Molecule Generation and Property Optimization By Deep Learning

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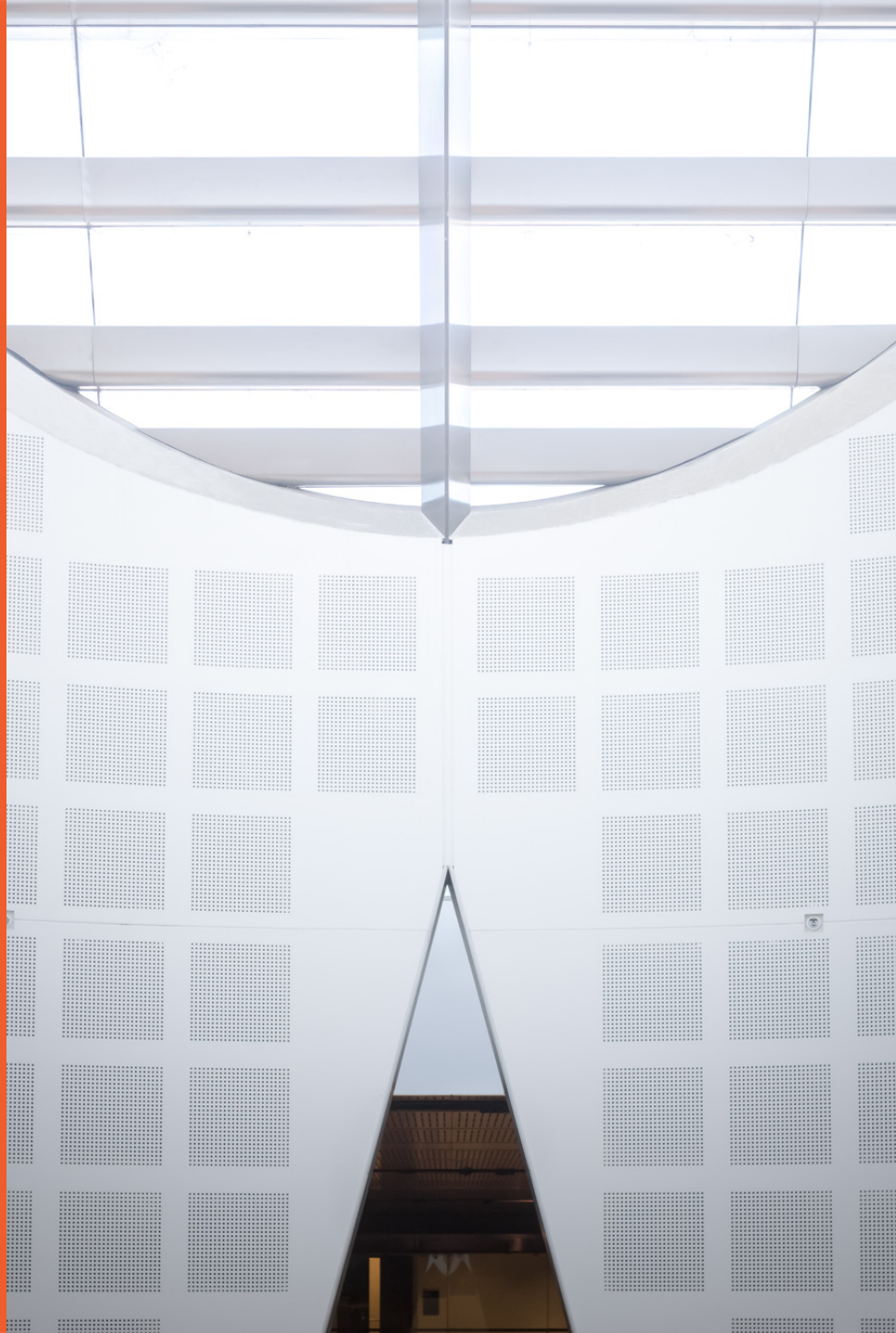
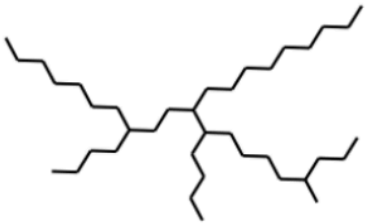


Molecules and Chemical Properties



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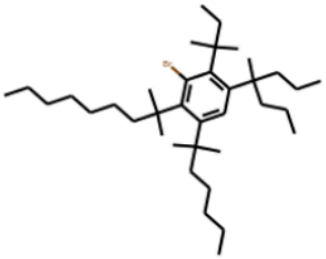

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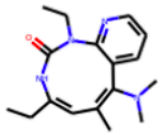

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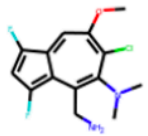

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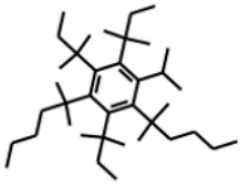

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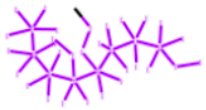

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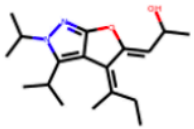

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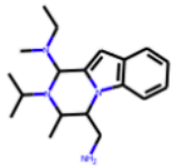

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(a) Penalized logP optimization

(b) QED optimization

Context and Importance of this research

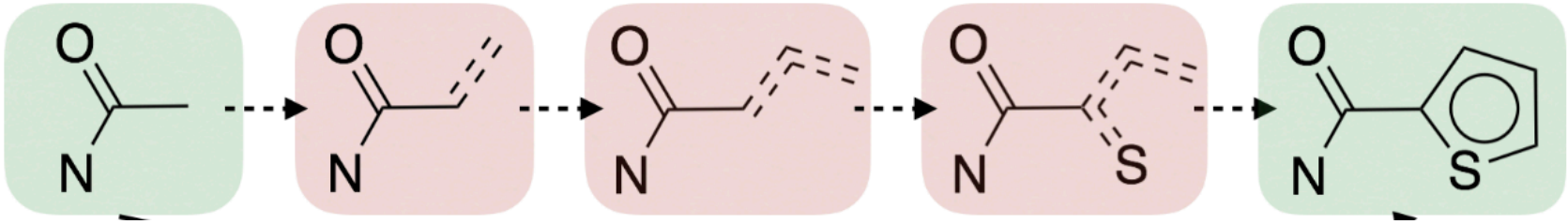
- Many important problems in drug discovery and material science are based on the principle of designing molecular structures with specific desired properties.

- This research is very meaningful in both medical and AI fields, which can benefits novel drug discovery for some diseases.

- It remains a challenging task due to the large size of chemical space(10^23 ~ 10^60).

Research Problem

- Explore a more effective generative model to sequentially generate novel molecules, along with achieving specific chemical property optimization(eg. Penalized LogP, QED and etc.).



How to Represent a Molecule

There are basically two representation types for molecule

- SMILES
- Graph

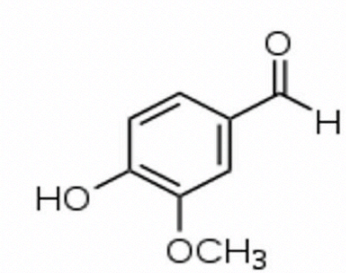
SMILES Representation

But it's hard to implement valency checking, and an incomplete SMILES string is meaningless.

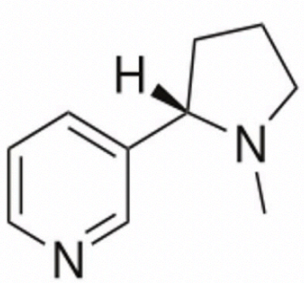
SMILES(Simplified Molecular Input Line Entry Specification): A text-based approach to simply represent a unique molecule, has its own syntax

- Easily to be processed by a simple language model.
- Contains general semantic global features of a molecule

Vanillin: O=Cc1ccc(O)c(OC)c1

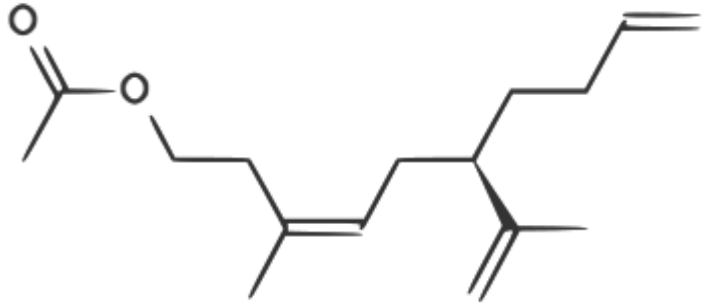


Nicotine: CN1CCC[C@H]1c2cccnc2



Graph Representation

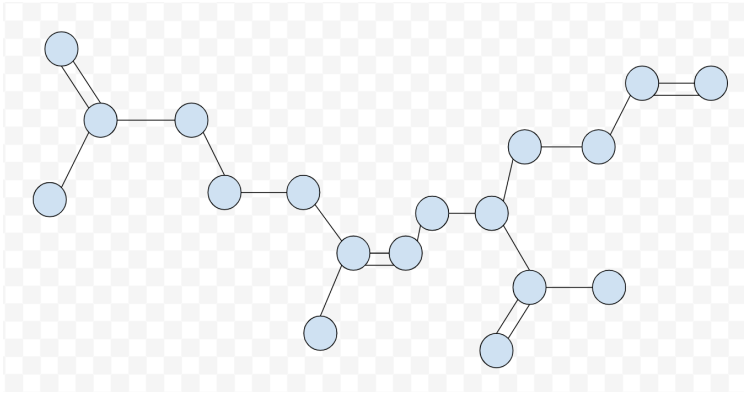
But it has to access to the domain specific priors indicating a big picture of the molecules to be generated.



Graph Structure: all molecules can be formulated into a graph structure,

Bonds→ Edges, Atoms→ Nodes

- Graph can be represented by matrix.
- G(A, F): A is a e*n*n adjacent matrix, F is a n*f node feature matrix.
- Easily to do valency check at each step of generation; more meaningful; can handle node's topology relationship, etc.



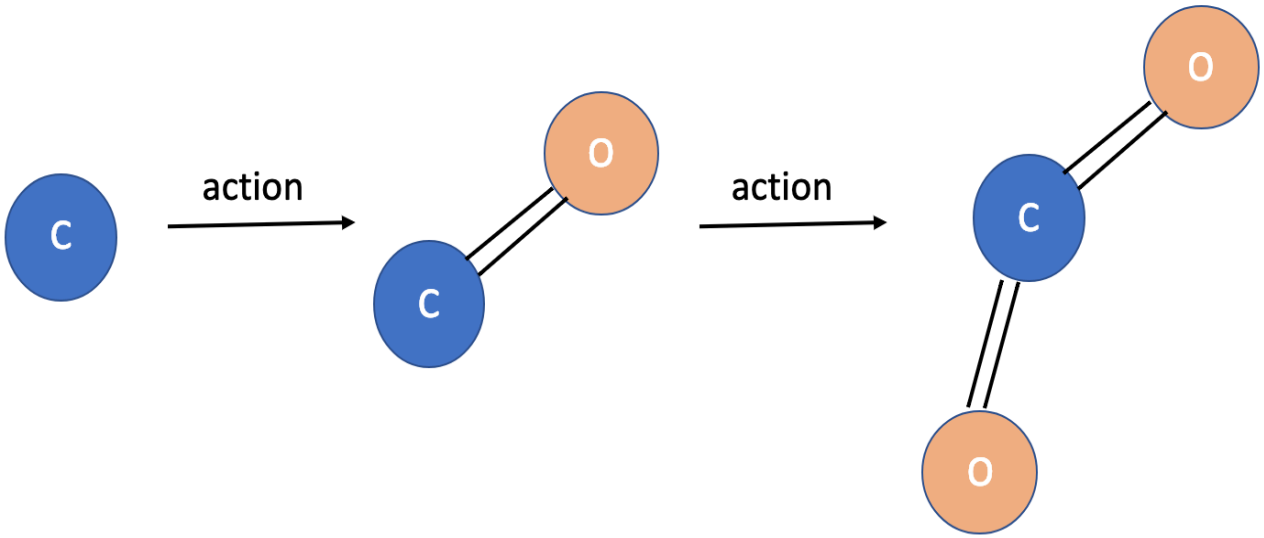
Traditional Methods VS Deep Learning

- **Traditionally** done by some heuristic search algorithms through a vast chemical space.(Expensive, and highly relys on domain knowledges.

- **Deep Learning:**
  - Texted-based(SMILES-based) generative models: leverage language model(RNNs, LSTM, GRU).
  - Graph-based generative models: leverage graph neural networks.

Reinforcement Learning

- **Reinforcement learning**: using policy network to sequentially build a molecule; can solve non-differential problem, directly optimize chemical properties.



Motivation

In the recent years, reinforcement learning-based methods have made use of either **graph** or **SMILES** representation of the molecule. Each type of representation has its own advantages and shortcomings.

However, there is not an approach that **leverage the information from both graph and SMILES representations** to generate novel molecules. **We should absorb their advantages!**

Proposed Method

01

Augment the origin graph state with SMILES context information at each step of graph generation.

02

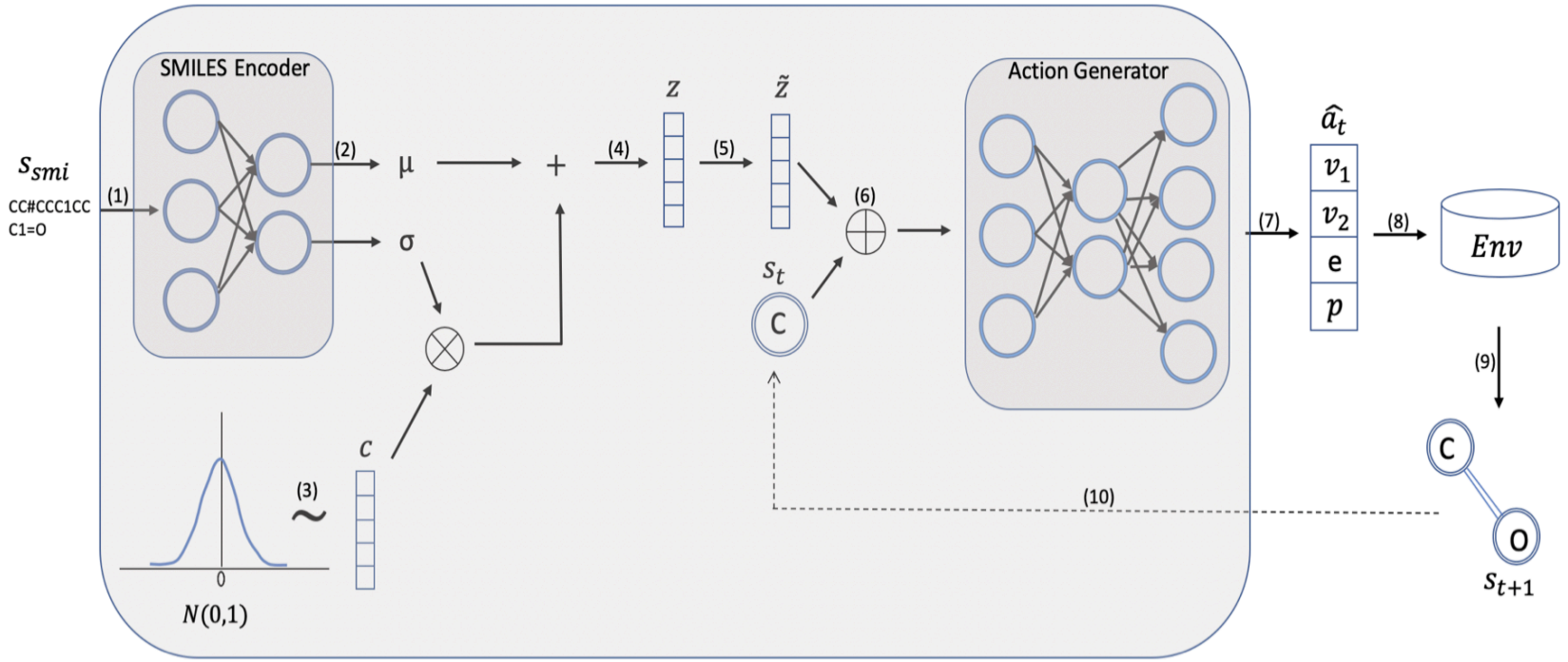
Propose two types of attention mechanism: action-attention and **graph-attention,** to further **select meaningful features** from the SMILES string,

03

Propose to **implement supervised learning to make initialization of the model,** which can aid the afterward reinforcement learning process.

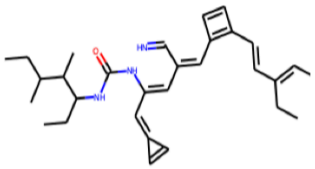
Framework Overview

- Supervised Learning followed by Reinforcement Learning

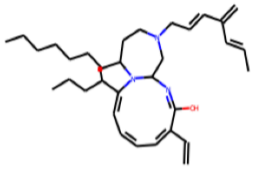


Experiment Results

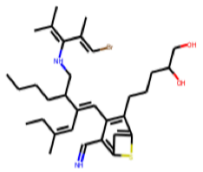
- Examples of molecules generated by our model with Penalized logP scores



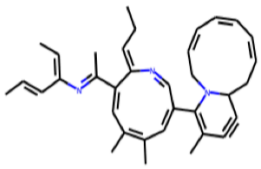
(a) 8.89



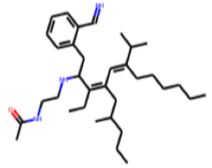
(b) 8.69



(c) 8.55



(d) 8.52



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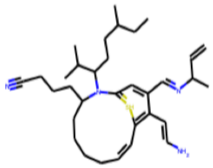

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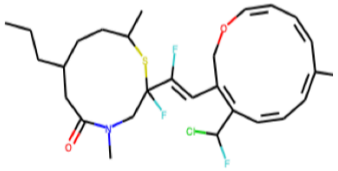
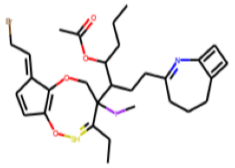


(g) 8.12



(h) 8.02

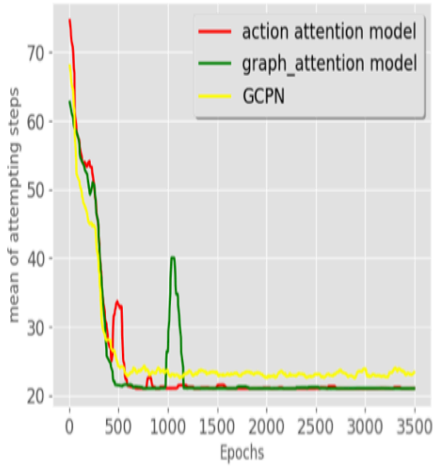
Experiment Results

- Comparison results for property optimization task on ZINC

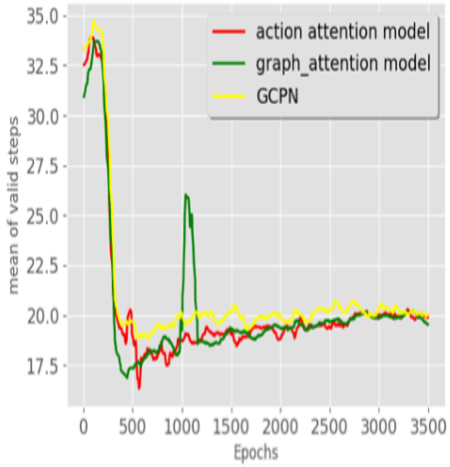
Algorithm	Penalized logP				QED			
	1st	2nd	3rd	Validity	1st	2nd	3rd	Validity
ZINC	4.52	4.30	4.23	100%	0.948	0.948	0.948	100%
ORGAN	3.63	3.49	3.44	0.4%	0.896	0.824	0.820	2.2%
JT-VAE	5.30	4.93	4.49	100%	0.925	0.911	0.910	100%
GCPN	7.98	7.85	7.80	100%	0.948	0.947	0.946	100%
Our Work	**8.89**	**8.69**	**8.55**	**100%**	**0.948**	**0.948**	**0.947**	**100%**

Experiment Results

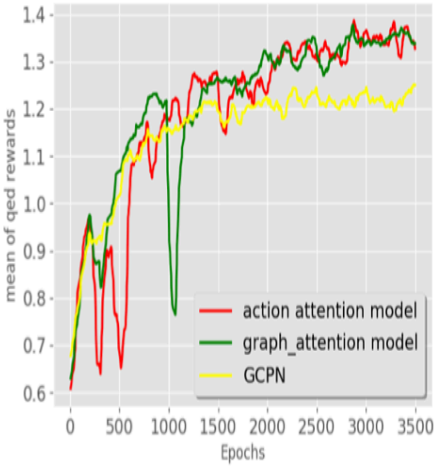
- Learning curves of our work configured with action attention mechanism, graph attention mechanism, comparing with GCPN.



(a) the mean of the number of attempting steps for generating a complete molecule performed by the agent in each training epoch



(b) the mean of the number of valid steps for generating a complete molecule in each epoch



(c) the property rewards returned from the environment when we doing the QED property optimization task in each epoch

The work presented here is published as "**Reinforced Molecule Generation with Heterogeneous States**" in the 19th IEEE International Conference on Data Mining(ICDM), 2019.

Reference

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Thank you!