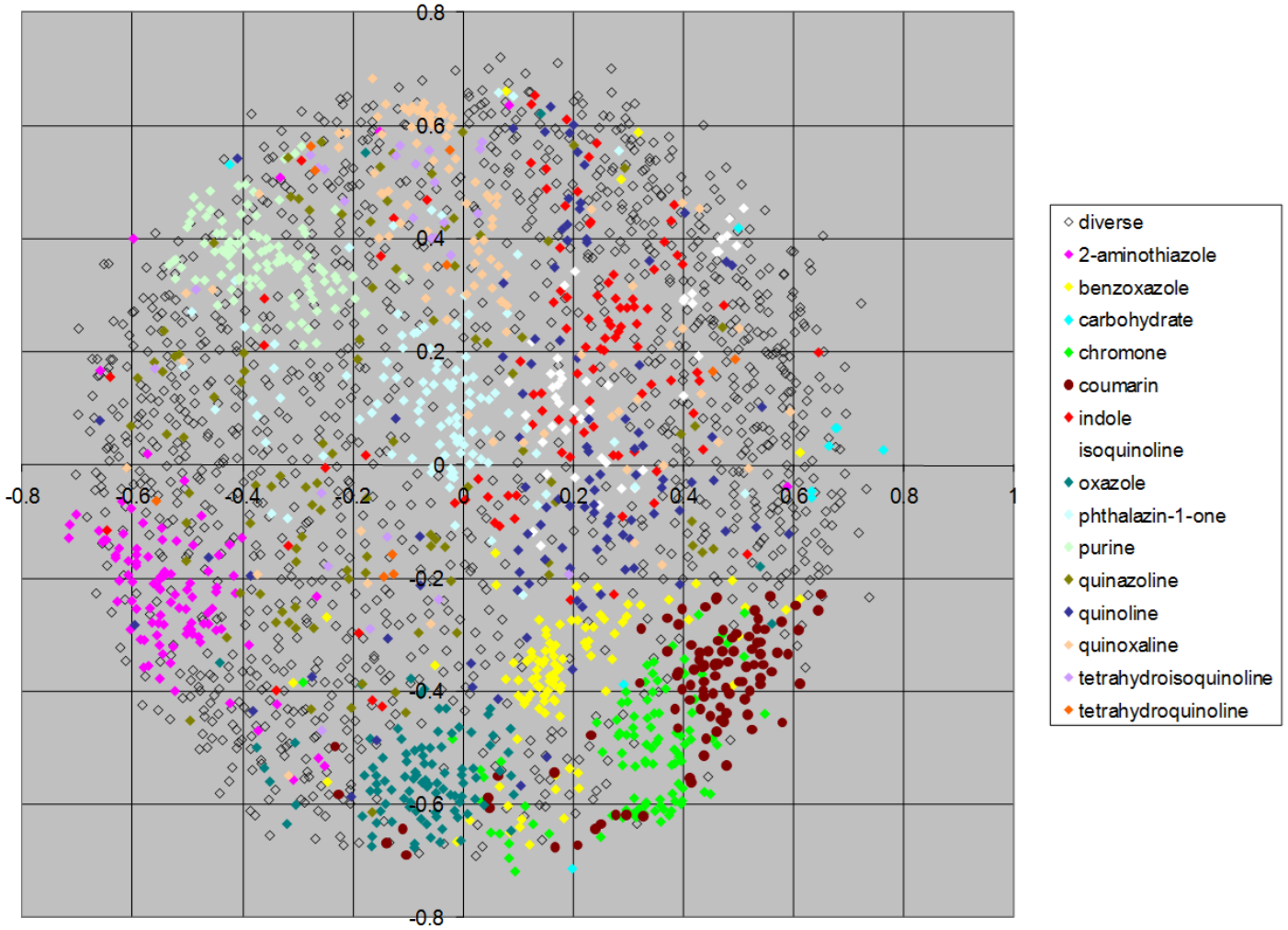
The NExT Diversity Library

- A total of 83,536 compounds
- Three non-separable subsets
  - Legacy MLSMR
  - Diversity 1
  - Diversity 2
- 15 privileged scaffold in the Diversity subsets
- Pre-plated and distributed only as the full combined set in 384-well single-use plates (Greiner 781280, 1uL @ 10mM in DMSO).

* The NCI Diversity Library is managed by NCI contractor, Evotec.

Privileged Scaffolds of the Diversity subsets



Scaffold	# of compounds
2-Aminothiazole	2097
Benzoxazole	1647
Carbohydrate	20
Chromone	1871
Coumarin	3110
Indole	3691
Isoquinoline	193
Oxazole	4943
Phthalazin-1-one	2306
Purine	2854
Quinazoline	1597
Quinoline	3964
Quinoxaline	1255
Tetrahydroisoquinoline	288
Tetrahydroquinoline	323

Lipinski's Rule of Five*

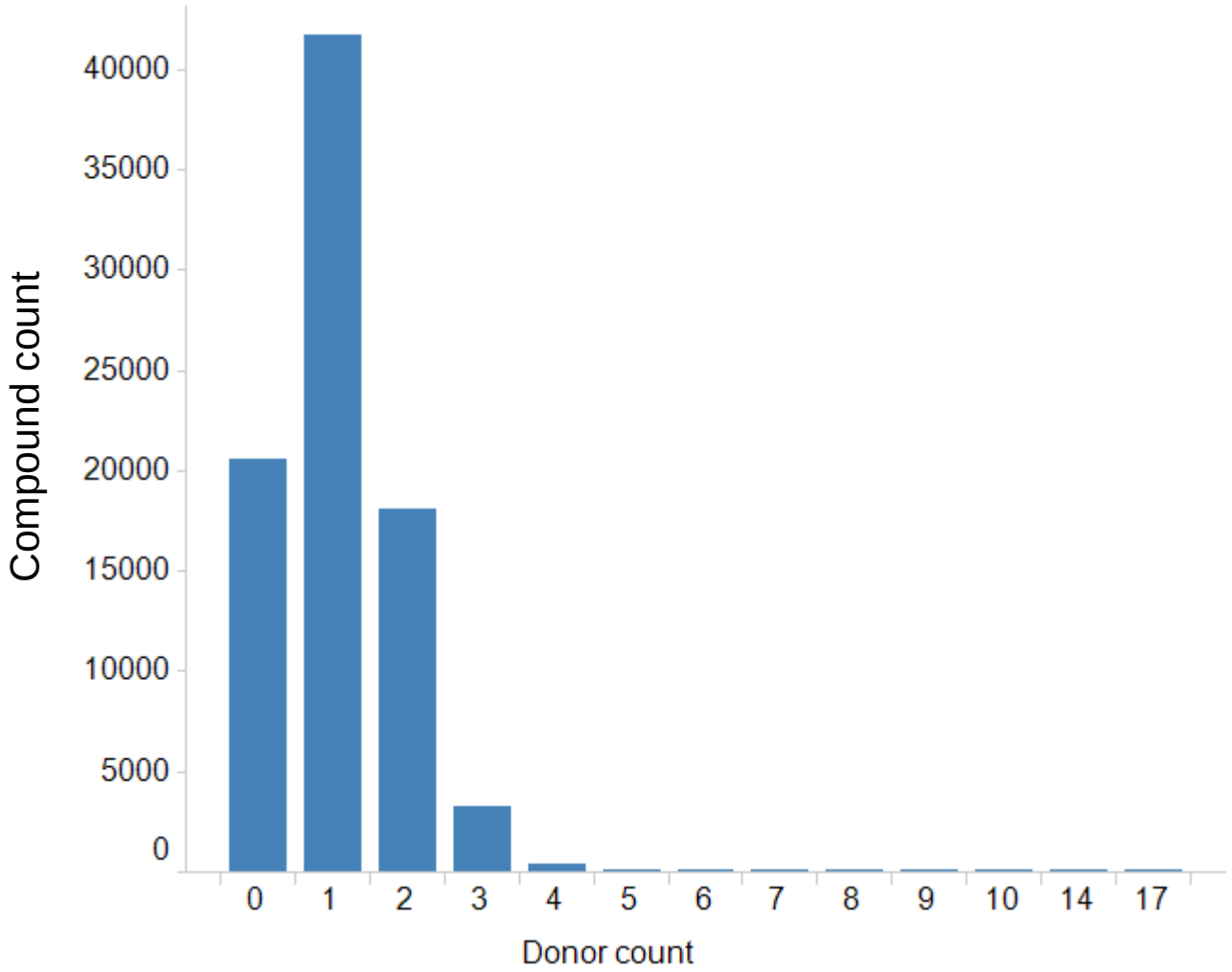
- For orally active drugs, no more than one violation of these rules:
  - Not more than 5 hydrogen bond donors
  - Not more than 10 hydrogen bond acceptors
  - A molecular mass less than 500 daltons
  - A log *P* not greater than 5
- All three sets have high Lipinski compliance:

	Legacy MLSMR	Diversity 1	Diversity 2	Combined
Pass all rules	98.7%	95.0%	82.2%	91.7%
Max. one violation	99.8%	100.0%	99.4%	99.8%

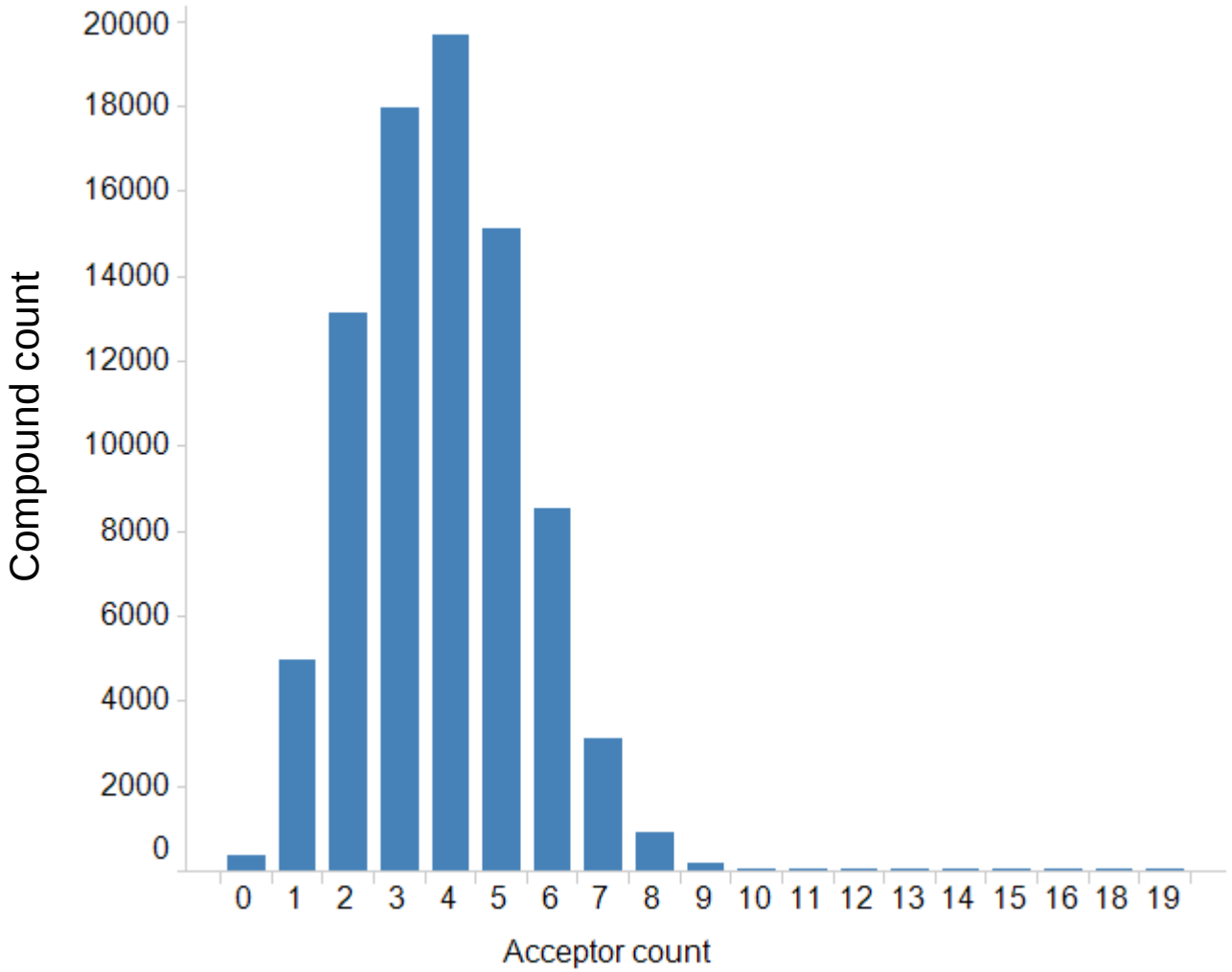
* The following library descriptions include all 83,536 compounds.

Lipinski CA, et al. *Adv. Drug Deliv. Rev.* **2001**, 3–26.

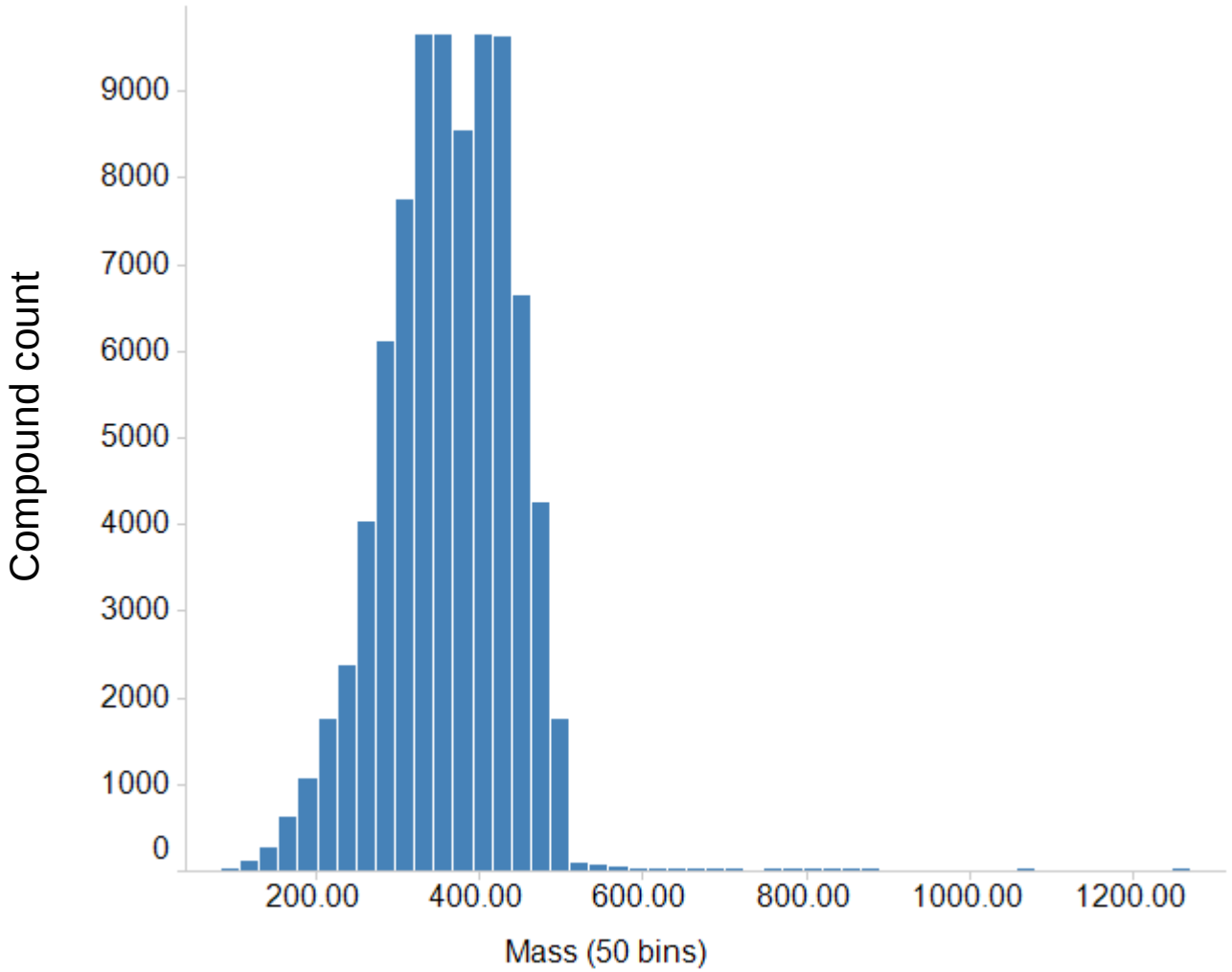
H-Bond Donor Count Distribution



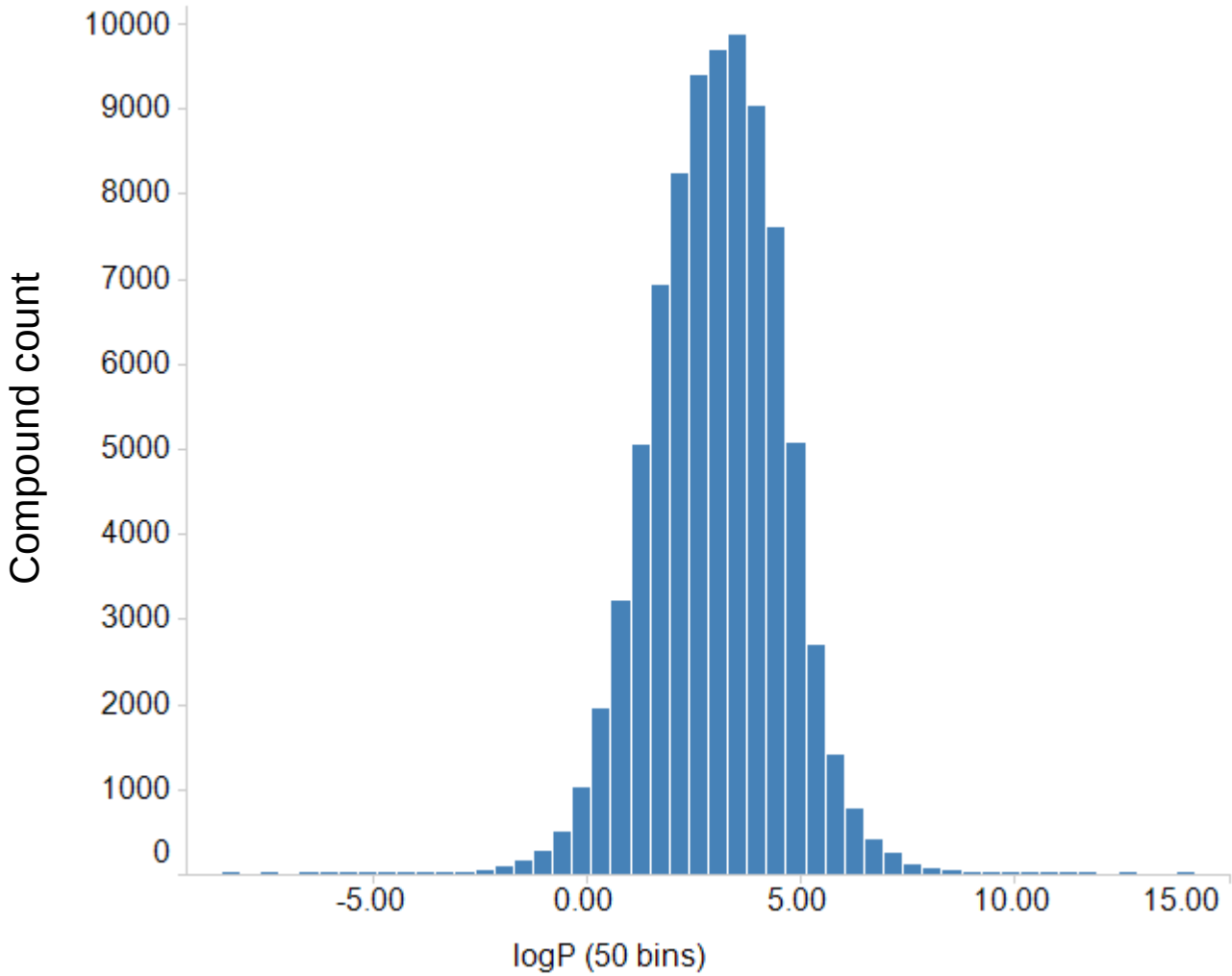
H-Bond Acceptor Count Distribution



Molecular Weight Distribution

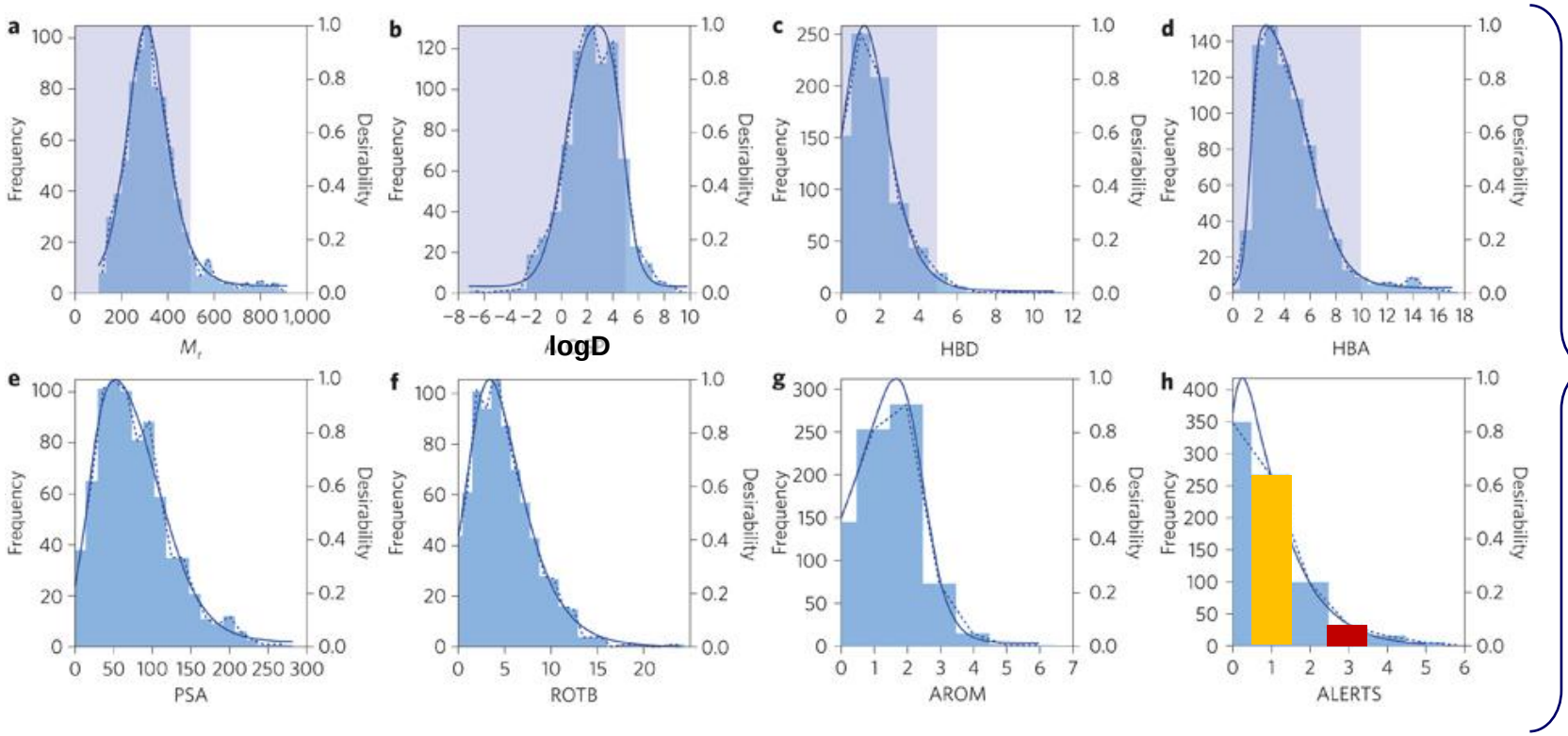


LogP(*calc*) Distribution



Beyond Lipinski: QED-Drug-likeness Score

- Going beyond simple Lipinski “Rule of Five” to guide for orally bioavailable drugs
- Properties are dependent on each other in terms of effect on drug-likeness, therefore they need to be considered in parallel → multi-parameter optimized (MPO) score



MPO score for druggability:

QED
(Quantitative Evaluation of Druglikeness)

Bickerton et al. *Nature Chem.* **2012**, 90-98.

QED Score of Diversity Library

Compounds in the NCI Diversity Library have a high QED score, which signifies high drug-likeness.

QED≥0.5	81.8%
Mean ± Std. deviation	0.637 ± 0.138