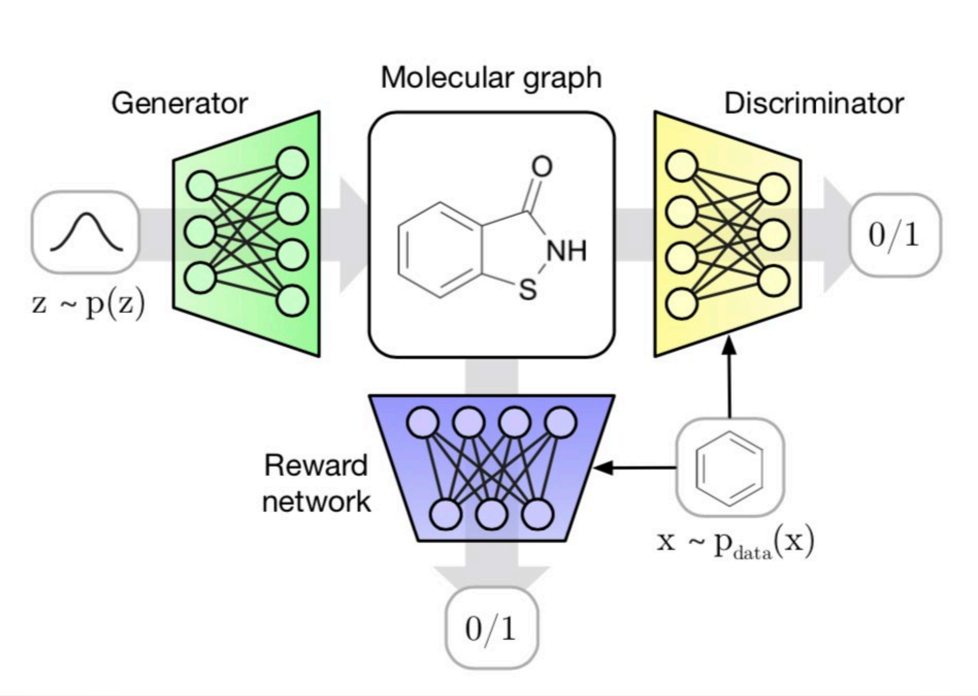
An effort of solving mode collapse in MolGAN

Li, Ziyao & Ma, Xiaojun; June 4, 2020

Schema of MolGAN



- Generator and Discriminator
- Reward Network

N. D. Cao, **T. Kipf**: MolGAN: An implicit generative model for small molecular graphs. CoRR abs/1805.11973 (2018)

Implicit Graph Gen.

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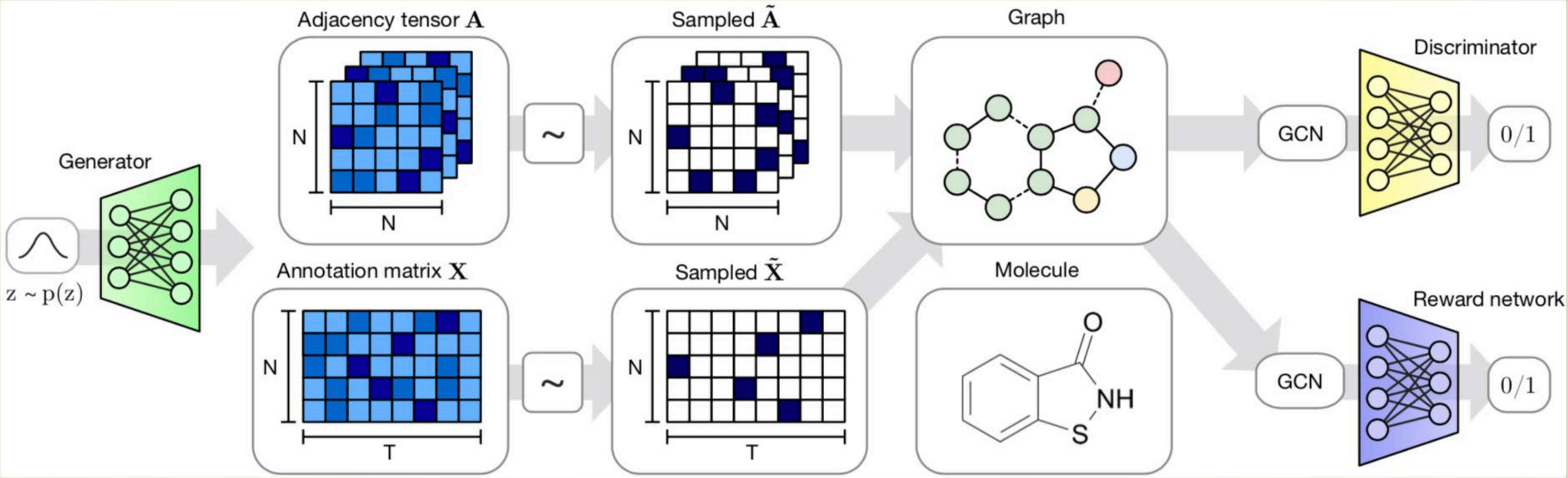
- Utilizing implicit, likelihood-free methods
- Generate G directly:
  - $\mathrm{en}\ \ (z) \sim G = (A, X)$
  - $A \in \mathbf{R}^{N \times N \times C_b}$, indication of edges *(binary)*
  - $X = [x_1, \ldots, x_n] \in \mathbf{R}^{N \times C_a}$, indication of node *(binary)*
  - ($N = 9$, $C_a = 4$ the types of atoms (C N O F), $C_b = 4$ the types of bonds)

MolGAN Overview



$$L(\theta) = \lambda \cdot L_{WGAN} + (1 - \lambda) \cdot L_{RL}$$

Overall techniques: GAN + Property Optimization

- Generate A and X, sample $\tilde{A}$ and $\tilde{X}$
- Train with Reward network and Discriminator

Generator

Predict the entire graph at once

- Generate A and X at once using a simple multi-layer perceptron:

$$\tilde{A} = \mathrm{reshape}(\mathrm{MLP}_A(z), N \times N \times C_b)$$

$$A = \frac{1}{2}(\tilde{A} + \tilde{A}^T)$$

$$X = \mathrm{reshape}(\mathrm{MLP}_X(z), N \times C_a)$$

- No explicit constraints over A (atom degrees et al)

Discriminator and Reward

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- Encode MolGraph with Relational-GCN & GG-NN readout fn.

$$
\begin{aligned}
\boldsymbol{h}_i^{\prime(\ell+1)} &= f_s^{(\ell)}(\boldsymbol{h}_i^{(\ell)}, \boldsymbol{x}_i) + \sum_{j=1}^{N}\sum_{y=1}^{Y} \frac{\tilde{\boldsymbol{A}}_{ijy}}{|\mathcal{N}_i|} f_y^{(\ell)}(\boldsymbol{h}_j^{(\ell)}, \boldsymbol{x}_i)\ , \\
\boldsymbol{h}_i^{(\ell+1)} &= \tanh(\boldsymbol{h}_i^{\prime(\ell+1)})\ , \qquad (5)
\end{aligned}
$$

$$
\begin{aligned}
\boldsymbol{h}'_{\mathcal{G}} &= \sum_{v\in\mathcal{V}} \sigma(i(\boldsymbol{h}_v^{(L)}, \boldsymbol{x}_v)) \odot \tanh(j(\boldsymbol{h}_v^{(L)}, \boldsymbol{x}_v)) \\
\boldsymbol{h}_{\mathcal{G}} &= \tanh \boldsymbol{h}'_{\mathcal{G}}\ ,
\end{aligned}
$$

- RewardNet: Approximating non-differentiable rewards of true / generated molecules. (logP, QED, Synthesizability…)
- Training: first train GAN and RewardNet separably; then add reward loss to the generator.

Data: QM9 (Quantum Mechanics)

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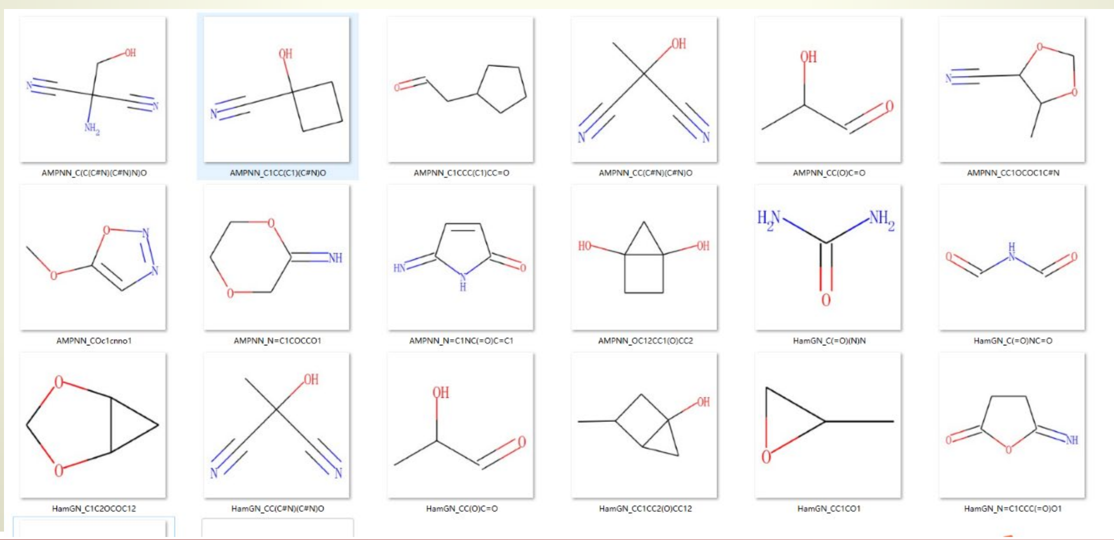
- Subset of GDB-17 with number of heavy atoms less than 9.
- Size: 130,000 (8:1:1 for train, val, test.)
- A very classic task of molecule representation. (with DFT properties)
- Not a popular task for molecule generation: QED scores et al are actually quite meaningless; generated molecules are usually useless.



Graph Generation

- Back to the ecosystem of *graph generation* research
- **VAE-based:** GraphVAE (2018) / Junction-Tree VAE (2018) / Constrained Graph VAE (2018) / HVGAE (2020)…
- **RL (sequential generation):** GCPN (2018) / MolRNN (2019) Quantum Mechanics (2020) / …
- **Flow-based:** GraphNVP (2019) / GraphAF (2020) / …
- **GAN?** MolGAN *(2018 ICML workshop on gen. models)*
- *Starting point: modify MolGAN*

Reported Mode Collapse

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Objective	Algorithm	Valid (%)	Unique (%)	Time (h)	Diversity	Druglikeliness	Synthesizability	Solubility
Druglikeliness	ORGAN	88.2	69.4*	9.63*	0.55	0.52	0.32	0.35
	OR(W)GAN	85.0	8.2*	10.06*	0.95	0.60	0.54	0.47
	Naive RL	97.1	54.0*	9.39*	0.80	0.57	0.53	0.50
	MolGAN	**99.9**	2.0	1.66	0.95	**0.61**	0.68	0.52
	MolGAN (QM9)	**100.0**	2.2	4.12	**0.97**	**0.62**	0.59	0.53
Synthesizability	ORGAN	96.5	45.9*	8.66*	0.92	0.51	0.83	0.45
	OR(W)GAN	97.6	30.7*	9.60*	**1.00**	0.20	0.75	0.84
	Naive RL	97.7	13.6*	10.60*	0.96	0.52	0.83	0.46
	MolGAN	**99.4**	2.1	1.04	0.75	0.52	**0.90**	0.67
	MolGAN (QM9)	**100.0**	2.1	2.49	0.95	0.53	**0.95**	0.68
Solubility	ORGAN	94.7	54.3*	8.65*	0.76	0.50	0.63	0.55
	OR(W)GAN	94.1	20.8*	9.21*	0.90	0.42	0.66	0.54
	Naive RL	92.7	100.0*	10.51*	0.75	0.49	0.70	0.78
	MolGAN	**99.8**	2.3	0.58	**0.97**	0.45	0.42	**0.86**
	MolGAN (QM9)	**99.8**	2.0	1.62	**0.99**	0.44	0.22	**0.89**
All/Alternated	ORGAN	96.1	97.2*	10.2*	0.92	**0.52**	0.71	0.53
All/Simultaneously	*MolGAN*	**97.4**	2.4	2.12	0.91	0.47	**0.84**	**0.65**
All/Simultaneously	*MolGAN (QM9)*	**98.0**	2.3	5.83	**0.93**	0.51	**0.82**	**0.69**

Proposal: Twd Mode Collapse

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- An idea of PacGAN, but with explicit *variance imitation*
- Original model: $D(x_1), D(x_2), D(x_3) \cdots$
- PacGAN: $D(x_1, \cdots, x_m)$; Instable in real training processes (rarely successful)
- Our proposal: $D\big(x_1; v_B(x)\big), D\big(x_2; v_B(x)\big) \cdots$
- Obs: std. dev may be too sensitive (instable training)
- Sol: *Elastic* Deviation: $v_B(d) = \lambda \sum_{i=1}^{|B|} \frac{|d_i - \bar{d}|}{|B|} + (1-\lambda)\sqrt{\sum_{i=1}^{|B|} \frac{(d_i - \bar{d})^2}{|B|}}$

Proposal: Better Discriminator

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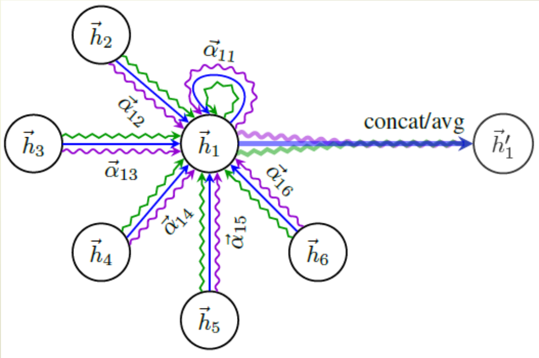
- More expressive discriminator helps to generate stronger samples
- Implement Graph Attentions in the discriminator.
- Detailly:
- MolGAN: $H^{(l+1)} = \sigma\left(\sum_{j \in N(i)} \hat{A}_{ij}\, h_j^{(l)} W^{(l)}\right)$
- MolAGAN: $H^{(l+1)} = \sigma\left(\sum_{j \in N(i)} \alpha_{ij}\, h_j^{(l)} W^{(l)}\right)$



Experiments.

MolGAN;
MolGAN+mean;
MolGAN+var(elastic)

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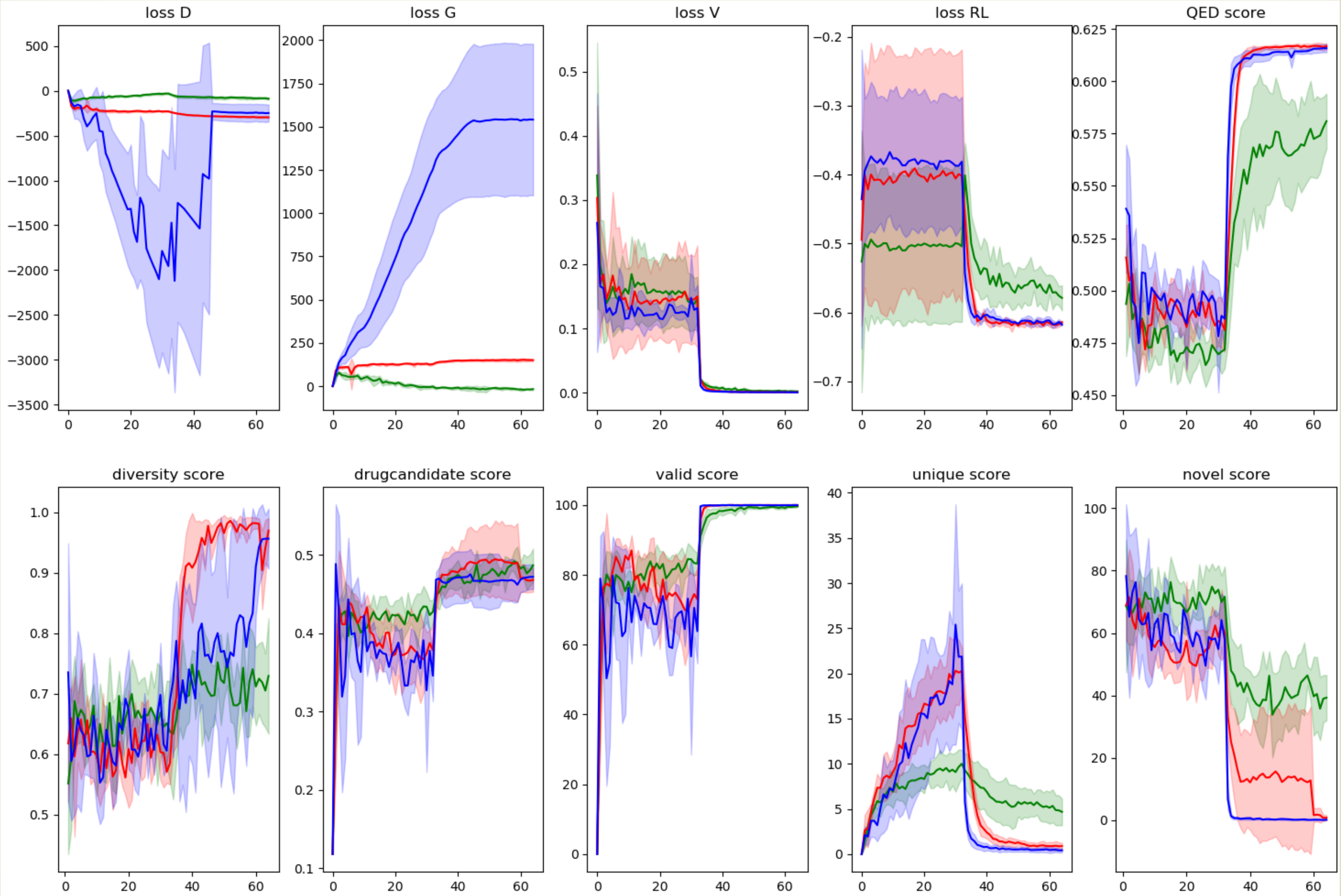
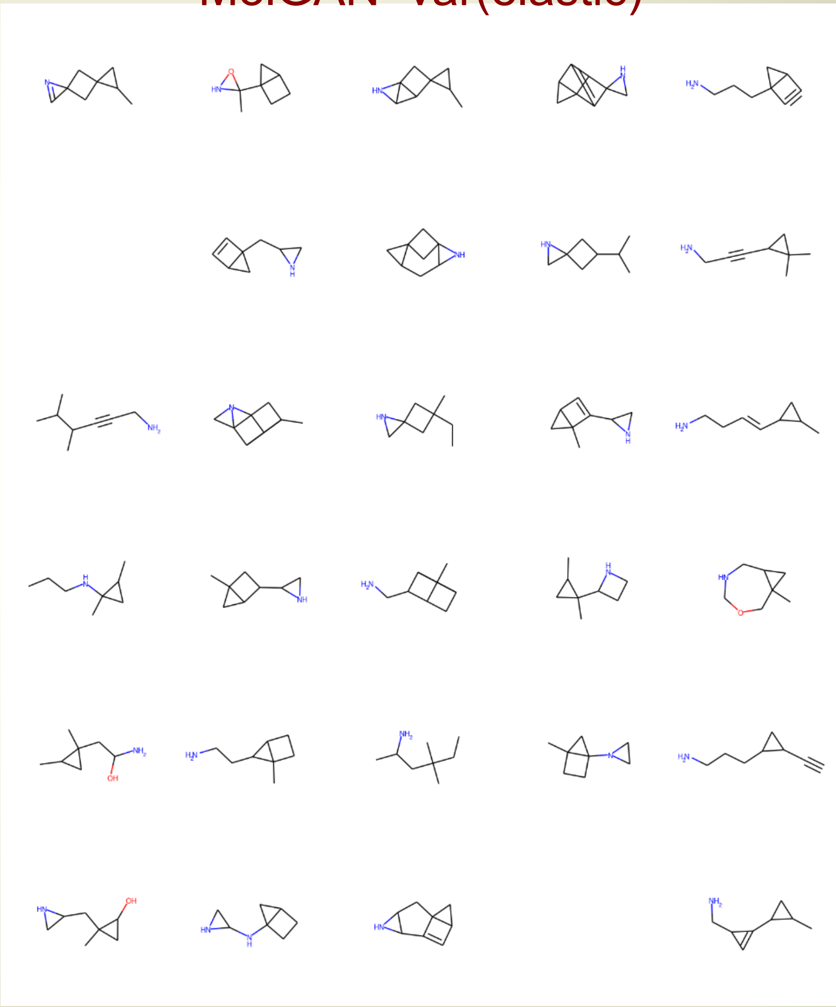
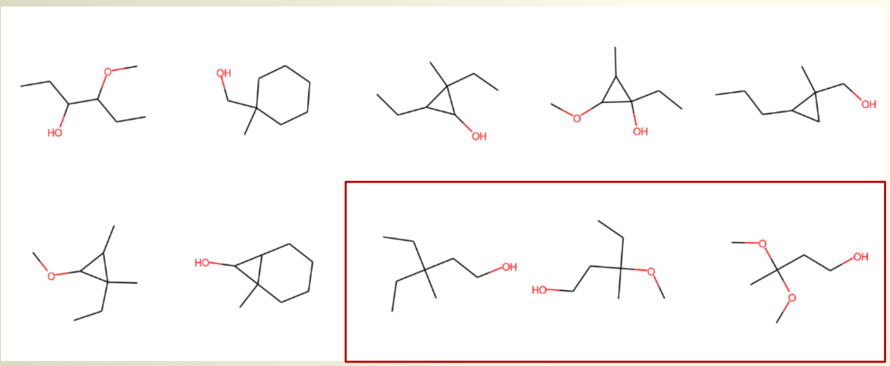


Demos.

MolGAN+var(elastic)



MolGAN



MolGAN+mean

A (newly raised) assumption.

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- What GANs learn is the distribution of data;
- Adding objectives over the generated samples in fact poses a condition.
- In MolGAN, the training of GAN still uses all the datasets when the rwd. objective is incorporated.
- This may be the major reason of mode collapse.
- Solution (naive): train the model with constrained data after the rwd. object is incorporated; i.e. pretrain the model with full data and finetune it according to objectives

TODO

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- Project-level:
  - The pre-train strategy we discussed;
  - Implement the GAT discriminator (in fact debug);
  - Conduct experiments on ZINC data…
- Research-level:
  - Meaningful latent space of molecules (recap the demo);
  - Resolve Mode Collapse (with targets) once-and-for-all:

    Conditional MolGAN

Thanks