A Community Based CURE Project to Explore Structure-Function Relationships in Malate Dehydrogenase

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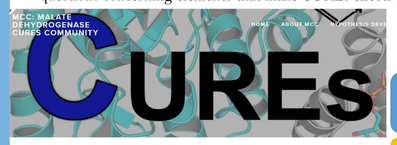
Visit the Project Web Page for More Details and Information about How to Participate

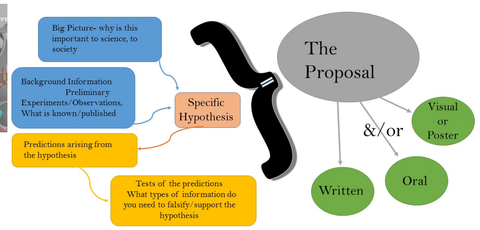
Visit the Bell Labs Web Site

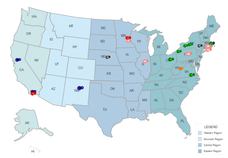
The Bell Laboratories: Systems Biology, Structural Biology, Biophysics & Bioinformatics

Abstract & Background

The Malate Dehydrogenase CUREs Community (MCC) project, funded by a grant from the National Science Foundation, involves protein-centric, Course-based Undergraduate Research Experiences, (CUREs), focusing on Malate Dehydrogenase. These are being conducted in introductory to advanced level courses in diverse institutions, ranging from Community Colleges to Research intensive institutions. MCC has developed, and made available, a variety of written and physical resources to facilitate incorporation of these CUREs into the curriculum. Research projects integrate foundational concepts of protein structure and function with basic research into a variety of aspects of malate dehydrogenase, organized around three cluster themes, protein conformation, cellular biochemistry, & mechanism. The projects frequently extend beyond the classroom into longer term, student-centered research projects, and have led to presentations at national meetings and publications. Recent projects, combining bioinformatics, computational approaches, and wet lab, have elucidated a mechanism for subunit interactions, explored the role of the flexible loop involved in substrate and effector binding, probed the formation of metabolons with Citrate Synthase, and investigated the role of "second sphere" residues around the active site. All CUREs implemented by MCC contain the same elements: Scientific Background, Hypothesis Development, Proposal, Experiments/Teamwork to test hypothesis, Data Analysis and Conclusions, and Presentation. Several of the projects include collaboration between institutions. In addition to the scientific questions being addressed, MCC is exploring several pedagogical questions concerning elements that make CUREs effective high impact teaching practices, including duration (whole semester versus 6-7 week mini CUREs) and scientific collaboration.

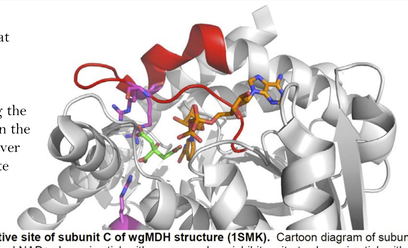






Faculty across the Country in diverse institution types are teaching CUREs focusing on Structure-Function relationships in Malate Dehydrogenase

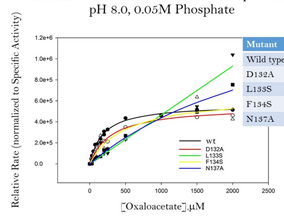
One coordinated project involving CURE classes at Research Intensive, PUI, Comprehensive, and Community Colleges is focused on understanding the roles of each amino acid in the flexible loop that closes over the active site on substrate binding.



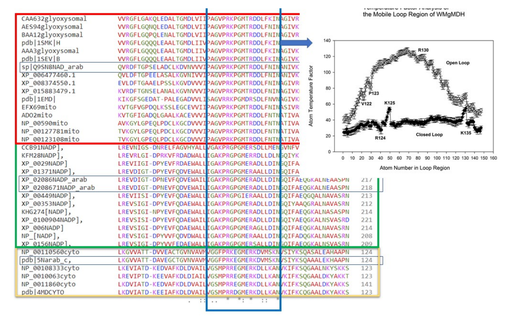
Active site of subunit C of wgMDH structure (1SMK). Cartoon diagram of subunit C of 1SMK with bound NAD+ shown in stick with orange carbon, inhibitor citrate shown in stick with green carbon. arginines (124, 130, 196) that coordinate substrate shown in stick with magenta carbon. loop is shown in red.

#	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	1
wt	P	A	G	V	P	R	K	P	G	M	T	R	D	D	L	F	K	I	N
mut	?	G	A	?	G	A	Q	G	F	Q	V	A	N	N	S	S	?	?	A

Michaelis Menten Plots of wt and Loop Mutants
pH 8.0, 0.05M Phosphate



Mutant	Km, µM	Standard Error
Wild type	186	11
D32A	302	36
L133S	nd	nd
F134S	492	224
N137A	3055	1102



Students and Faculty collaborate in hypothesis development, proposal presentations, experiments and data analysis.

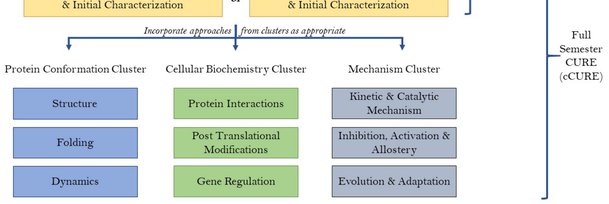
Contributing Faculty and Students will share authorship on manuscripts submitted for publication

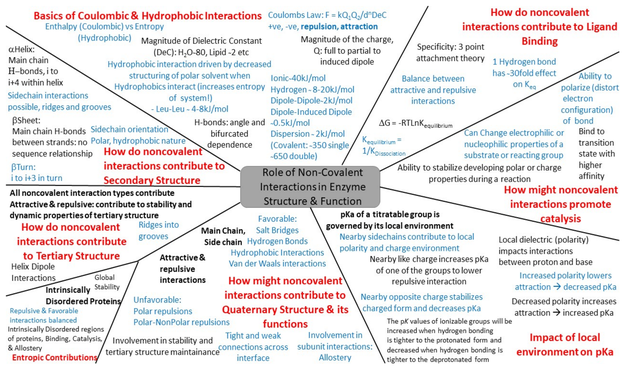
Kevin Callahan, SJRC, Kristin Fox, Union, Tamara Mans, NHCC, Zing Zhang, UNL, John Rakus , Marshall, and Jessica & Ellis Bell, USD have combined to explore the role of each residue in the mobile loop of Malate Dehydrogenase sharing data and resources, focusing on a variety of CUREs (full semester and miniCUREs). Experimental data is subsequently validated outside of the CURE setting by other students and participating faculty.

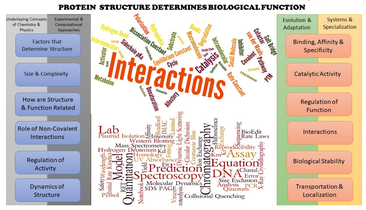
Subsequent CUREs at the 6 institutions will further explore organelle and species differences as well as develop other experimental approaches to explore structure-function relationships.

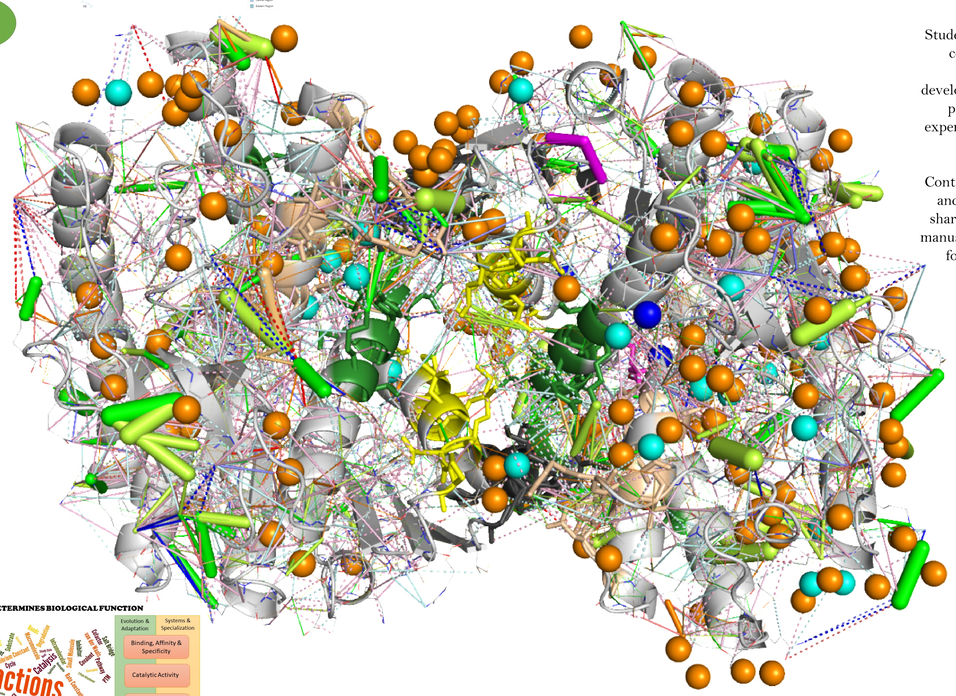
In all cases students in a CURE class will have access to validated preliminary data and will develop their own hypothesis and predictions for further exploration.

CUREs









Exploring the Role Non Covalent Interactions Play in Structure & Function

JOIN MCC:

Currently Full Members of the Community (MCCv1.0) commit to the following: Teach an MCC CURE in a course on a regular basis, Contribute pedagogical and scientific data to the overall project: this requires working with USD to develop the appropriate IRB etc. and contribute "control" courses as well as "treatment" courses, Contribute resources to the community, Join one or more of the three cluster areas, Participate in the annual workshop, Work on MCC manuscripts as appropriate for both CourseSource and or the scientific literature.

In addition to full members, faculty who wish to use MCC resources can join as Affiliate Members and sign the relevant MTAs etc. They join a cluster area and can interact with the MCC in terms of course design/development but do not contribute to the pedagogical research. As appropriate they can contribute to the scientific research, and can if they choose, participate virtually in appropriate aspects of the annual workshop.

Finally, the resources developed and validated by the community are freely available to anyone who executes the appropriate MTA.

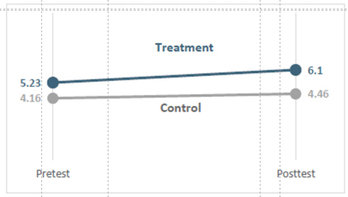
View our NSF STEM4ALL 2019 Video Showcase Video about the Project.

Impact of CURE Duration: Preliminary Results

STEM Interest by CURE length (cCURE versus mCURE)

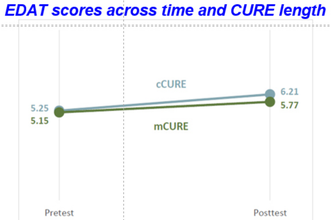
Within the CURE condition, 112 students who participated in cCUREs and 34 students who participated in mCUREs completed the student posttest survey. Independent samples *t*-tests were conducted to compare students in cCUREs to students in mCUREs on each of the three STEM interest subscales. ***There were no differences between students in cCUREs and students in mCUREs on any of the STEM interest subscales.***

EDAT scores across time and condition



Treatment N=139, Control N=142. difference from pretest to posttest and difference between treatment and control is significant at p<0.001. Interaction between time and condition is significant at p<0.5.

EDAT scores across time and CURE length

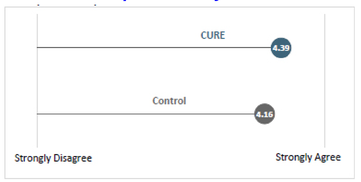


Note: cCURE N=106, mCURE N=33. Difference from pretest to posttest is significant at p<0.001.

These findings suggests that students can receive a high-quality CURE experience in either a full course or a more feasible, mini-CURE if time and/or resources are limited.

Impact of CUREs on Student Perceptions & Career Goals

STEM importance by condition



STEM career interest by condition

CURE N=146, Control N=131. Scale: 1 = Strongly Disagree to 5 = Strongly Agree. Differences are significant at p<0.01.

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