Química Medicinal

Espaço químico-biológico

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O espaço químico

Enumeration from first principles shows that almost all small molecules (>99.9%) have never been synthesized and are still available to be prepared and tested.

Table 1. The Known Chemical Space[a]

database	description	size[a]	Web address	ref
PubChem	known molecules from various public sources	32.5 M	http://pubchem.ncbi.nlm.nih.gov	11
Chemspider	online resource from the Royal Society of Chemistry	26.0 M	http://www.chemspider.com/	12
ZINC	commercially available small molecules	21.0 M	http://zinc.docking.org	13
NCI Open	anticancer and AIDS compounds with screening data	0.25 M	http://cactus.nci.nih.gov/ncidb2.1	14
ChemDB	commercially available small molecules	4.1 M	http://cdb.ics.uci.edu	15
BindingDB	bioactive molecules with binding affinity data	0.36 M	http://www.bindingdb.org	16
ChemBank	small molecules annotated with screening data	1.2 M	http://chembank.broadinstitute.org/	17
ChEMBL	small molecules annotated with experimental data	1.1 M	https://www.ebi.ac.uk/chembldb	18
CTD	comparative toxicogenomics database	0.17 M	http://ctdbase.org	19
HMDB	human metabolome database	0.0085 M	http://www.hmdb.ca	20
SMPDB	small molecule pathway database	0.001 M	http://www.smpdb.ca	21
DrugBank	experimental and approved small molecule drugs	0.0065 M	http://www.drugbank.ca	22

[a]Open access collections as of April 2012. Corporate collections and nonopen access sources are not listed.

Reymond, J.L.; Awale, M. Exploring Chemical Space for Drug Discovery Using the Chemical Universe Database. *ACS Chem. Neurosci.* **2012**, *3*, 649-657.

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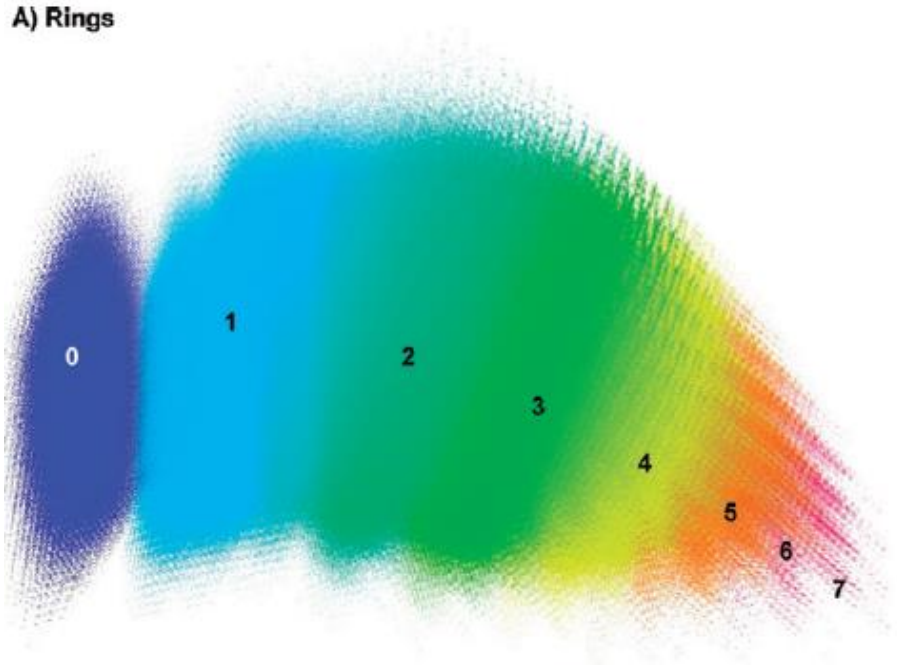
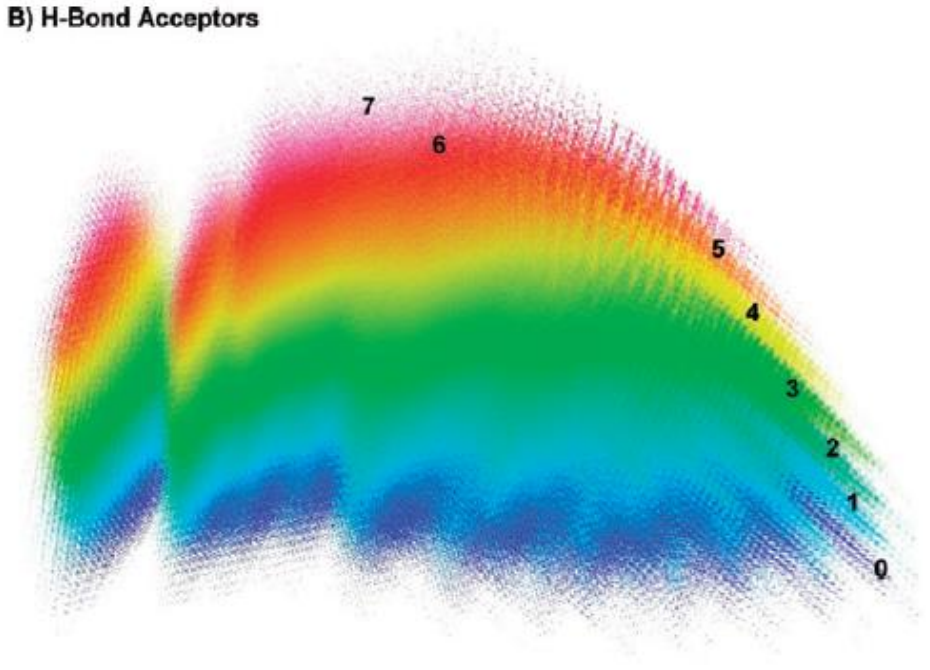
Table 1. Databases of the Known and Unknown Chemical Space

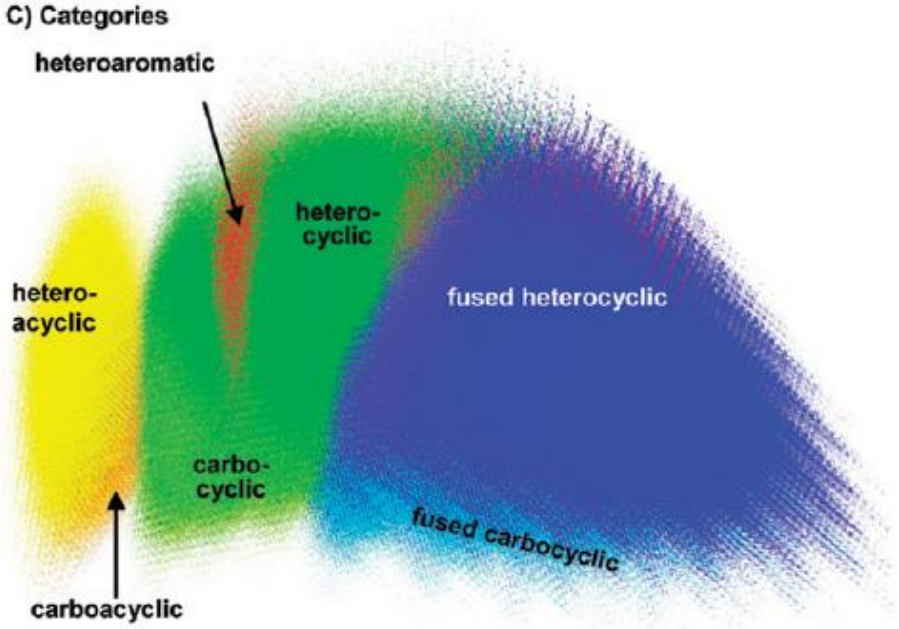
database	description	size[a]	ref
DrugBank	approved and investigational drugs	7 584	59
SuperScent	scents from literature	2 300	60
Flavornet	volatile compounds from literature	738	61
SuperSweet	carbohydrates and artificial sweeteners	642	62
BitterDB	bitter cpds from literature and Merck index	606	63
PubChem	NIH repository of molecules	63 095 535	64,65
ZINC	commercial small molecules	22 724 825	66,67
ZINC.FL	fragrance-like subset of ZINC	69 724	68
BindingDB	small molecules annotated with bioactivity data	453 657	69,70
ChEMBL	small molecules annotated with bioactivity data	1 411 786	71
GDB-11	molecules of up to 11 atoms of C, N, O, and F	26 434 571	36
GDB-13	molecules of up to 13 atoms of C, N, O, S, and Cl	977 468 314	37
GDB-13.subset	simplicity-selected GDB-13 molecules	43 729 989	72
GDB-13.FL	fragrance-like subset of GDB-13	59 482 898	68
GDB-17	molecules of up to 17 atoms of C, N, O, S, and halogens	166 443 860 262	38

[a]For the latest version of each database as available in November 2014

Reymond, J.L. The Chemical Space Project. *Acc. Chem. Res.* **2015**, *48*, 722-730.







O espaço químico
Análise do PubChem

Reymond, J.L.; Awale, M. Exploring Chemical Space for Drug Discovery Using the Chemical Universe Database. *ACS Chem. Neurosci.* **2012**, *3*, 649-657.

Viagem no espaço químico

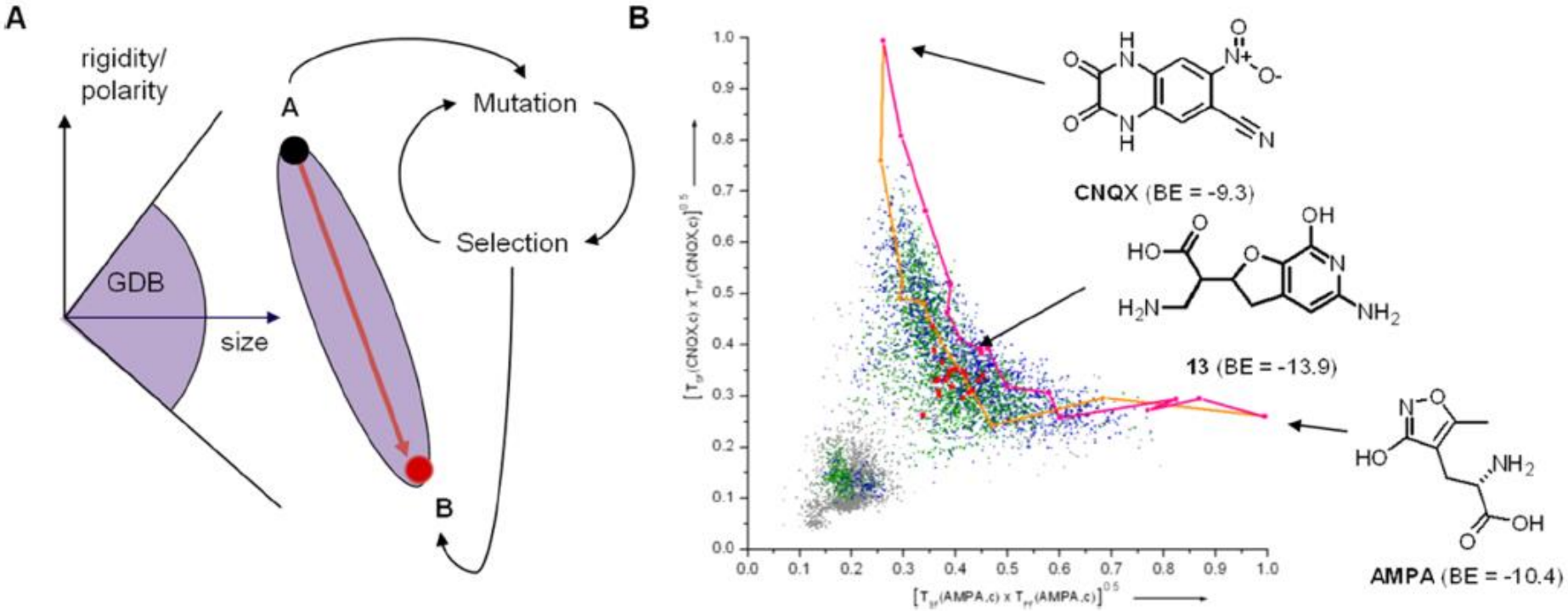


Figure 2. Chemical space travel. (A) Concept of chemical space travel. (B) Application to AMPA receptor ligands.

Reymond, J.L. The Chemical Space Project. *Acc. Chem. Res.* **2015**, *48*, 722-730.

As propriedades físico-químicas e o espaço químico

Geração aleatória de moléculas com 1 ou 2 átomos de C, N, O, H.

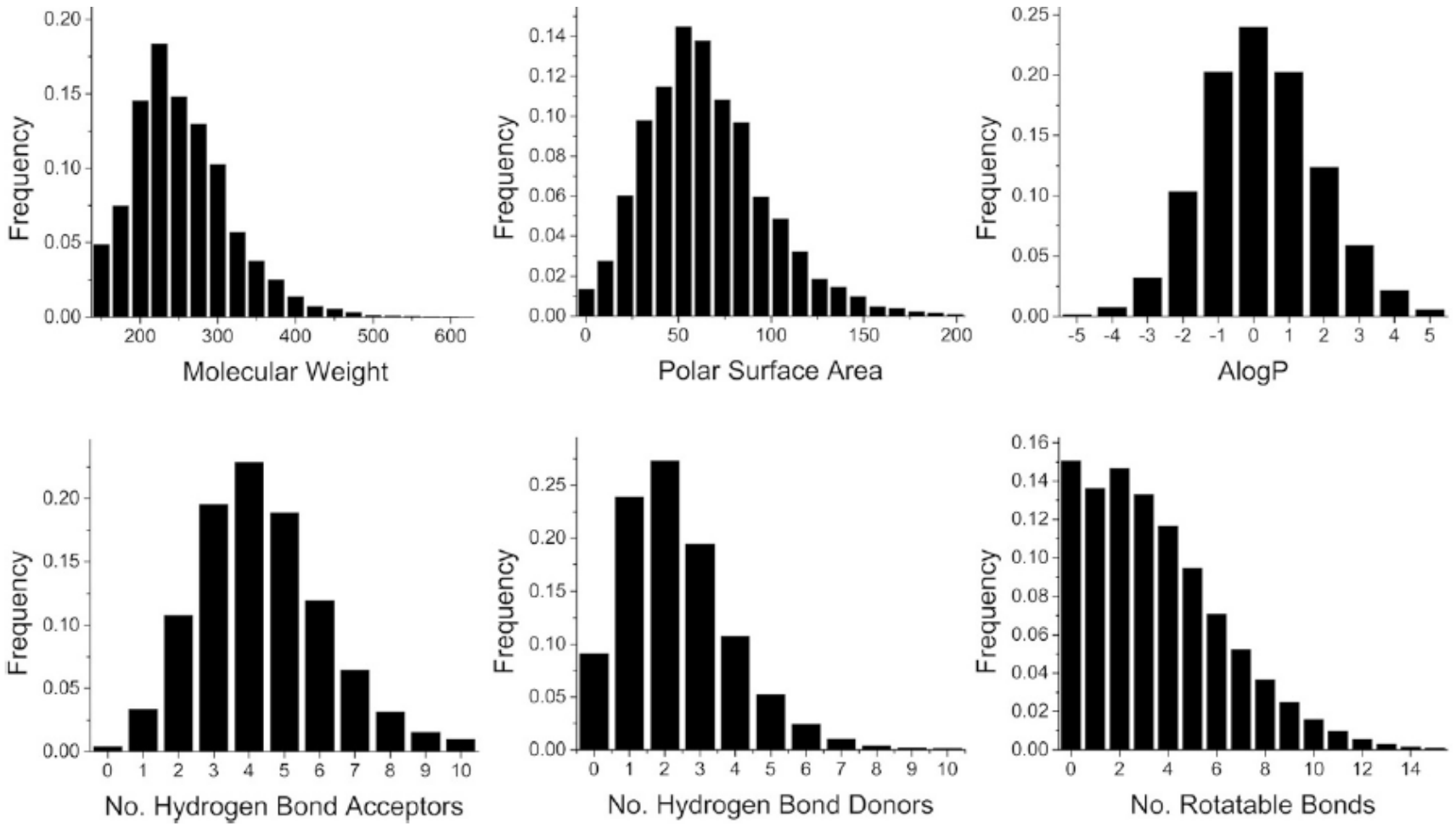
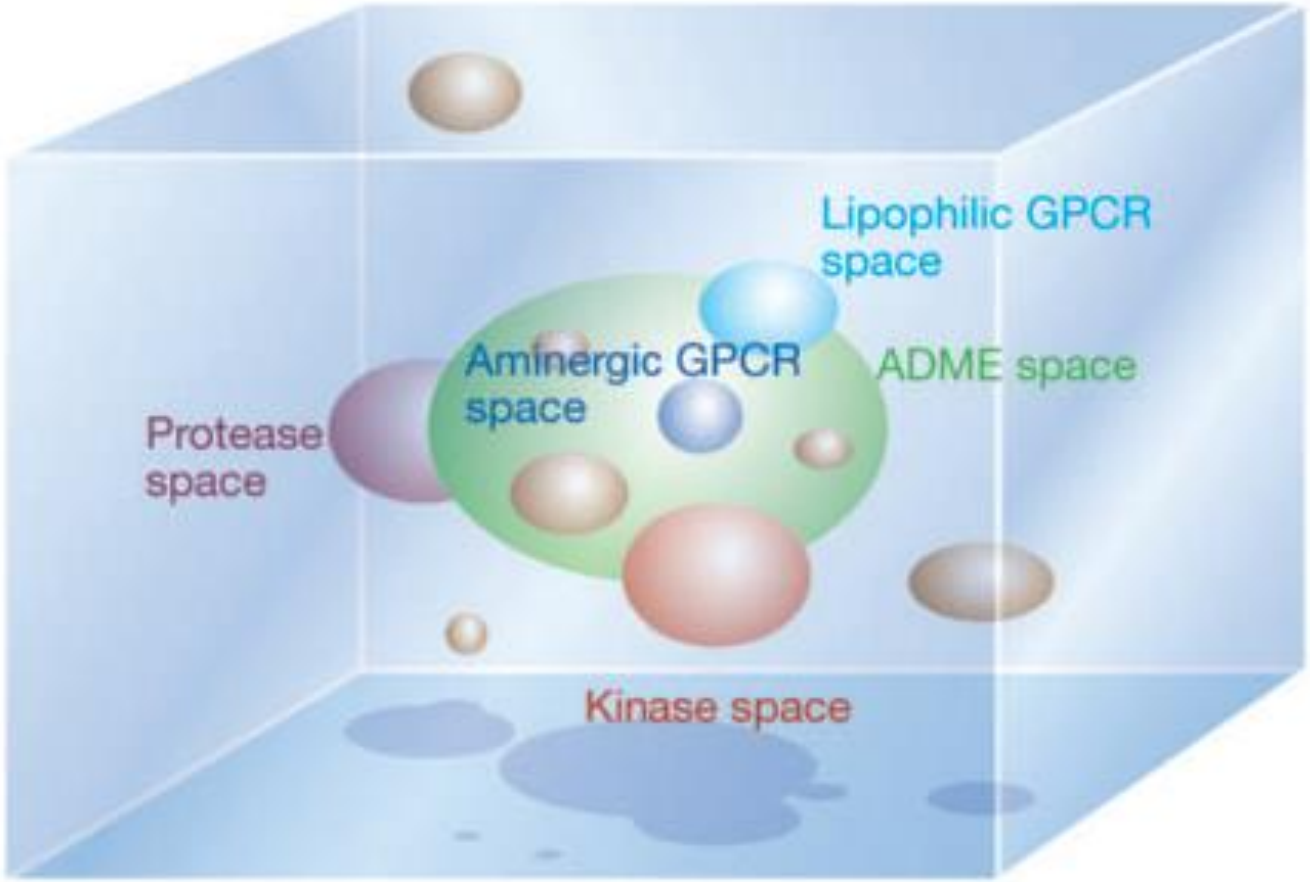


Figure 2 Histogram analysis of the 250,000 member enumerated virtual compound set.

Yu, M.J. Druggable chemical space and enumerative combinatorics. *J. Cheminf.* **2013**, *5*, 19.

O que é o espaço químico-biológico?



Lipinski, C.; Hopkins, A. Navigating chemical space for biology and medicine. *Nature* **2004**, *432*, 855.

O que é *druggability*?

The concept of druggability postulates that since the binding sites on biological molecules are complementary with their ligands in terms of volume, topology and physicochemical properties, then only certain binding sites on putative drug targets will be compatible with high-affinity binding to compounds with drug-like properties.

Hopkins, A. L. & Groom, C. R. Target analysis: a priori assessment of druggability. *Ernst Schering Res. Found. Workshop* **42,** 11–17 (2003).