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6. AUTHORS
Christopher W. Bielawski

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAMES AND ADDRESSES
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14. ABSTRACT
A primary objective of this project is to use externally-applied mechanical forces to control the intrinsic activities displayed by enzymes and other materials. It was demonstrated that the application of forces to enzymes properly outfitted with polymers resulted in distortions at the active sites of the corresponding enzymes. For example, polymer-protein composites were found to display photophysical properties that were dependent on the applied force. Recent efforts have focused on new classes of polymeric materials that effectively resist mechanical degradation.

15. SUBJECT TERMS

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a. REPORT	b. ABSTRACT	c. THIS PAGE			Adrian Keatinge-Clay
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Report Title

Final Report: Mechanobiocatalysis: Modulating Enzymatic Activity with Mechanical Force

ABSTRACT

A primary objective of this project is to use externally-applied mechanical forces to control the intrinsic activities displayed by enzymes and other materials. It was demonstrated that the application of forces to enzymes properly outfitted with polymers resulted in distortions at the active sites of the corresponding enzymes. For example, polymer-protein composites were found to display photophysical properties that were dependent on the applied force. Recent efforts have focused on new classes of polymeric materials that effectively resist mechanical degradation.

Enter List of papers submitted or published that acknowledge ARO support from the start of the project to the date of this printing. List the papers, including journal references, in the following categories:

(a) Papers published in peer-reviewed journals (N/A for none)

Received		Paper
08/30/2014	4.00	Constance B. Bailey, Joe R. Cannon, Katie A. Clark, David A. Vanden Bout, Jennifer S. Brodbelt, Johnathan N. Brantley, Adrian T. Keatinge-Clay, Christopher W. Bielawski. Mechanically Modulating the Photophysical Properties of Fluorescent Protein Biocomposites for Ratio- and Intensiometric Sensors, Angewandte Chemie International Edition, (04 2014): 5088. doi: 10.1002/anie.201306988
09/14/2013	1.00	Christopher W. Bielawski, Johnathan N. Brantley, Constance B. Bailey, Kelly M. Wiggins, Adrian T. Keatinge-Clay. Mechanobiochemistry: harnessing biomacromolecules for force-responsive materials, Polymer Chemistry, (2013): 0. doi: 10.1039/c3py00001j
09/14/2013	2.00	Sai Sriharsha M. Konda, Johnathan N. Brantley, Bibin T. Varghese, Kelly M. Wiggins, Christopher W. Bielawski, Dmitrii E. Makarov. Molecular Catch Bonds and the Anti-Hammond Effect in Polymer Mechanochemistry, Journal of the American Chemical Society, (08 2013): 0. doi: 10.1021/ja4051108
09/14/2013	3.00	Kelly M. Wiggins, Johnathan N. Brantley, Christopher W. Bielawski. Methods for activating and characterizing mechanically responsive polymers, Chemical Society Reviews, (2013): 0. doi: 10.1039/c3cs35493h
TOTAL:	**4**	

Number of Papers published in peer-reviewed journals:

(b) Papers published in non-peer-reviewed journals (N/A for none)

Received		Paper
TOTAL:		

Number of Papers published in non peer-reviewed journals:

(c) Presentations

(1) Eastman Chemical

(2) Plenary Lecturer, International Symposium on Mechanochemistry in Synthesis and Nanoscience (ISMECh 2013), Warsaw

(3) ACS-PMSE/CCS-PD 3rd Joint Symposium on Polymers, Chinese Chemical Society (CCS), Shanghai, China

(4) Tsinghua University, ACS-PMSE/CCS-PD 3rd Joint Symposium on Polymers, Chinese Chemical Society (CCS), Beijing, China

(5) Texas State University

(6) UT Southwestern

Number of Presentations: 6.00

Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Received Paper

TOTAL:

Number of Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Peer-Reviewed Conference Proceeding publications (other than abstracts):

Received Paper

TOTAL:

Number of Peer-Reviewed Conference Proceeding publications (other than abstracts):

(d) Manuscripts

Received Paper

TOTAL:

Number of Manuscripts:

Books

Received Book

TOTAL:

Received Book Chapter

TOTAL:

Patents Submitted

Patents Awarded

Awards

(1) Fellow of the Royal Society of Chemistry, 2014

(2) Visiting Professorship for Senior Int'l Scientists, Chinese Academy of Sciences, 2013

Graduate Students

NAME	PERCENT_SUPPORTED	Discipline
Blake, Garrett	0.36	
Lastovickova, Dominika	0.36	
Liu, Di	0.36	
Moerdyk, Jonathan	0.36	
Teator, Aaron	0.36	
Todd, Alexander	1.00	
FTE Equivalent:	**2.80**	
Total Number:	**6**	

Names of Post Doctorates

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Names of Faculty Supported

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Names of Under Graduate students supported

NAME	PERCENT_SUPPORTED	Discipline
Carroll, Valyn	0.52	Chemistry
Larsen, Eric	0.41	Chemistry
FTE Equivalent:	**0.93**	
Total Number:	**2**	

Student Metrics

This section only applies to graduating undergraduates supported by this agreement in this reporting period

The number of undergraduates funded by this agreement who graduated during this period: 2.00

The number of undergraduates funded by this agreement who graduated during this period with a degree in science, mathematics, engineering, or technology fields:..... 2.00

The number of undergraduates funded by your agreement who graduated during this period and will continue to pursue a graduate or Ph.D. degree in science, mathematics, engineering, or technology fields:..... 1.00

Number of graduating undergraduates who achieved a 3.5 GPA to 4.0 (4.0 max scale):..... 0.00

Number of graduating undergraduates funded by a DoD funded Center of Excellence grant for Education, Research and Engineering:..... 0.00

The number of undergraduates funded by your agreement who graduated during this period and intend to work for the Department of Defense 0.00

The number of undergraduates funded by your agreement who graduated during this period and will receive scholarships or fellowships for further studies in science, mathematics, engineering or technology fields:..... 0.00

Names of Personnel receiving masters degrees

NAME
Total Number:

Names of personnel receiving PHDs

NAME	
Brantley, Johnathan	
Moerdyk, Jonathan	
Total Number:	**2**

Names of other research staff

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Sub Contractors (DD882)

Inventions (DD882)

Scientific Progress

A primary aim of this project is to use externally-applied mechanical forces to change the intrinsic activities displayed by various proteins and other materials. After selectively attaching synthetic and other types of polymers to enzymes and other functional species at predetermined locations, the forces created under ultrasound and other conditions was expected to result in changes at the corresponding active sites. As a part of these efforts, a large range of of solution- and solid-state techniques used to activate polymers using mechanical force was employed. In parallel, the characterization of the mechanically-activated systems was performed using various spectroscopic techniques as well as chemical methodologies.

Efforts over the past year have been directed toward the synthesis of novel polymeric materials that are designed to resist mechanical degradation. This ambition project sought to develop molecular scaffolds that reinforce the overall polymeric architecture under the action of exogenous forces through “catch bond” effects. Although recent efforts have been primarily focused on the acceleration of chemical processes, the mechanical suppression of chemical reactivity is an underexplored phenomenon with significant implications for the design of new synthetic and biological materials that resist mechanical degradation under stress. One mechanism by which exogenous forces could reduce bond scissile processes in a broad range of molecular scaffolds is through catch bond effects, where certain covalent bonds dissociate only when force is applied to them through a specific vector. For example, we recently showed that appending polymer chains to the 2-position of the anthracene moiety inhibited the corresponding cycloreversion reaction. Building on these results, efforts were directed toward embedded these and other functionalities within poly(urethane), and divided into two categories: (a) polymers designed to exhibit enhanced mechanical properties in response to stress and (b) stress-sensing composites that are undergo mechanical activation only when above a certain force threshold. To prepare materials that reinforce themselves under mechanical stress, various functionalized were condensed with various difunctional isocyanates; for comparison, analogous control poly(urethanes) derived from the known mechanically-labile diols were also prepared. To tune the threshold at which mechanical activation occurs, which could have important implications for the design of force sensors or materials that degrade at predetermined stresses, other designed diols were prepared and polymerized with various bis(isocyanate)s to afford the corresponding poly (urethane)s and compared to analogous materials containing the known mechanically-labile systems. The direct measurement of a catch bond has not yet been reported outside of the context of biomolecular adhesion complexes; thus, such experiments would provide new insights into the fundamental interactions between chemical systems and macroscopic forces.

In parallel, we also demonstrated that mechanical forces may be used to vary the intrinsic photophysical properties displayed by various fluorescent proteins that were embedded within synthetic polymeric matrices. Indeed, we successfully modulated the emission wavelength of eYFP-containing polymer composites via the application of mechanical force, as well as showing that the photophysical properties displayed by GFPuv may also be changed. Additionally, the mechanical perturbation of various fluorescent proteins were shown to vary the intrinsic photophysical properties of the aforementioned materials in ratiometric or intensiometric manner. An ability to influence the optical characteristics of composite materials containing active biological agents is expected to result in new stress-responsive materials with specified sensitivities. In addition, it was shown that mechanochemical phenomena involving chemical systems can be translated to force-sensitive systems. An ability to synthesize the responsive biocomposites described is expected to lead to the development of new classes of materials and systems that respond to mechanical force.

Technology Transfer