MassSpecGym: A benchmark for the discovery and identification of molecules

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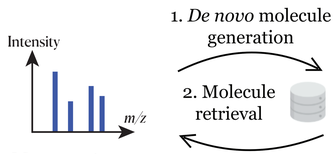
The MassSpecGym benchmark

Three new challenges



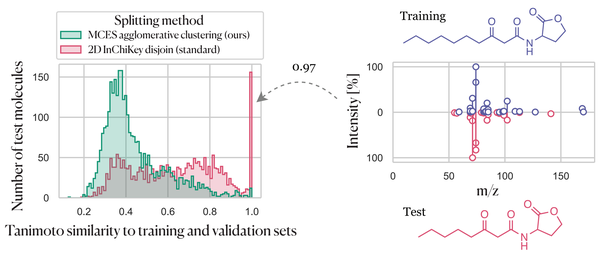
$V \in \mathbb{V}^N$, $|\mathbb{V}| = 118$ (atom/node types)

$E \in \mathbb{E}^M$, $|\mathbb{E}| = 4$ (bond/edge types)

New largest public dataset of mass spectra labeled with molecules

Dataset	Spectra	High-quality spectra	Molecules	Split
GNPS (Wang et al., 2016)	**322K**	104K	16K	✗
MoNA (Fiehn lab)	98K	62K	10K	✗
MassBank (Horai et al., 2010)	62K	58K	4K	✗
MIST CANOPUS (Goldman et al., 2023)	11K	≤ 11K	≤ 9K	✓
MassSpecGym (ours)	231K	**231K**	**29K**	✓

New generalization-demanding data split



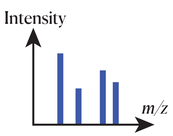
How many molecules have not yet been discovered in a randomly picked organism (e.g., this plant)?

E. coli bacteria < 19% molecules discovered

Plant kingdom < 7% molecules discovered

Human < 4% molecules discovered

Mass spectrometry (LC-MS/MS)

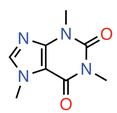


Mass spectra of molecules (MS/MS)

WANTED

New molecular generative models conditioned on mass spectra needed!

Major bottleneck!



Discovery of new molecular structures

Percentage estimates based on Alseekh et al., 2021, Nat Methods, https://doi.org/10.1038/s41592-021-01197-1

MassSpecGym baseline results

1. *De novo* molecule generation

	Top-1			Top-10		
	Accuracy ↑	MCES ↓	Tanimoto ↑	Accuracy ↑	MCES ↓	Tanimoto ↑
Random chemical generation	0.00	**28.59 (28.33-28.84)**	0.07 (0.07 - 0.07)	0.00	25.72 (25.49-25.95)	0.10 (0.10 - 0.10)
SMILES Transformer	0.00	53.80 (52.95-54.61)	0.07 (0.07 - 0.08)	0.00	21.97 (21.79-22.16)	**0.17 (0.17 - 0.17)**
SELFIES Transformer	0.00	33.28 (33.00-33.57)	**0.10 (0.10 - 0.10)**	0.00	**21.84 (21.67-22.00)**	0.15 (0.15 - 0.15)
Bonus chemical formulae challenge						
SMILES Transformer	0.00	79.39 (78.64-80.08)	0.03 (0.03 - 0.04)	0.00	52.13 (51.45-52.81)	0.10 (0.09 - 0.10)
SELFIES Transformer	0.00	38.88 (38.57-39.20)	**0.08 (0.08 - 0.08)**	0.00	26.87 (26.66-27.11)	**0.13 (0.13 - 0.13)**
Random chemical generation	0.00	**21.11 (20.97-21.26)**	**0.08 (0.08 - 0.08)**	0.00	**18.25 (18.14-18.35)**	0.11 (0.11 - 0.11)

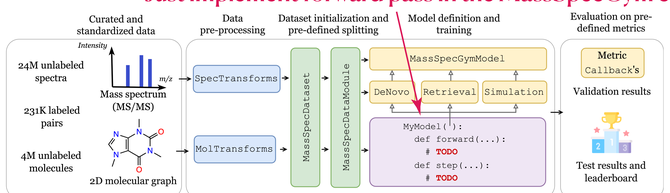
2. Molecule retrieval

The performance of current methods is limited!

	Hit rate @ 1 ↑	Hit rate @ 5 ↑	Hit rate @ 20 ↑	MCES @ 1 ↓
Random	0.37 (0.24-0.54)	2.01 (1.68-2.39)	8.22 (7.53-8.89)	30.81 (30.40-31.21)
DeepSets	1.47 (1.18-1.77)	6.21 (5.64-6.82)	19.23 (18.24-20.26)	25.11 (24.84-25.39)
Fingerprint FFN	2.54 (2.17-2.99)	7.59 (6.96-8.28)	20.00 (19.01-20.98)	24.66 (24.38-24.94)
DeepSets + Fourier features	5.24 (4.71-5.83)	12.58 (11.80-13.42)	28.21 (27.10-29.36)	22.13 (21.85-22.43)
MIST	**14.64 (13.82-15.54)**	**34.87 (33.69-36.10)**	**59.15 (57.89-60.39)**	**15.37 (15.12-15.62)**
Bonus chemical formulae challenge				
Random	3.06 (2.64-3.52)	11.35 (10.60-12.12)	27.74 (26.52-28.84)	13.87 (13.70-14.03)
DeepSets	4.42 (3.92-4.97)	14.46 (13.58-15.36)	30.76 (29.67-31.93)	15.04 (14.89-15.19)
Fingerprint FFN	5.09 (4.57-5.66)	14.69 (13.83-15.56)	31.97 (30.86-33.10)	14.94 (14.79-15.09)
DeepSets + Fourier features	6.56 (5.95-7.16)	16.46 (15.58-17.35)	33.46 (32.39-34.59)	14.14 (13.98-14.31)
MIST	**9.57 (8.88-10.30)**	**22.11 (21.10-23.13)**	**41.12 (39.98-42.34)**	**12.75 (12.59-12.91)**

3. Spectrum simulation

	Cosine Similarity ↑	Jensen-Shannon Similarity ↑	Hit Rate @ 1 ↑	Hit Rate @ 5 ↑	Hit Rate @ 20 ↑
Precursor m/z	0.15 (0.14-0.17)	0.41 (0.40-0.42)	0.38 (0.21-0.62)	1.72 (1.32-2.18)	7.17 (6.32-8.04)
FFN Fingerprint	0.25 (0.24-0.26)	0.48 (0.47-0.48)	8.44 (7.56-9.34)	21.43 (20.10-22.79)	38.57 (36.99-40.23)
GNN	0.19 (0.18-0.20)	0.44 (0.44-0.45)	3.95 (3.37-4.62)	11.92 (10.87-13.00)	26.27 (24.83-27.82)
FraGNNet	**0.52 (0.51-0.53)**	**0.63 (0.63-0.64)**	**46.64 (44.98-48.26)**	**72.56 (71.18-74.00)**	**83.58 (82.34-84.75)**
Bonus chemical formulae challenge					
Precursor m/z	-	-	2.09 (1.66-2.59)	8.52 (7.65-9.53)	22.65 (21.26-24.01)
FFN Fingerprint	-	-	7.62 (6.77-8.54)	22.70 (21.32-24.12)	44.12 (42.51-45.75)
GNN	-	-	3.63 (3.05-4.29)	13.55 (12.46-14.68)	33.77 (32.26-35.37)
FraGNNet	-	-	**31.93 (30.40-33.50)**	**63.20 (61.64-64.76)**	**82.70 (81.45-83.93)**

Evaluating new methods is easy

Just implement forward pass in the MassSpecGym codebase!