# DOE Bioenergy Technologies Office (BETO) 2021 Project Peer Review

# Identifying Performance Advantaged Biobased Chemicals Utilizing Bioprivileged Molecules

## DOE BETO BEEPS DE-EE0008492
## Topic Area 3: Performance Advantaged Bioproducts (PABP)

3/10/21

Performance Advantaged BioProducts

Brent H. Shanks

Iowa State University

# Performance Advantaged Molecules

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Center for Biorenewable Chemicals

- Challenges:
  - Biobased chemicals developed primarily through retrosynthesis.
  - Chemical structures available through biology nearly “infinite.”
  - Performance advantaged chemical structure in end use application difficult to predict *a priori.*
  - No systematic strategies.
- Opportunities:
  - Bioprivileged molecules as synthetic platform species.
  - Developments in computational methods (automated reaction network generation, data mining).
  - Literature over the past 100 years contains many examples of molecule screening.
  - Team had interesting set of initial structures for organic corrosion inhibitors and flame retardant polymers (nylon 6,6) and these areas are searching for new molecules.

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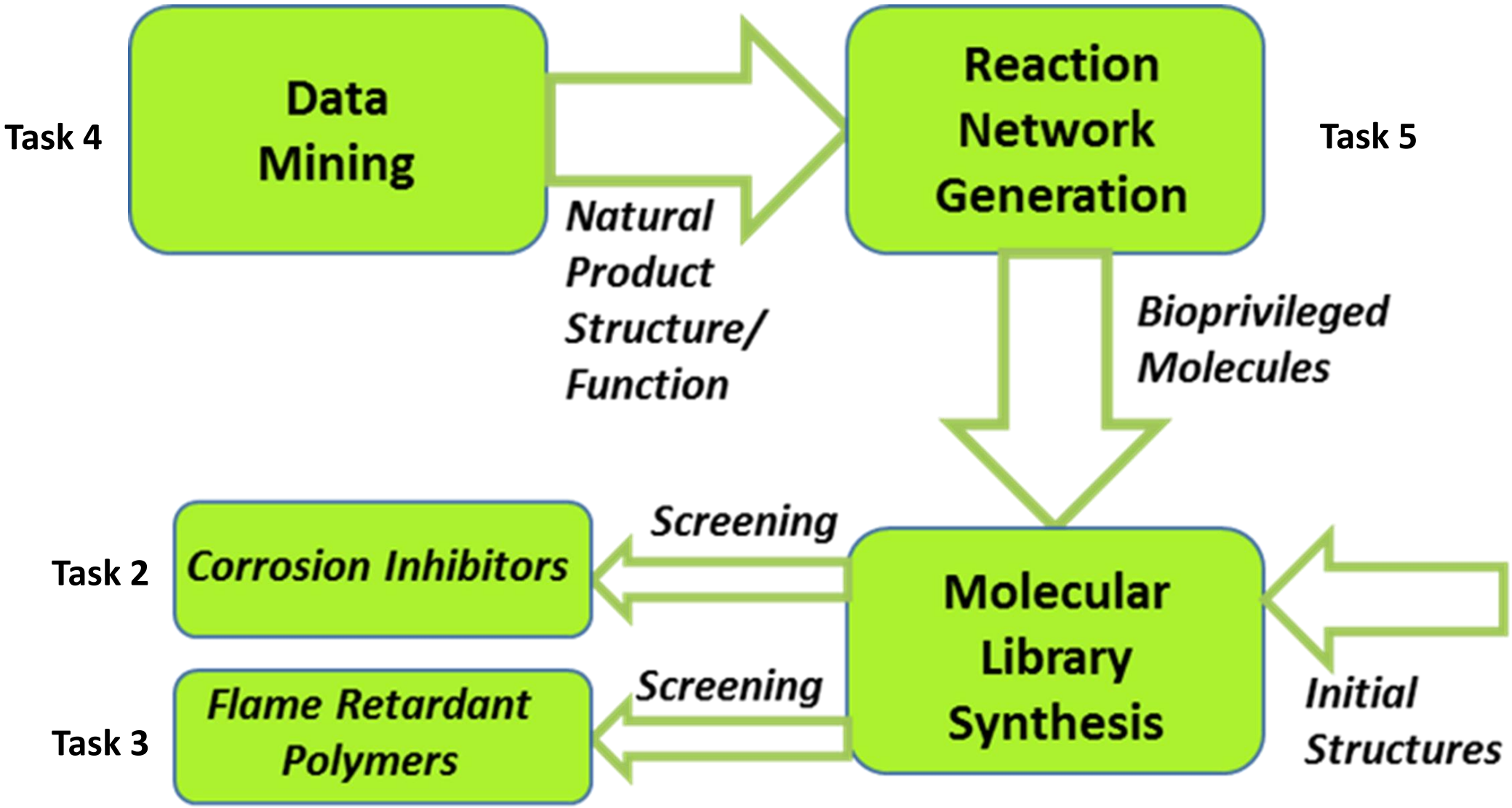
# Project Overview



# Project Management

***Overall Lead:*** B. Shanks (*ISU*)

***Task 2**: Identification of Novel Enhanced Organic Corrosion Inhibitors*

- G. Kraus, B. Shanks *(ISU)*

***Task 3:** Identification of Novel Enhanced Flame Retardant Nylons*

- J.P. Tessonnier, E. Cochran, B. Shanks (*ISU)*

***Task 4:** Construction and Application of Recurrent Neural Network Model*

- J. Pfaendtner, D. Beck *(UW)*

***Task 5:** Construction and Application of Reaction Network Generation Framework*

- L. Broadbelt *(NU)*

# Technology Risks/Mitigation

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- Screening protocol for novel molecules
  - Developing representative test
  - Sample size
- Computational strategy
  - Data mining has precedent
  - Reaction network generation builds from existing platform
  - Integration is unique
- Technology translation
  - Industrial connection

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# Approach

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## Phase 1: Project Component Development

- Initial synthetic “libraries” for each application
- Development of recurrent neural network (RNN) and reaction network generation (RNG) framework
- Second iteration of synthetic libraries for each application

## Phase 2: Integration of Project Components

- Passing structures from RRN to RNG for candidate molecule identification
- Synthesize libraries from candidate molecules

| | Key Milestones & Deliverables |
|---|---|
| **Year 1** | • Identification of at least two novel corrosion inhibitors<br>• Nylon modified with 3-hexenedioic acid screened |
| **Year 2** | • Initial set of at least 5 novel molecules identified<br>• First set of data mined candidate molecules found |
| **Year 3** | • Data mined candidate molecules synthesized and tested - ≥5 novel molecules identified<br>• Integrated computational process developed for finding novel chemicals. |

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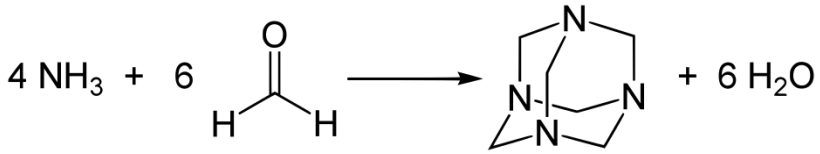
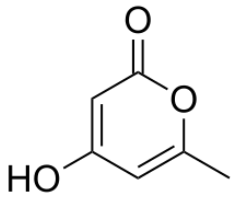
# Initial Corrosion Inhibitor Set



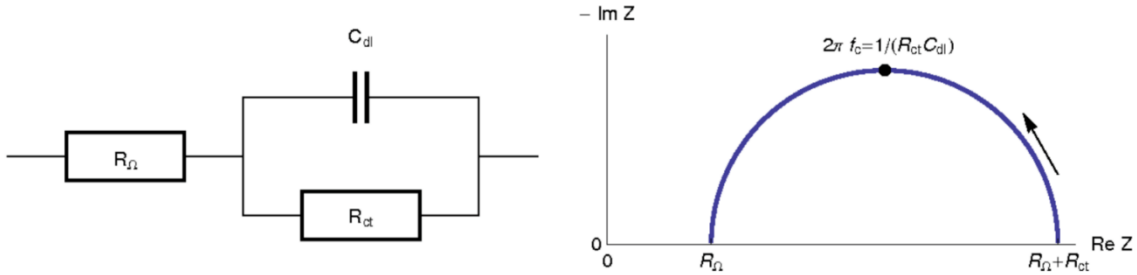

Urotropin synthesis


Opuntiol speculated as promising performance (*Opuntia elatior*)*




CBiRC triacetic acid lactone

***Electrochemical impedance spectroscopy screening***

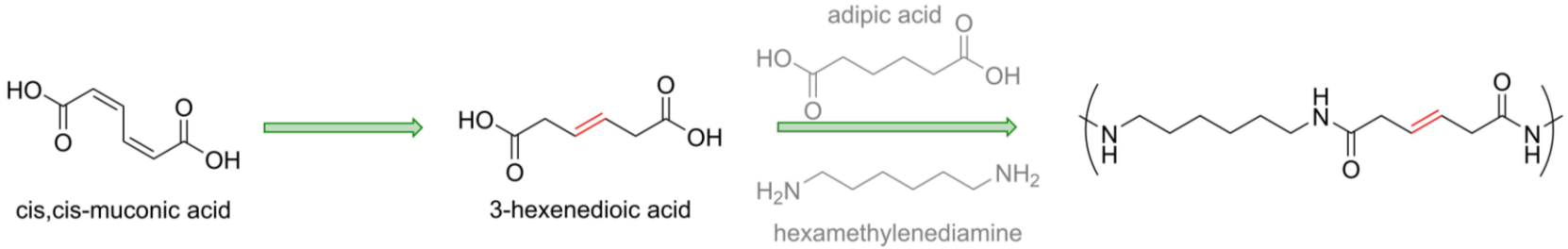



$$IE\% = \left(\frac{R_p - R_{po}}{R_p}\right) \times 100$$

where $R_p$ and $R_{po}$ are the values of the polarisation resistance with and without inhibitor, respectively.

*Loganayagi et al., *ACS Sustainable Chemistry & Engineering* (2014), **2**, 606-613.

# Initial Polymer Set




Conventional nylon 6,6: adipic acid + hexamethylenediamine

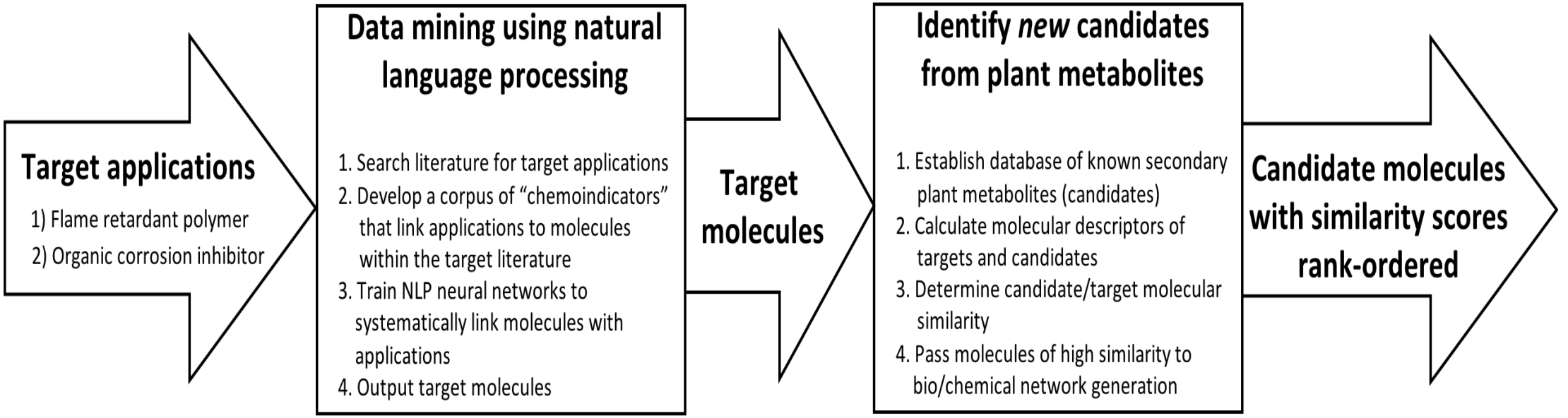
Flame retardant nylon 6,6: (adipic acid/3-hexenedioic acid) + hexamethylenediamine

} Same polymerization procedure
Similar thermal and mechanical properties

**UPA-x** polymers formed from blends of **x** mol % AA and HAD (10 samples)

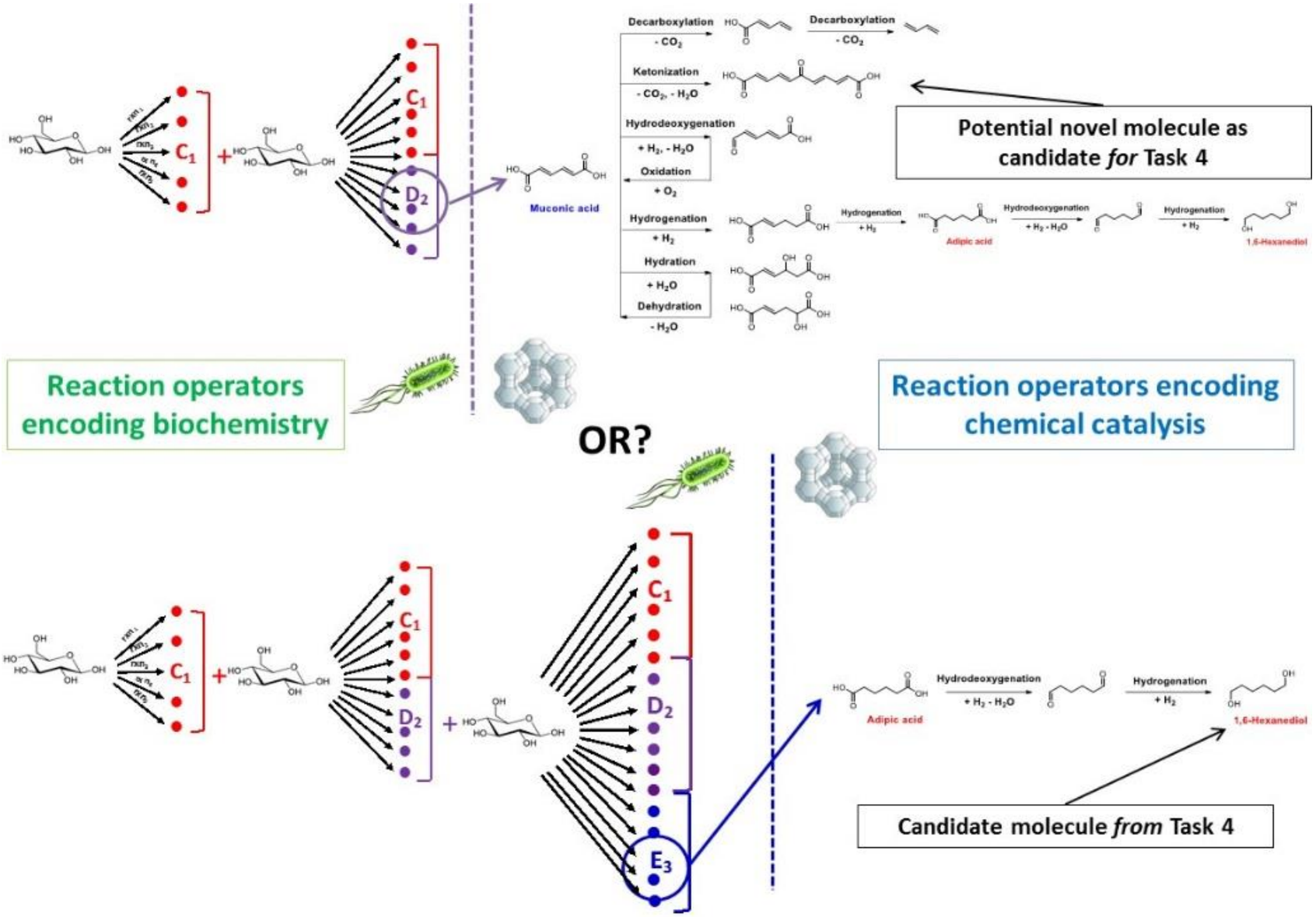
***TGA Screening for Char Formation***

# Recurrent Neural Network Framework

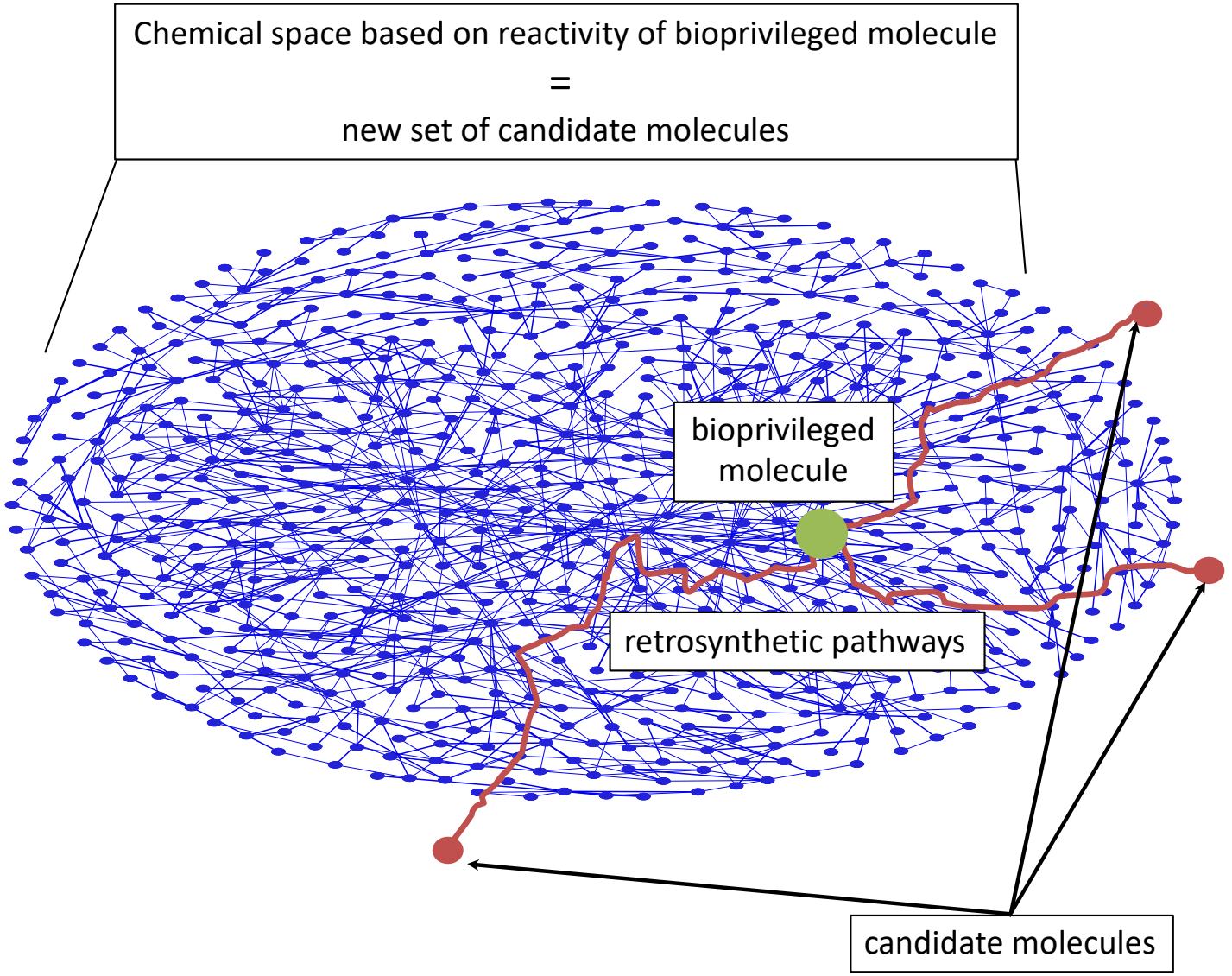



- Concept: the "data mining + similarity" workflow will produce candidate molecules for the reaction network generator
  - Hypothesis: "target" molecules will have ideal properties for applications, can be readily synthetically upgraded from "candidates" due to chemical similarity

# Reaction Network Generation Framework



# Integration of Computational Tasks



# Impact

**Specific Product Impact: Performance and environmental impact**

- Organic corrosion inhibitors to replace inorganics
- Flame retardant polymers without co-extruded molecules

**Broader Impact**:

- Value-added products that can help enable biorefineries
- Systematic strategy to identify and develop performance advantaged biobased chemicals

# Corrosion Inhibitor Libraries

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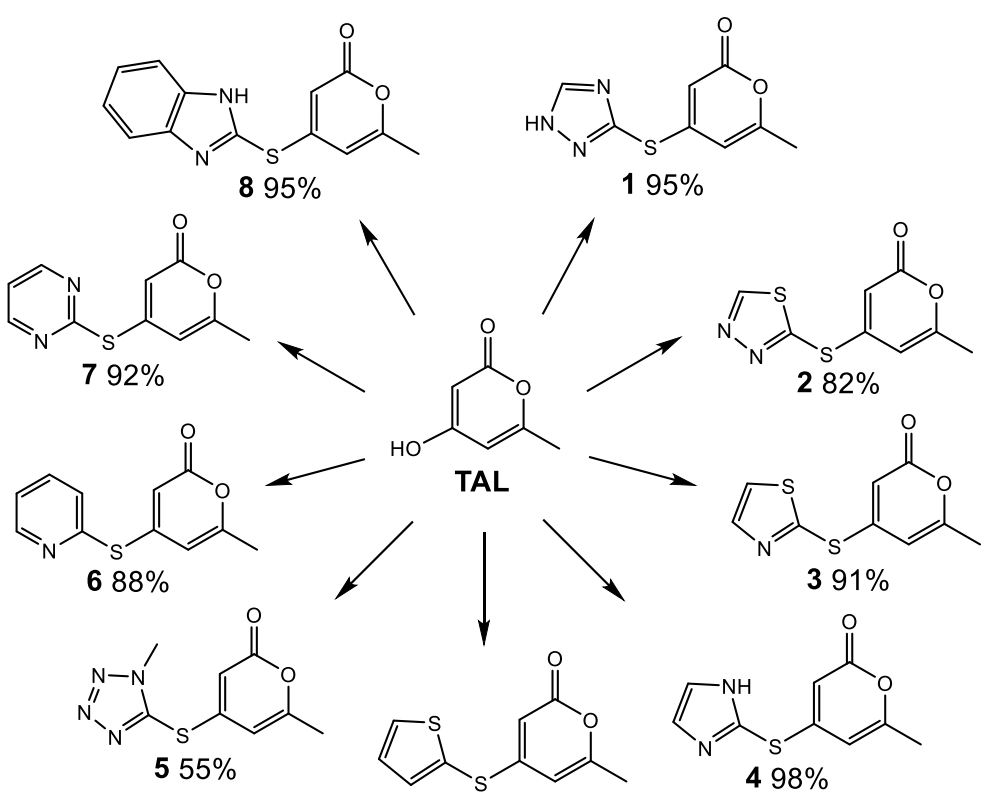
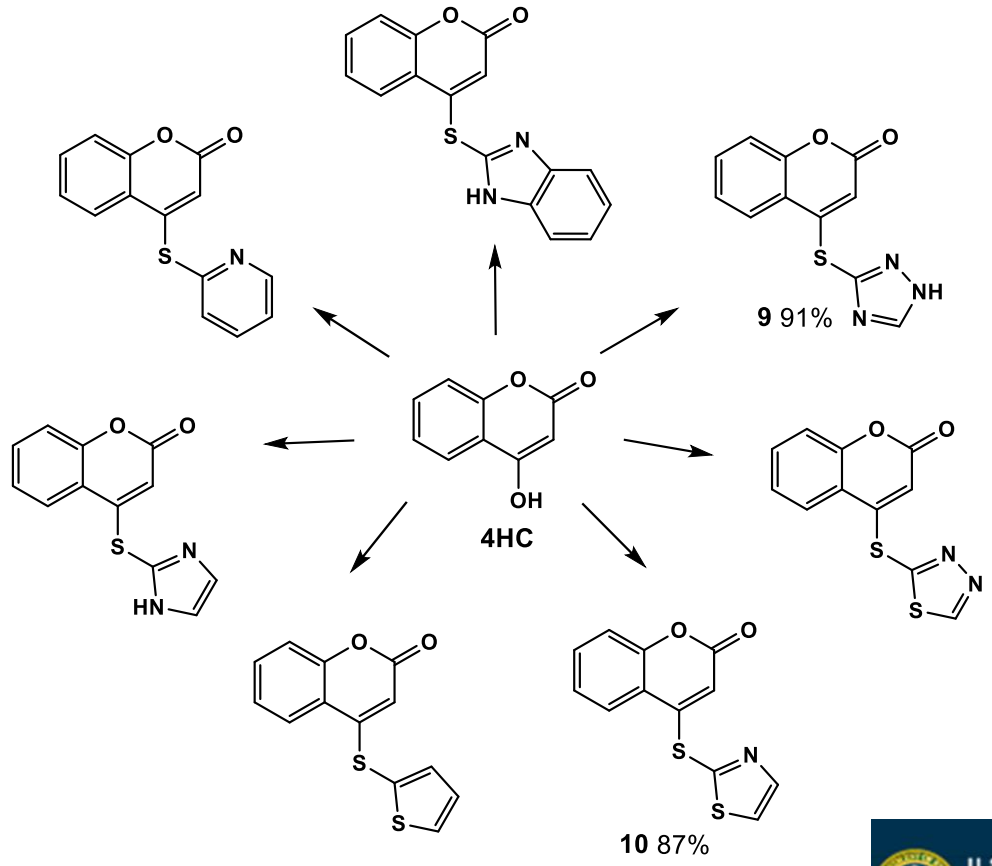
## 1st and 2nd Generation Libraries

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# Corrosion Inhibitor Libraries – $H_2SO_4$

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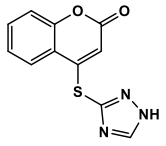
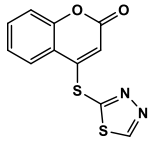
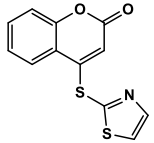
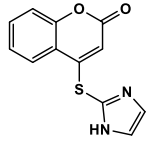
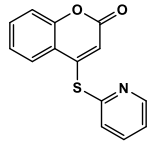
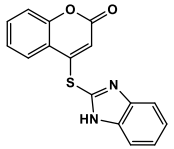
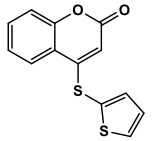
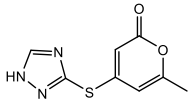
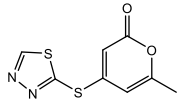
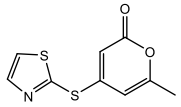
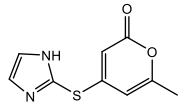
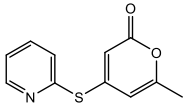
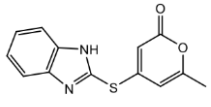
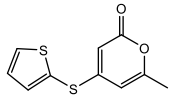
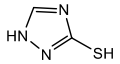
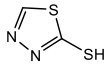
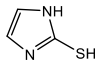
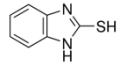
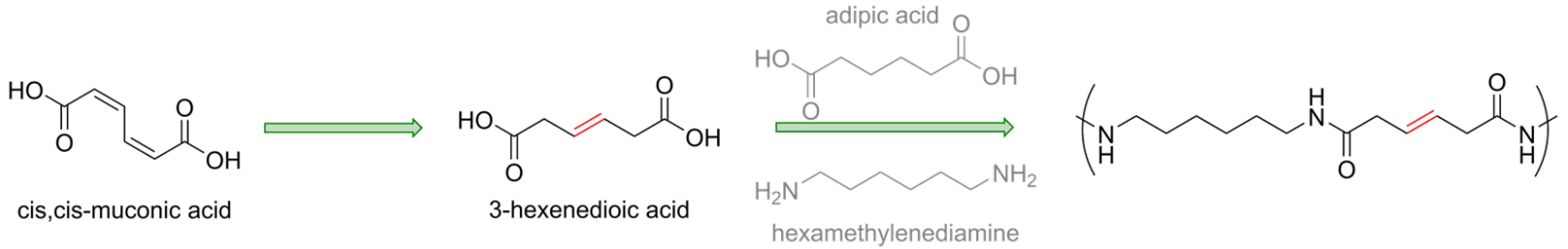
| Label | **4HC** |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|
| Rct/Ohm | 13 | 430 | 397 | 478 | 269 | 398 | 133 | 11 |
| IE | **-23%** | **96%** | **96%** | **97%** | **94%** | **96%** | **88%** | -45% |
| Label | **TAL** |  |  |  |  |  |  |  |
| Rct/Ohm | 16 | 77 | 73 | 126 | 44 | 306 | 415 | 229 |
| IE | **0%** | **79%** | **78%** | **87%** | **64%** | **95%** | **96%** | **93%** |
| Label | **Urotropin** |  |  |  |  |  |  | |
| Rct/Ohm | 23 | 18 | 19 | 99 | 71 | 145 | 270 | |
| IE | **30%** | 11% | 16% | 84% | 77% | 89% | 94% | |

# Polymer: 3HDA Content Evaluated

- UPA-x polymers with blends of x mol % HDA replacement of AA

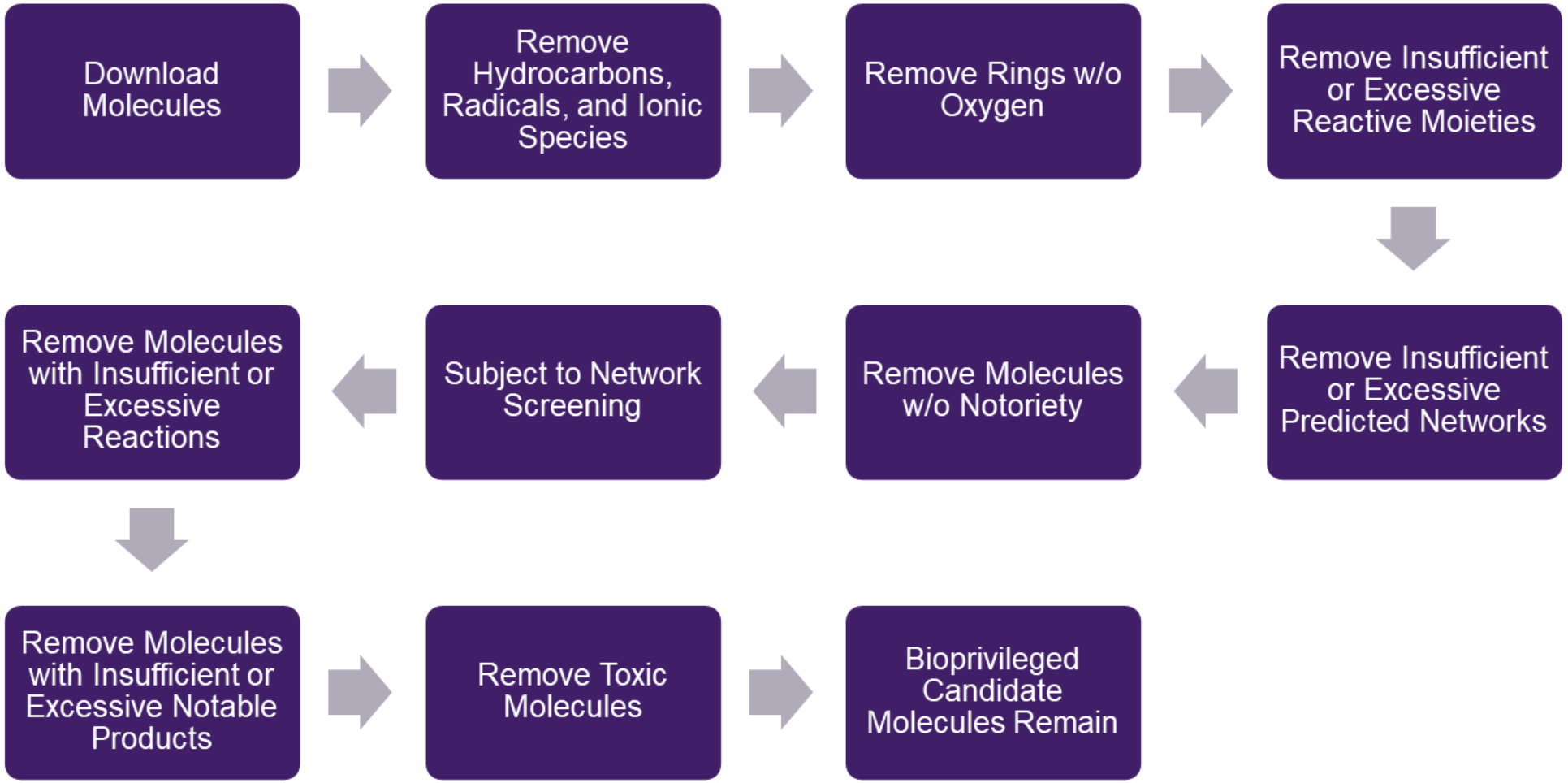



| Sample | Anaerobic Char (%) | Aerobic Char (%) |
|---|---|---|
| Commercial | 4.4 ± 0.8 | 25.1 ± 0.9 |
| UPA-0 | 3.7 ± 1.3 | 26 ± 2 |
| UPA-5 | 6.7, 6.7 | 30.6, 26.3 |
| UPA-10 | 7.0, 8.3 | 29.9, 30.3 |
| UPA-20 | 10.0, 8.9 | 28.6, 28.9 |
| UPA-30 | 9.7, 10.5 | 30.2, 27.9 |

| Sample | $T_m$ (°C) | $\Delta H_m$ (J/g) | $T_c$ (°C) | $\Delta H_c$ (J/g) | $M_n$ (kDa) | Mw (kDa) | PDI |
|---|---|---|---|---|---|---|---|
| UPA-0 | 257.1 | 49.6 | 223.9 | 43.6 | 17.1 | 34.3 | 2.01 |
| UPA-5 | 253.6 | 38.6 | 219.3 | 42.2 | 16.7 | 34.0 | 2.04 |
| UPA-10 | 247.0 | 35.8 | 211.3 | 38.7 | 16.3 | 33.2 | 2.04 |
| UPA-20 | 233.4 | 25.6 | 192.1 | 32.1 | 16.2 | 33.0 | 2.03 |

Annealed ISO 527-2 1BB bars, 7-10 replicates: Similar **toughness, tensile modulus, max stress, mass strain**

# Workflow for Generic Candidate Molecules



# Reaction Network Candidate Pruning

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## Starting Candidates

| Formula | Compounds |
|---|---|
| $C_4H_xO_y$ | 5,706 |
| $C_5H_xO_y$ | 13,271 |
| $C_6H_xO_y$ | 35,542 |
| $C_7H_xO_y$ | 57,043 |

## Final Pruning

| Step | C5 | C6 |
|---|---|---|
| Product Count | 277 | 390 |
| Product Rank | - | 14 |
| Thermodynamics | 91 | 41 |
| Known Products | 4 | 34 |
| Literature of Products | 4 | 57 |
| % Unknown | 51 | 314 |
| Patents/Literature | 113 | 45 |
| Toxicity | 12 | 35 |
| **CANDIDATES** | **104** | **103** |

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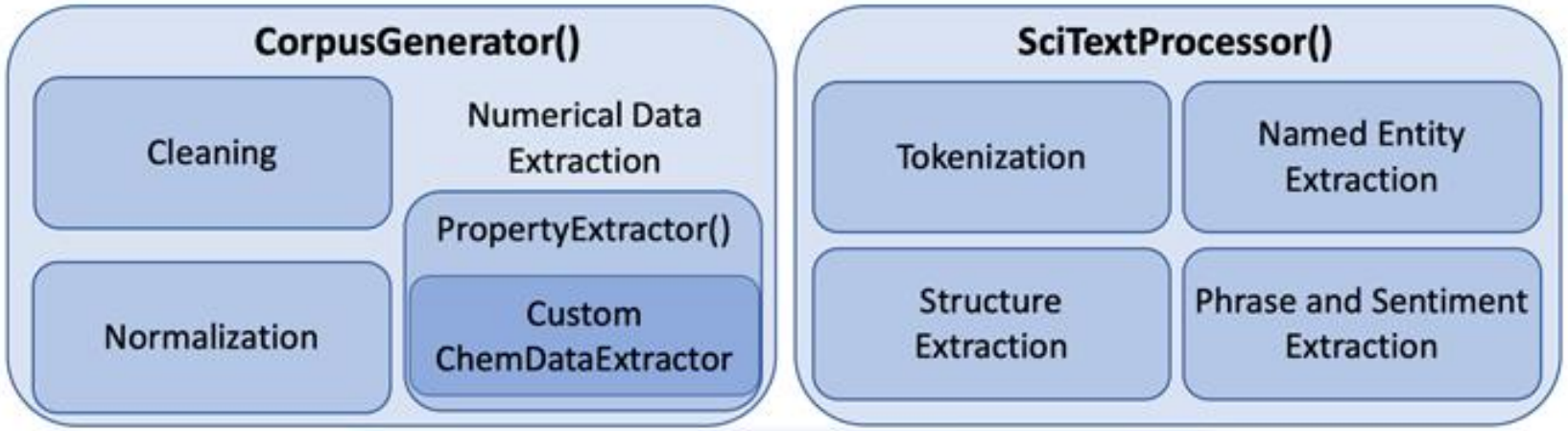
# RNN for Corrosion Inhibitors





{'name': ['imidazoline', '2-imidazoline],
'role': 'product',
'inhibition_efficiency': {'value': '99.3', 'units': '%'},
'LUMO': {'value': '6.048 – 6.720', 'units': 'eV'},
...
'SMILES': 'N\1=C\NCC/1',
'sentiment_phrase': 'good corrosion inhibitor'}


Articles: **~100,000**

Extracted molecules: **~22,000**

Initial candidates: **60***

* High similarity scores

# Future Work – Corrosion Inhibitors

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- Additional characterizations with best candidates
  - Electron microscopy
  - Quantum chemical calculations
  - Molecular dynamic simulations
  - Adsorption isotherm studies
- Chemical structures suggested by computational work
- Technology translation
  - Connect with corrosion inhibitor companies
  - Understand commercial requirements for further development of identified organic corrosion inhibitors

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# Future Work – Flame Retardant Nylon

- Additional testing with best polymer candidates
  - Polymer physical properties (thermal - <20 mg, mechanical - ~10 g)
  - Microcalorimetry screening
  - Flammability testing
- Initial tethered chemical structures
- Tethered chemical structures suggested by computational work
- Technology translation
  - Connect with polymer companies
  - Establish plan for further development of identified flame retardant nylons

# Summary

- 13 high performing organic corrosion inhibitors identified
- Improved charring “nylon 6,6” synthesized with good physical properties
- RNN and RNG computational frameworks established
- First set of prospective corrosion inhibitors handed off from RNN to RNG
- Key future work
  - Proposed biopriviledged molecules for corrosion inhibitor library generation
  - Second test of computational framework for tethered moieties to create flame retardant nylon polymers

# Quad Chart Overview

## Timeline

- 10/1/18
- 12/31/21

| | FY20 Costed | Total Award |
|---|---|---|
| **DOE Funding** | $923,061 | $2,500,000 |
| **Project Cost Share** | $326,676 | $625,000 |

## Project Partners

- Northwestern University
- University of Washington

## Project Goal

Advance two technological areas; a) novel molecules with improved performance in the end use application of organic corrosion inhibitors and flame retardant nylon polymers and b) development of a systematic process for identifying biomass-derived molecules with improved performance in end use applications. Use the two application areas for aiding the construction of a broader systematic process for novel molecule identification.

## End of Project Milestones

- Data mined candidate molecules synthesized and tested - ≥ 5 novel molecules identified with >10% performance improvement
- Integrated computational process developed for finding novel chemicals.

## Funding Mechanism

FOA-0001916 Bioenergy Engineering for Products Synthesis (BEEPS) - 2018

Topic Area 3: Performance Advantaged Bioproducts (PABP)

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*Thank You*

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# Responses to Previous Reviewers' Comments

- If your project has been peer reviewed previously, address 1-3 significant questions/criticisms from the previous reviewers' comments which you have since addressed
- Also provide highlights from any Go/No-Go Reviews

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# Publications, Patents, Presentations, Awards, and Commercialization

- Carraher, J.M., Carter, P., Rao, R.G., Forrester, M.J., Pfennig, T., Shanks, B.H., Cochran, E.W., and Tessonnier, J.-P., "Solvent-driven isomerization of cis,cis-muconic acid for the production of specialty and performance-advantaged cyclic biobased monomers," *Green Chemistry*, **22**, 6444-6454 (2020)
- Dollar, O., Joshi, N., Beck, D.A.C., and Pfaendtner, J. "Giving Attention to Generative VAE Models for *de novo* Molecular Design," *Nature Communications*, submitted (2020)
- Lopez, L.M., Shanks, B.H., and Broadbelt, L.J., "Identification of Bioprivileged Molecules: Expansion of a Computational Approach to Broader Molecular Space," *Molecular Systems Design & Engineering,* submitted (2021)
- Abdolmohammadi, S., Forrester, M.J., Lin, F.-Y., Gansebom, D., Nelson, J.W., Matthiesen, J.E., Hernández, N., Shanks, B.H., Tessonnier, J.-P., and Cochran, E.W., "Analysis of the Amorphous and Interphase Influence of Comonomer Loading on Polymer Properties Towards Forwarding Bioadvantaged Copolyamides," *Green Chemistry,* submitted (2021).

- Tessonnier, J.P., Shanks, B.H., Cochran, E.W., Hadel, J.E., Dell'Anna, M.N. and Carter, P., "Isomerization of Cyclohexenedicarboxylic Acid and its Derivatives," United States Patent application, 2020.
- Shanks, B.H., Kraus, G.A., Bradley, W., Huo, J. and Podolak, K., "Heteroaryl-Thio-Substituted Pyrones," United States Patent application, 2020.

- "Developing Performance-Advantaged Chemicals Utilizing Bioprivileged Molecules: Organic Corrosion Inhibitors" with Huo, J., Bradley, W., Podolak, K., Ryan, B., Roling, L.K., Kraus, G.A., Annual Meeting, American Institute of Chemical Engineers, virtual, November, 2020.

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