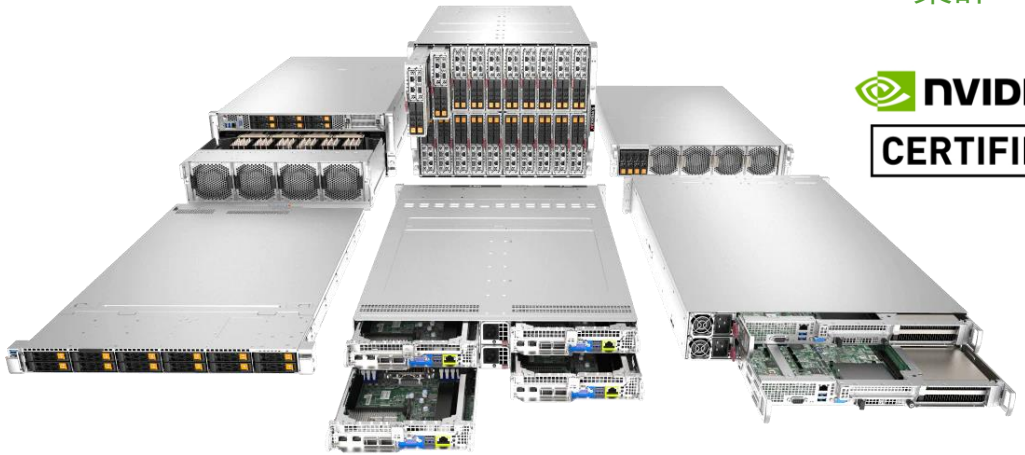


一体机

私有云部署

- 量身定制 硬件配置 高度集成
- 预装 WeMol 完全兼容
- CUDA 加速技术 AI/MD Ready
- NVIDIA 官方认证 质量保证
- 现场部署 开箱即用

HPC集群



NVIDIA CERTIFIED

感谢观看 Thanks

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