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Small Molecule Interactions with
Membranes Final Report CRADA No.
TC02321 Date Technical Work Ended:
1/29/20

H. Peck, I. Gomez

March 15, 2021

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Small Molecule Interactions with Membranes

Final Report
CRADA No. TC02321
Date Technical Work Ended: 1/29/20

Date: January 24, 2020

Revision: 0

A. Parties

This project was a relationship between Lawrence Livermore National Security, LLC and Procter & Gamble Company.

Lawrence Livermore National Security, LLC
Lawrence Livermore National Laboratory
7000 East Avenue
Livermore, CA 94550
Felice Lightstone
Tel: (925) 423-8657
Email: lightstone1@llnl.gov

Procter & Gamble Company
8700 Mason-Montgomery Road
Mason, OH 45040
Mark Meili
Tel: (513) 394-7361
Email: meili.ma@pg.com

B. Project Scope

This was a collaborative effort between Lawrence Livermore National Security, LLC (LLNS) as manager and operator of Lawrence Livermore National Laboratory (LLNL) and Procter & Gamble (P&G) to develop and use a multiscale simulation method to explore and evaluate the nature of industrially relevant compounds in the presence of models that represent microbial membranes.

The project was a six (6) month project, and consisted of four (4) major tasks and the following major deliverables:

- Deliverable 1** P&G and LLNL will select industrial compounds (Month 1)
- Deliverable 2** P&G will deliver existing simulation protocols (Month 1)

Deliverable 3 LLNL and P&G deliver the Final Report and Abstract due within thirty (30) days of completion or termination of the project, as required under Article X of the CRADA. (Month 6)

All of the deliverables for this project were successfully completed on time. LLNL and P&G are working to sign a long term CRADA to build on this work.

C. Technical Accomplishments

The specific technical accomplishments were building a multiscale model of a gram-positive bacterial membrane. This model was simulated using atomistic and coarse-grained molecular dynamics computer simulations. Small molecules of interest to P&G were also parameterized and simulated to assess their impact on the bacterial membrane. After running the simulations detailed analysis of the bilayer's structural and elastic properties was conducted. This work is a step towards a multiscale computational method to assess the effect of P&G surfactant small molecules on bacterial membranes.

D. Expected Economic Impact

This work resulted in a multiscale simulation protocol for simulating small molecules interacting with gram-positive bacterial membranes. As a result of this work, we are in the process of signing a new CRADA between LLNL and P&G to expand this computational capability.

D.1 Specific Benefits

Benefits to DOE

This CRADA project will benefit the DOE because the focus is to develop and use a high-performance computing multiscale simulation method to explore and evaluate the nature of industrially-relevant compounds in the presence of models that represent microbial membranes. The technologies evaluated for this effort tests the robustness of these technologies for use in different applications, and the compounds evaluated are of interest to our mission in Biosecurity.

Benefits to Industry

The benefit for P&G from this project was the simulation data on a number of their industrial relevant small molecules interacting with a bacterial membrane. The simulations in this work were conducted on LLNL's high-performance computing systems. This work is a step towards a machine-learned multiscale model that can be used by P&G for investigating specific formulations and their effect on bacterial membranes. Understanding the underlying molecular mechanisms for bacterial membrane disruption will allow P&G to build and select novel small molecules for their products.

E. Participant Contribution

Work during this project was conducted by both P&G and LLNL. Molecules and protocols were specified by P&G, in addition to work to parameterize the peptidoglycan layer, that will be added in future CRADA work. This work is a step towards automated multiscale simulation methods that will be used by P&G for product development. No subject inventions were created during this CRADA project.

F. Documents/Reference List

Reports

A detailed technical report for the simulation workflow and results is in preparation and will be provided to P&G by January 29, 2020.

Copyright Activity

No copyright material was developed.

Subject Inventions

No subject inventions were produced during this CRADA.

Background Intellectual Property

Background Intellectual Property was not used during this CRADA.

G. Acknowledgement

Industrial Participant's signature of the final report indicates the following:

- 1) The Participant has reviewed the final report and concurs with the statements made therein.
- 2) The Participant agrees that any modifications or changes from the initial proposal were discussed and agreed to during the term of the project.
- 3) The Participant certifies that all reports either completed or in process are listed and all subject inventions and the associated intellectual property protection measures generated by his/her respective company and attributable to the project have been disclosed and included in Section E or are included on a list attached to this report.
- 4) The Participant certifies that if tangible personal property was exchanged during the agreement, all has either been returned to the initial custodian or transferred permanently.
- 5) The Participant certifies that proprietary information has been returned or destroyed by LLNL.

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2/6/2020

Mark Meili, R&D Director, Modeling & Simulation
Procter & Gamble Company

Date

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2/6/2020

Felice Lightstone, LLNL Principal Investigator
Lawrence Livermore National Security, LLC

Date



Els\f,Quaite-Randa II, Deputy Director
Innovation and Partnerships Office
Lawrence Livermore National Security, LLC


Date

Attachment I-Final Abstract

Small Molecule Interactions with Membranes

Final Abstract (Attachment I)
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B. Purpose and Description

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molecules on bacterial membranes. All deliverables were completed on time and LLNL and P&G are working on signing a new long term CRADA to expand this work.

C. Benefit to Industry

The benefit for P&G from this project was the simulation data on a number of their industrial relevant small molecules interacting with a bacterial membrane. The simulations in this work were conducted on LLNL's high-performance computing systems. This work is a step towards a machine-learned multiscale model that can be used by P&G for investigating specific formulations and their effect on bacterial membranes. Understanding the underlying molecular mechanisms for bacterial membrane disruption will allow P&G to build and select novel small molecules for their products.

D. Benefit to DOE/LLNL

This CRADA project benefits the DOE by developing and using high-performance computing multiscale simulation methods to explore and evaluate the nature of industrially relevant compounds in the presence of models that represent microbial membranes. The technologies evaluated for this effort tests the robustness of these technologies for use in different applications, and the compounds evaluated are of interest to our mission in Biosecurity.

E. Project Dates

5/31/19 - 1/29/20