Exploring Chemical Reaction Space with Intrinsically Motivated Agent

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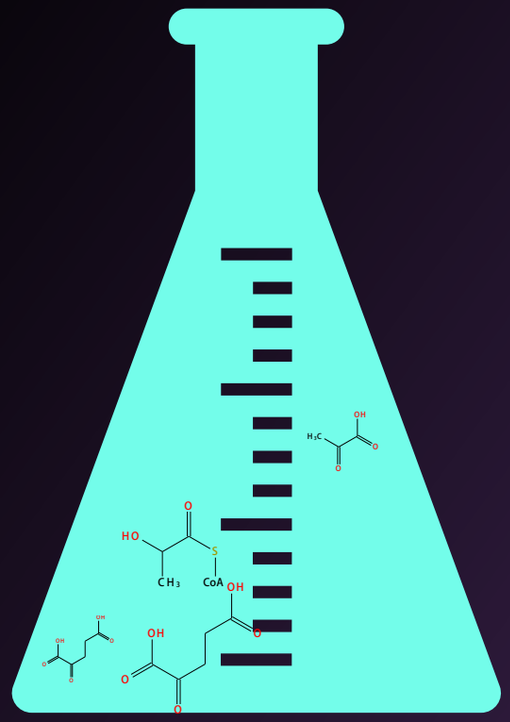
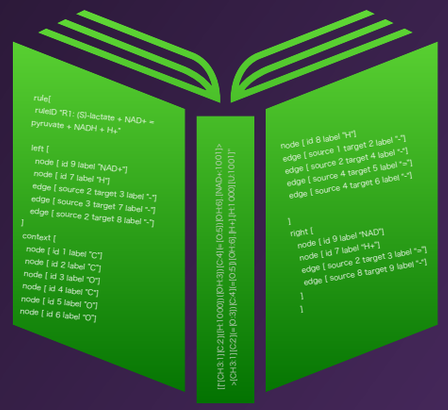
39 TBI Winterseminar Bled

Data Mining & Machine Learning tbi universität wien TU WIEN

Problem Setting

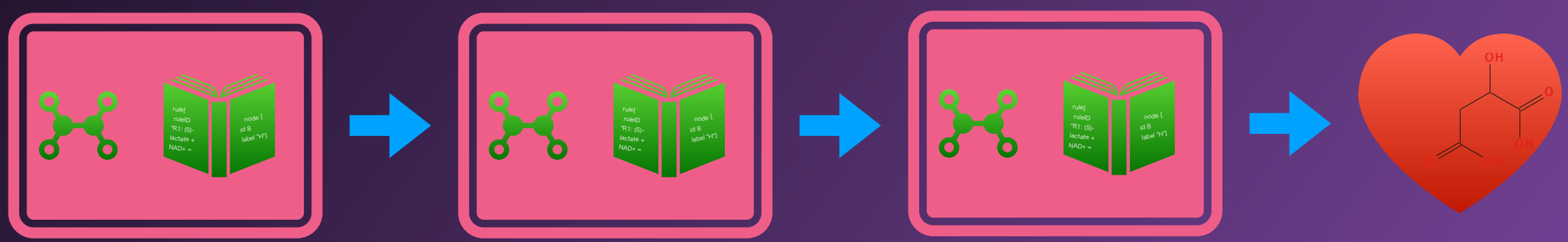




Target Mols

Shortest Path
rule sequence

Source Mols



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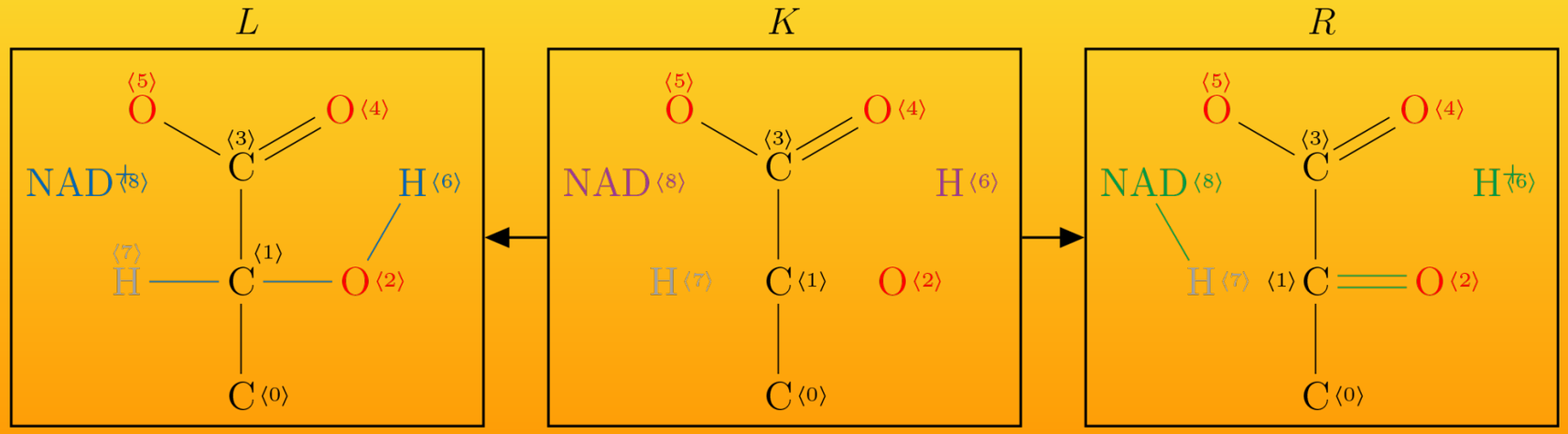
Chemical Reaction Rules and Data Structure

0.0.1 R1: (S)-lactate + NAD+ = pyruvate + NADH + H+



Left Graph

- Features of the Changed Atoms
- Changed Bonds idx and features

Transition Graph

- Features of the Unchanged Atoms
- Unchanged Bonds idx and features

Right Graph

- Features of the Changed Atoms
- Newly Formed Bonds idx and features

JL Anderson, et.al. A software package for chemically inspired graph transformation
Luo, Yizhen et.al. MolFM: A Multimodal Molecular Foundation Model

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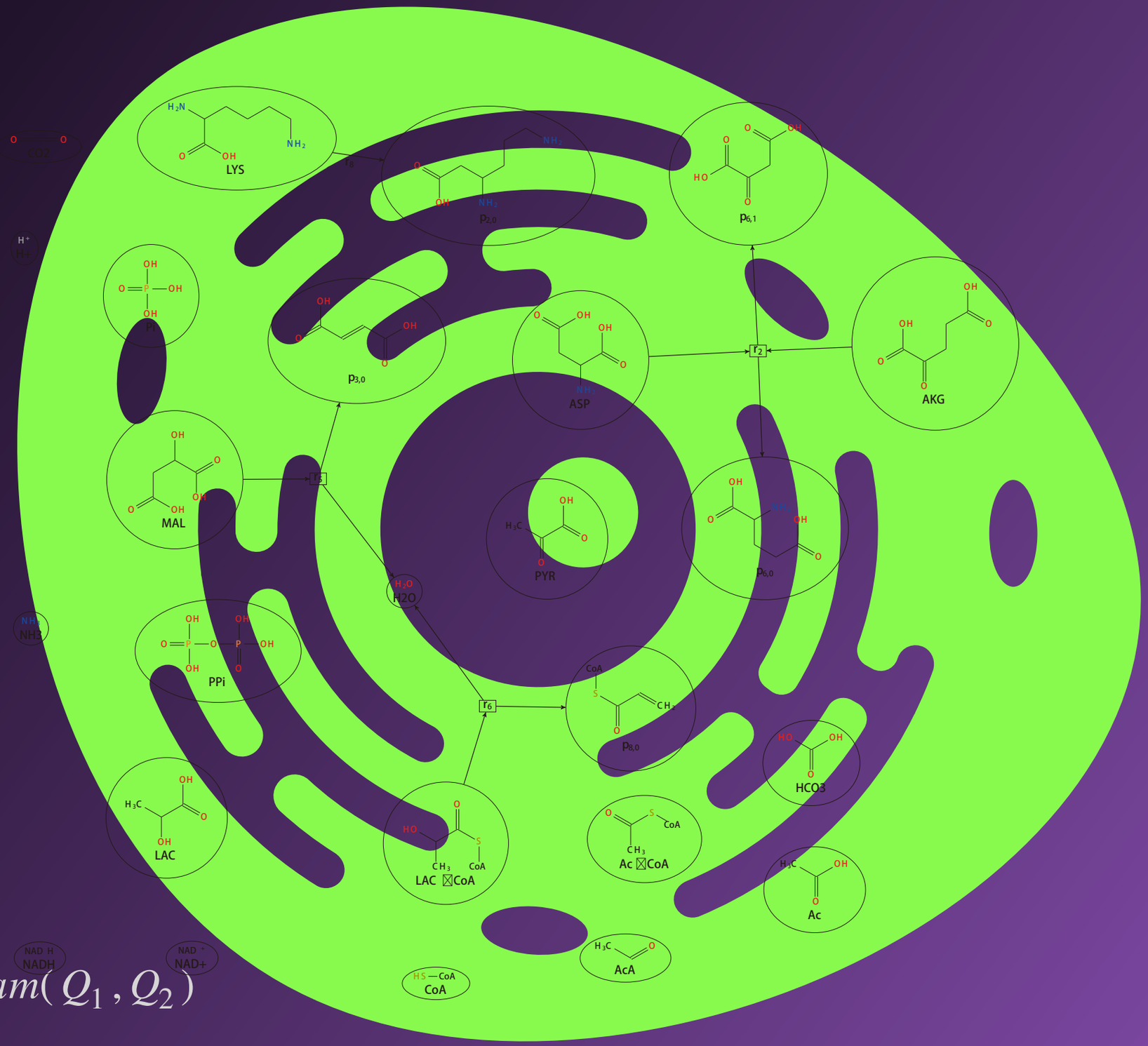
```python
class RuleGraphFeaturizer(BaseFeaturizer):
    allowable_features = {
        'possible_atomic_num_list':       list(range(1, 119)) + ['misc'],
        'possible_formal_charge_list':    [-5, -4, -3, -2, -1, 0, 1, 2, 3, 4, 5, 'misc'],
        'possible_chirality_list':        [
            Chem.rdchem.ChiralType.CHI_UNSPECIFIED,
            Chem.rdchem.ChiralType.CHI_TETRAHEDRAL_CW,
            Chem.rdchem.ChiralType.CHI_TETRAHEDRAL_CCW,
            Chem.rdchem.ChiralType.CHI_OTHER
        ],
        'possible_hybridization_list':    [
            Chem.rdchem.HybridizationType.SP,
            Chem.rdchem.HybridizationType.SP2,
            Chem.rdchem.HybridizationType.SP3,
            Chem.rdchem.HybridizationType.SP3D,
            Chem.rdchem.HybridizationType.SP3D2,
            Chem.rdchem.HybridizationType.UNSPECIFIED,
            'misc'
        ],
        'possible_numH_list':             [0, 1, 2, 3, 4, 5, 6, 7, 8, 'misc'],
        'possible_implicit_valence_list': [0, 1, 2, 3, 4, 5, 6],
        'possible_degree_list':           [0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 'misc'],
        'possible_number_radical_e_list': [0, 1, 2, 3, 4, 'misc'],
        'possible_is_aromatic_list':      [False, True],
        'possible_is_in_ring_list':       [False, True],
        'possible_bond_type_list':        [
            Chem.rdchem.BondType.SINGLE,
            Chem.rdchem.BondType.DOUBLE,
            Chem.rdchem.BondType.TRIPLE,
            Chem.rdchem.BondType.AROMATIC,
            'misc'
```

```python
data = Data(atom_attr=x, edge_index=edge_index, edge_attr=edge_attr)
```

Chemical Reaction Space

Gymnasium + MOD
Chemical Reaction
Environment

State: Derivation Graph
(pymod)
Action: choose reactant
and Apply Rule



$$D_{shortest} = TorgansinZimmeram(Q_1, Q_2)$$

$$ExtrinsicReward = SimilarityScore / min(D_{shortest}[:N_{mol}, target]) * \epsilon$$

JL Anderson, et.al. A software package for chemically inspired graph transformation
S Torgasin, KH Zimmermann. An all-pairs shortest path algorithm for bipartite graphs

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Learning Process

State 0

Q(S,A)

a1: R 2 /M 2

a2: R 1 / M1

a3: R 3 / M 3

Policy:

$\pi(M \mid s_t, \theta, \pi(R \mid s_t, \phi))$

State 1

V(S)

a1: R 2/M1

a3: R 3/M2

state 2

state space

a2: R 1/M2

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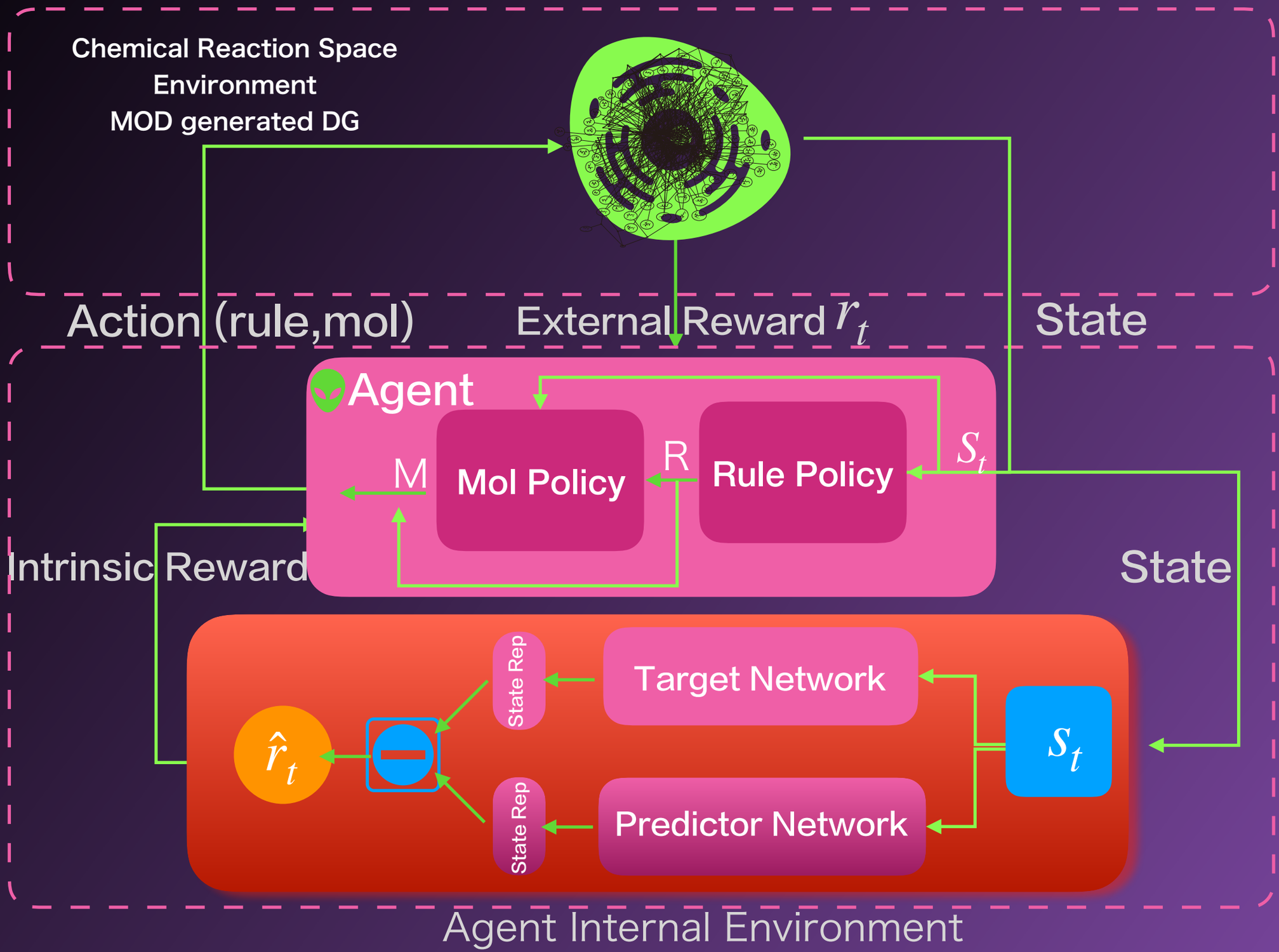
Model Architecture

Intrinsically Motivated Agent



Philip Becker-Ehmck et.al. Exploration via empowerment gain: combining novelty, surprise and learning progress
Sun, Chenyu et.al. From psychological curiosity to artificial curiosity: curiosity-driven learning in artificial intelligence tasks.
Yuan,Mingqi. Intrinsically-Motivated reinforcement learning: A brief introduction.
Sai Krishna Gottipati et.al. Learning to Navigate The Synthetically Accessible Chemical Space Using Reinforcement Learning

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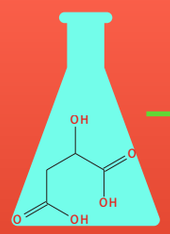
Policy Architecture



Molecule Graph

Substructure Aware GNN

MoI Rep

[O:1]=[C:2]([OH:3])[CH2:4][C@H:5]([OH:6])[C:7](=[O:8])[OH:9]>>[O:1]=[C:2]([OH:3])/[CH:4]=[CH:5]/[C:7](=[O:8])[OH:9].[OH2:6]

RXN Graph

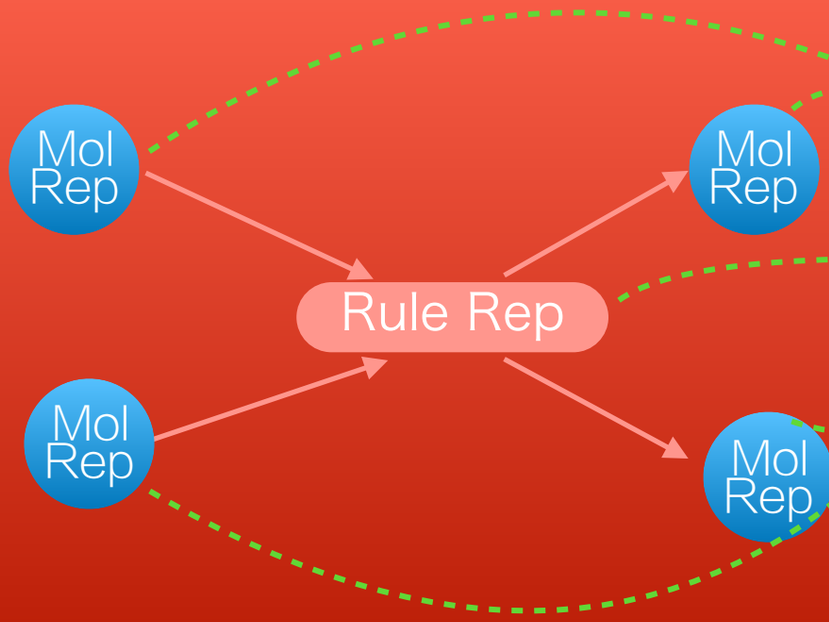
L Graph Data

K Graph Data

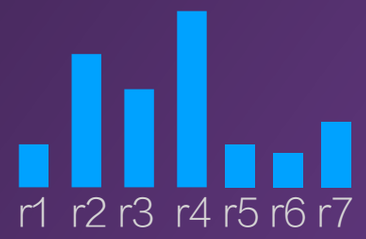
R Graph Data

Substructure Aware GNN

Rule Rep



Graph Multihead Attention for Hypergraph



Actor

Action Output

MLP

Critic

Value Output

V(S)

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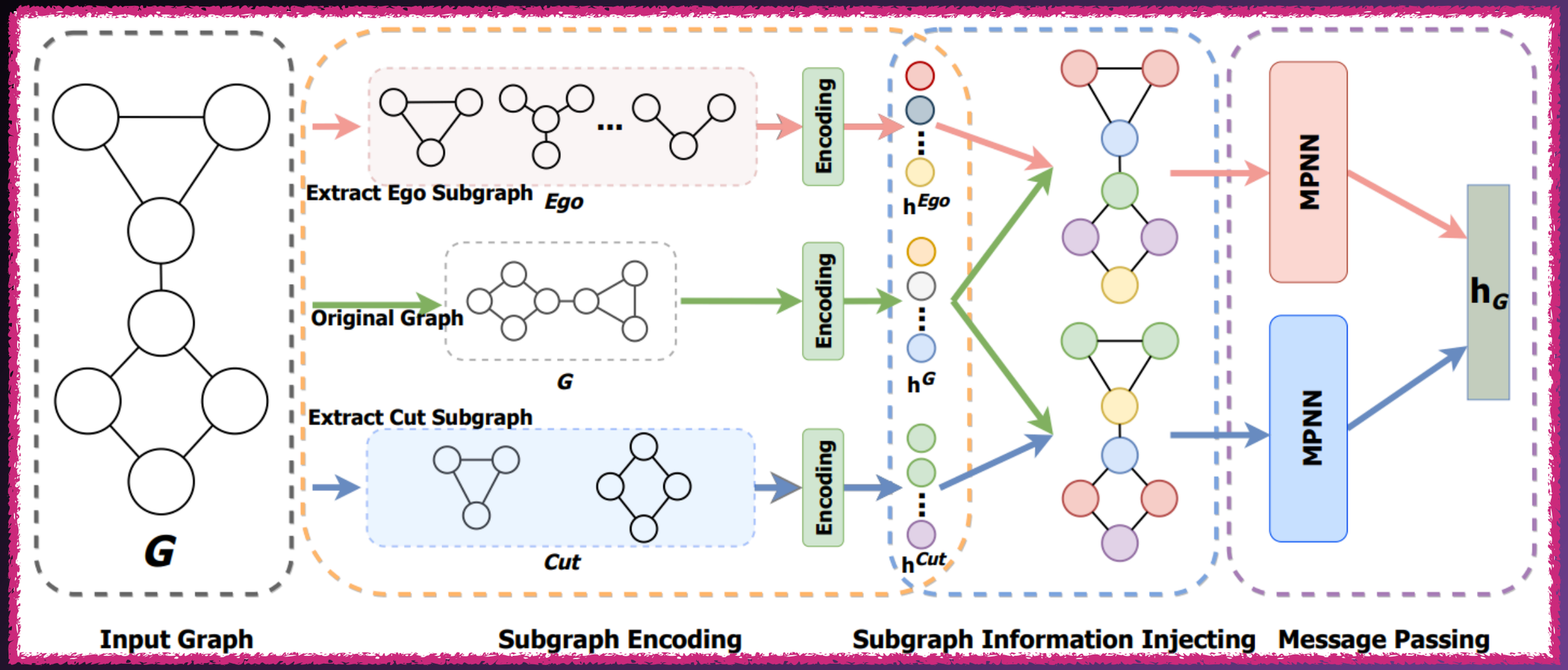
Supplement & Prospective



- Incorporate pretrained BioMed LLM to form multimodal Chemical Reaction Exploration Agent
- Topolgy guided graph neural network for hypergraph structure learning

Pretrained LLM → **MultiModal Agent**

Zeng, Dingyi et.al., Substructure Aware Graph Neural Networks
Luo, Yizhen et.al. BioMedGPT: Open Multimodal Generative Pre-trained Transformer for BioMedicine

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Happy Chinese New Year
The year of 龍 Long