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Cooperative Research and Development Agreement (CRADA) Final Report - MITRE Domain Specific Language (DSL) for synthetic biology workflows

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Cooperative Research and Development Agreement (CRADA) Final Report

Report Date: March 10, 2025

In accordance with Requirements set forth in the terms of the CRADA, this document is the CRADA Final Report, including a list of Subject Inventions. It is to be forwarded to the DOE Office of Scientific and Technical Information upon completion or termination of the CRADA, as part of the commitment to the public to demonstrate results of federally funded research.

Parties to the Agreement: Lawrence Berkeley National Laboratory (hereafter LBNL) and Mitre Corporation (hereafter MITRE)

CRADA number: FP00019840

CRADA Title: MITRE Domain Specific Language (DSL) for synthetic biology workflows

Responsible Technical Contact at Berkeley Lab: Nathan Hillson

Name and Email Address of POC at Partner Company(ies): Marc Salit msalit@mitre.org

Sponsoring DOE Program Office(s): N/A (no DOE sponsor)

LBNL Report Number: LBNL-2001649

OSTI Number: *[SPO to complete]*

Joint Work Statement Funding Table showing DOE funding commitment:

DOE Funding to LBNL	$0.00
Participant Funding to LBNL	$50,000.00
Participant In-Kind Contribution Value	$135,040.00
Total of all Contributions	$185,040.00

Provide a list of publications, conference papers, or other public releases of results, developed under this CRADA: None.

Provide a detailed list of all subject inventions, to include patent applications, copyrights, and trademarks: None.

Executive Summary of CRADA Work:

MITRE is currently developing BioNet, a network designed to facilitate the work of biologist collaborators that are distributed across multiple organizations. BioNet is envisaged to break down traditional barriers in biology, allowing for an integrated, service-based approach to

projects which can utilize expertise from any participating entity. This disaggregation fosters innovation by enabling contributions from multiple sources. The public will benefit from the development of the BioNet (to which this project contributes), in that this fostered innovation could positively contribute to our economy.

As MITRE works to develop the BioNet, it is seeking relevant examples of distributed biologist collaboration across multiple organizations. LBNL has completed a number of such collaborations that are relevant for these purposes. The outputs of the work performed in this project, primarily the learnings derived from efforts to describe how three different LBNL distributed biological collaborations could be conducted on the BioNet, added to MITRE's understanding of how the BioNet should be further developed.

The approach used in this project, namely detailing the structures of the distributed LBNL biologist collaborations (including information and material flows between contributors within them), via MITRE/LBNL project team meetings and LBNL written documentation, was very effective in enabling MITRE staff to further improve and focus their future BioNet development efforts.

Summary of Research Results:

The technical objectives of this work were to scope three BioNet workflows, based on LBNL workflows, expressed in the BioNet Domain Specific Language (DSL) or with recommended DSL extensions, to provide feedback that will enable MITRE subject matter experts and software engineers to further improve and focus future development efforts of the BioNet and its associated DSL. This scoping of three BioNet workflows and their expression in the DSL (or recommended DSL extensions) were to be a collaboration between MITRE and LBNL staff, which were to include meetings that uncover detailed procedural disclosures by LBNL staff that enable the MITRE team to develop BioNet workflows. Workflow review meetings were to evaluate and refine the workflows, leading to revision of BioNet content as needed. As needed MITRE staff were to visit the LBNL EmeryStation East (ESE) research facility to observe the workflows being performed by LBNL staff. These three scoped BioNet workflows were to include the full data packages needed to complete them, including (as relevant to the particular workflow): the project concept, organism and processing designs, genetic designs and composition, strain engineering approaches and results, analytical chemical and other performance assessment, design of manufacturing and scaleup, downstream processing engineering, and/or any translation to practice. It was recognized that these objectives were to make productive contributions towards MITRE's refining of their means and approaches to extend the DSL for additional Operations.

The deliverables for the project were:
- The Parties agreed to complete and submit a final report, as stated in Article X of the CRADA, prior to the project's end-date or termination.
- LBNL was to shall complete the following deliverables, and submit as appropriate to msalit@mitre.org:

- - BioNet workflows: Work with MITRE staff to scope and revisit three (3) BioNet workflows, based on established LBNL workflows, expressed in the MITRE-developed DSL, or with recommended DSL extensions.
    - Ad hoc reports: Ad hoc status reports and technical updates via email and meetings with MITRE staff.
    - Final report: Work with MITRE staff to generate a final project report evaluating the sufficiency of the DSL to encode the three LBNL workflows, the ease of coding workflows in the BioNet DSL; and making recommendations for revising and refining the DSL for increased utility, functionality and ease of use.
  - MITRE was to complete the following deliverables:
    - BioNet workflows: Work with LBNL staff to scope, test, refine, and revisit three (3) BioNet workflows, based on established LBNL workflows, expressed in the MITRE-developed DSL, or with recommended DSL extensions.
    - Final report: Work with LBNL staff to generate a final project report evaluating the sufficiency of the DSL to encode the three LBNL workflows, the ease of coding workflows in the BioNet DSL; and making recommendations for revising and refining the DSL for increased utility, functionality and ease of use.

During the pursuit of the project's activities, it was recognized by the MITRE team that, since the BioNET DSL was undergoing rapid and fairly radical changes, it would not be maximally productive to proceed from the "Establish I/II/III" (scoping) task activities, to the next set of task activities (e.g. test, refine, revisit). Instead, the MITRE team pivoted the project direction to do a deeper, more extended and intensive variation of the "Establish I/II/III" task activities. In particular, the business processes used in Workflow II concerning new user/customer onboarding and sample/input intake for proteomics services, were of keen interest to MITRE in terms of a use-case study (with fairly extensive LBNL documentation) that seemed generalizable (e.g. similar processes were employed at the Broad Institute for their sequencing products/services) and prospectively a good test of the DSL and demonstration of how service interface friction could be reduced through a BioNET DSL-stylized and -documented process. As a consequence, work within the extended and intensified "Establish I/II/III" task activities continued through the duration of this project, and subsequently planned task activities were deferred and not initiated in this project.

This report constitutes the project's final report (the primary deliverable). As mentioned above, the "test, refine, and revisit" planned activities were deferred, and are thereby not included in the final deliverables. All other deliverables were delivered.

Plans for an extension to this project (as a CRADA amendment) were prepared (see attached PDF document). While the MITRE BioNet project has been paused, these plans are an additional output of this project, and could be helpful should a continuation of this work be desired in the future.