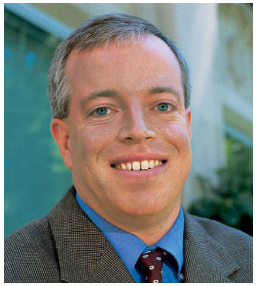
The **mission** of the CBM is to collaborate with member organizations to focus faculty innovation and student training on critically important emerging needs and opportunities in measurement science and instrumentation

cbm.nd.edu

Leadership and Mission

Chris Welch
Center Director and
Industry Liaison

Chris Crittenden
Genentech
Chair, IAB



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Nari Talaty
AbbVie
Vice-Chair, IAB

Garth J. Simpson
Purdue University
Site Director

Jessica Schiller
Operations Director

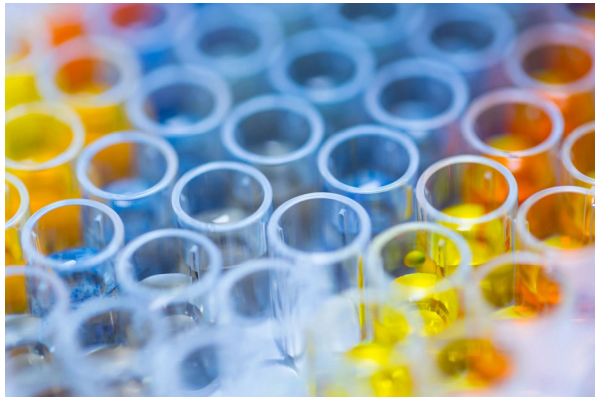
Merlin Bruening
Notre Dame University
Site Director

The **mission** of the CBM is to collaborate with member organizations to focus faculty innovation and student training on critically important emerging needs in measurement science and instrumentation

About 12 new research projects initiated each year

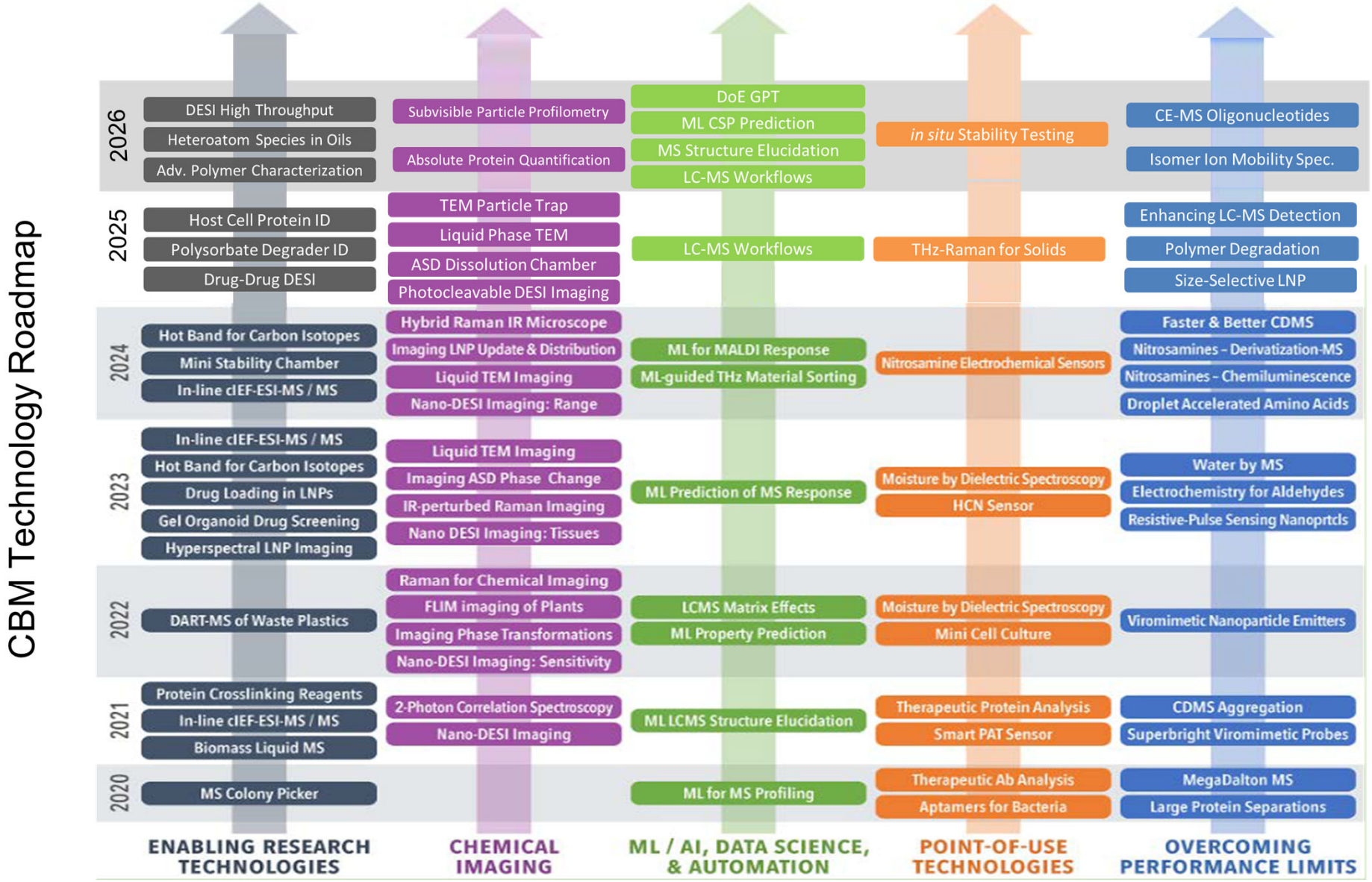
Typically PI + 1 graduate student for 1 year duration, ~$60,000 (no overhead $)

Often Analytical Chemistry faculty, but CBM can carry out projects with any professor in any department at Purdue, IU or Notre Dame



- Collaborative projects involving interested parties from any CBM member organization (typically 4-5 companies/project)
- Monthly group meetings; minutes and presentations stored in CBM data repository
- Publication is the goal – about 25% with industry member co-authors
- Research topics chosen by member organizations based on changing needs and priorities
- Constantly evolving, with core focus on advances in measurement science

CBM Research Roadmap



JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
pubs.acs.org/JACS
Article

Heterogeneity of Glycan Processing on Trimeric SARS-CoV-2 Spike Protein Revealed by Charge Detection Mass Spectrometry

Lohra M. Miller, Lauren F. Barnes, Shannon A. Raab, Benjamin E. Draper, Tarick J. El-Baba, Corinne A. Lutomski, Carol V. Robinson, David E. Clemmer, and Martin F. Jarrold*

Cite This: J. Am. Chem. Soc. 2021, 143, 3959−3966 Read Online

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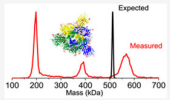
ABSTRACT: The heterogeneity associated with glycosylation of the 66 N-glycan sites on the protein trimer making up the spike (S) region of the SARS-CoV-2 virus has been assessed by charge detection mass spectrometry (CDMS). CDMS allows simultaneous measurement of the mass-to-charge ratio and charge of individual ions, so that mass distributions can be determined for highly heterogeneous proteins such as the heavily glycosylated S protein trimer. The CDMS results are compared to recent glycoproteomics studies of the structure and abundance of glycans at specific sites. Interestingly, average glycan masses determined by "top-down" CDMS measurements are 35−47% larger than those obtained from the "bottom-up" glycoproteomics studies, suggesting that the glycoproteomic measurements underestimated the abundances of larger, more-complex glycans. Moreover, the distribution of glycan masses determined by CDMS is much broader than the distribution expected from the glycoproteomics studies, assuming that glycan processing on each trimer is not correlated. The breadth of the glycan mass distribution therefore indicates heterogeneity in the extent of glycan processing of the S protein trimers, with some trimers being much more heavily processed than others. This heterogeneity may have evolved as a way of further confounding the host's immune system.



analytical chemistry
pubs.acs.org/ac
Article

Characterization of Classical Vaccines by Charge Detection Mass Spectrometry

Lohra M. Miller, Kevin M. Bond, Benjamin E. Draper, and Martin F. Jarrold*

Cite This: Anal. Chem. 2021, 93, 11965−11972 Read Online

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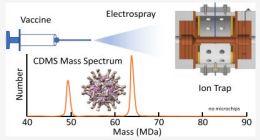
ABSTRACT: Vaccines induce immunity by presenting disease antigens through several platforms ranging from individual protein subunits to whole viruses. Due to the large difference in antigen size, the analytical techniques employed for vaccine characterization are often platform-specific. A single, robust analytical technique capable of widespread, cross-platform use would be of great benefit and allow for comparisons across manufacturing processes. One method that spans the antigen mass range is charge detection mass spectrometry (CDMS). CDMS is a single-ion approach where the mass-to-charge ratio (m/z) and charge are measured simultaneously, allowing accurate mass distributions to be measured for heterogeneous analytes over a broad size range. In this work, CDMS was used to characterize the antigens from three classical multivalent vaccines, inactivated poliomyelitis vaccine (IPOL), RotaTeq, and Gardasil-9, directly from commercial samples. For each vaccine, the antigen purity was inspected, and in the whole virus vaccines, empty virus particles were detected. For IPOL, information on the extent of formaldehyde cross-linking was obtained. RotaTeq shows a narrow peak at 61.06 MDa. This is at a slightly lower mass than expected for the double-layer particle, suggesting that around 10 pentonal trimers are missing. For Gardasil-9, buffer exchange of the vaccine resulted in very broad mass distributions. However, removal of the virus-like particles from the aluminum adjuvant using a displacement reaction generated a spectrum with narrow peaks.



ACS Partner Journal
Journal of the American Society for Mass Spectrometry
pubs.acs.org/jasms
Research Article

Fragmentation of Polyfunctional Compounds Recorded Using Automated High-Throughput Desorption Electrospray Ionization

MyPhuong T. Le,‖ Nicolás M. Morato,‖ Andreas Kaerner, Christopher J. Welch, and R. Graham Cooks*

Cite This: J. Am. Soc. Mass Spectrom. 2021, 32, 2261−2273 Read Online

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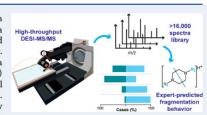
ABSTRACT: Using desorption electrospray ionization (DESI) as part of an automated high-throughput system, tandem mass spectra of the compounds in a pharmaceutical library were recorded in the positive mode under standardized conditions. Quality control filtering yielded an MS/MS library of 16 662 spectra. Fragmentation of subsets of the compounds in the library chosen to contain a single instance of a particular functional group (amide, piperazine, sulfonamide) was predicted by experts, and the results were compared with the experimental data. Expert performance was good to excellent for all the cases evaluated. Substituents on the functional groups were found to exert important secondary control over the fragmentation, with the main effect observed being product ion stabilization by aromatic substitution, which was consistent across the different groups evaluated. These substituent effects are generally explicable in terms of standard physical organic chemistry considerations of product ion stability as controlling fragmentation. A somewhat unexpected feature was the incidence of homolytic cleavages, driven by the stability of substituted amine radical cations. The findings of this study are intended to lay the groundwork for machine learning approaches to performing MS/MS spectrum → structure and structure → MS/MS spectrum operations on the same experimental data set. The effort involved and the success achieved in computer-aided interpretation, now underway, will be compared with the expert performance as described here.



KEYWORDS: tandem mass spectrometry, ambient ionization, fragmentation, ion chemistry, spectral interpretation

OL Organic Letters
pubs.acs.org/OrgLett
Letter

Accelerated Reactivity Mechanism and Interpretable Machine Learning Model of *N*-Sulfonylimines toward Fast Multicomponent Reactions

Krupal P. Jethava,‖ Jonathan Fine,‖ Yingqi Chen, Ahad Hossain, and Gaurav Chopra*

Cite This: Org. Lett. 2020, 22, 8480−8486 Read Online

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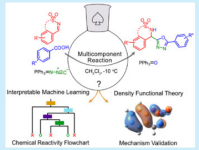
ABSTRACT: We introduce chemical reactivity flowcharts to help chemists interpret reaction outcomes using statistically robust machine learning models trained on a small number of reactions. We developed fast *N*-sulfonylimine multicomponent reactions for understanding reactivity and to generate training data. Accelerated reactivity mechanisms were investigated using density functional theory. Intuitive chemical features learned by the model accurately predicted heterogeneous reactivity of *N*-sulfonylimine with different carboxylic acids. Validation of the predictions shows that reaction outcome interpretation is useful for human chemists.



So far…

78 publications, > 1,475 citations, h factor = 20

Growing rapidly…

Check out our [Google Scholar page]

Analytical Methods
ROYAL SOCIETY OF CHEMISTRY
TECHNICAL NOTE
View Article Online
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Characterization of DNA aptamer–protein binding using fluorescence anisotropy assays in low-volume, high-efficiency plates†

Simon D. Weaver [a] and Rebecca J. Whelan [*b]

Aptamers have many useful attributes including specific binding to molecular targets. After aptamers are identified, their target binding must be characterized. Fluorescence anisotropy (FA) is one technique that can be used to characterize affinity and to optimize aptamer–target interactions. Efforts to make FA assays more efficient by reducing assay volume and time from mixing to measurement may save time and resources by minimizing consumption of costly reagents. Here, we use thrombin and two thrombin-binding aptamers as a model system to show that plate-based FA experiments can be performed in volumes as low as 2 μL per well with 20 minute incubations with minimal loss in assay precision. We demonstrate that the aptamer–thrombin interaction is best modelled with the Hill equation, indicating cooperative binding. The miniaturization of this assay has implications in drug development, as well as in the efficiency of aptamer selection workflows by allowing for higher throughput aptamer analysis.

Check for updates
Cite this: Anal. Methods, 2021, 13, 1302
Received 10th December 2020
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DOI: 10.1039/d0ay02256j
rsc.li/methods

THE JOURNAL OF PHYSICAL CHEMISTRY B
pubs.acs.org/JPCB
Article

Subset of Fluorophores Is Responsible for Radiation Brightening in Viromimetic Particles

Arathi Anil Sushma, Bingqing Zhao, Irina B. Tsvetkova, Carolina Pérez-Segura, Jodi A. Hadden-Perilla, James P. Reilly, and Bogdan Dragnea*

Cite This: J. Phys. Chem. B 2021, 125, 10494−10505 Read Online

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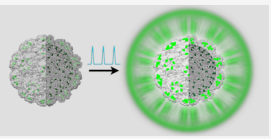
ABSTRACT: In certain conditions, dye-conjugated icosahedral virus shells exhibit suppression of concentration quenching. The recently observed radiation brightening at high fluorophore densities has been attributed to coherent emission, *i.e.*, to a cooperative process occurring within a subset of the virus-supported fluorophores. Until now, the distribution of fluorophores among potential conjugation sites and the nature of the active subset remained unknown. With the help of mass spectrometry and molecular dynamics simulations, we found which conjugation sites in the brome mosaic virus capsid are accessible to fluorophores. Reactive external surface lysines but also those at the lumenal interface where the coat protein N-termini are located showed virtually unrestricted access to dyes. The third type of labeled lysines was situated at the intercapsomeric interfaces. Through limited proteolysis of flexible N-termini, it was determined that dyes bound to them are unlikely to be involved in the radiation brightening effect. At the same time, specific labeling of genetically inserted cysteines on the exterior capsid surface alone did not lead to radiation brightening. The results suggest that lysines situated within the more rigid structural part of the coat protein provide the chemical environments conducive to radiation brightening, and we discuss some of the characteristics of these environments.



JACS
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Communication

Fluorescence-Detected Mid-Infrared Photothermal Microscopy

Minghe Li,‖ Aleksandr Razumtcev,‖ Ruochen Yang, Youlin Liu, Jiayue Rong, Andreas C. Geiger, Romain Blanchard, Christian Pflueg l, Lynne S. Taylor, and Garth J. Simpson*

Cite This: J. Am. Chem. Soc. 2021, 143, 10809−10815 Read Online

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ABSTRACT: We demonstrate instrumentation and methods to enable fluorescence-detected photothermal infrared (F-PTIR) microscopy and then demonstrate the utility of F-PTIR to characterize the composition within phase-separated domains of model amorphous solid dispersions (ASDs) induced by water sorption. In F-PTIR, temperature-dependent changes in fluorescence quantum efficiency are shown to sensitively report on highly localized absorption of mid-infrared radiation. The spatial resolution with which infrared spectroscopy can be performed is dictated by fluorescence microscopy, rather than the infrared wavelength. Intrinsic ultraviolet autofluorescence of tryptophan and protein microparticles enabled label-free F-PTIR microscopy. Following proof of concept F-PTIR demonstration on model systems of polyethylene glycol (PEG) and silica gel, F-PTIR enabled the characterization of chemical composition within inhomogeneous ritonavir/polyvinylpyrrolidone-vinyl acetate (PVPVA) amorphous dispersions. Phase separation is implicated in the observation of critical behaviors in ASD dissolution kinetics, with the results of F-PTIR supporting the formation of phase-separated drug-rich domains upon water sorption in spin-cast films.

Trends in Analytical Chemistry 140 (2021) 116241
Contents lists available at ScienceDirect
Trends in Analytical Chemistry
journal homepage: www.elsevier.com/locate/trac

Nonlinear optical characterization of pharmaceutical formulations

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ARTICLE INFO
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Available online 13 March 2021
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Active pharmaceutical ingredients
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Second harmonic generation
Stimulated Raman spectroscopy
Coherent anti-Stokes Raman spectroscopy
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Amorphous solid dispersions
Dissolution
Differential scanning calorimetry

ABSTRACT
Unique challenges in formulating the next generation of active pharmaceutical ingredients (APIs) into stable formulations demand analytical tools not currently available using common benchtop methods. Herein, we review approaches to address some of these challenges through leveraging nonlinear optical (NLO) interactions between light and matter. Applications in dissolution testing, polymorphism, and accelerated stability testing highlight the breadth of these methods. The specificity of second harmonic generation (SHG) to chiral crystals supports rapid polymorphism analysis at the limit of individual crystals and informs formulations designs to address solubility challenges common in emerging drug candidates. Coherent anti-Stokes Raman spectroscopy (CARS) and stimulated Raman spectroscopy (SRS) provide vibration-specific microscopy of final dosage forms to inform composition at video-rate acquisition speeds and ~1 μm spatial resolution. Recent results are reviewed to illustrate challenges in designing formulations for emerging drug candidates and opportunities for the development of NLO tools tailored to meet them.

January

- New projects begin with participation by PI, student(s), industry members, and a Principal Industry Mentor and monthly project team meetings

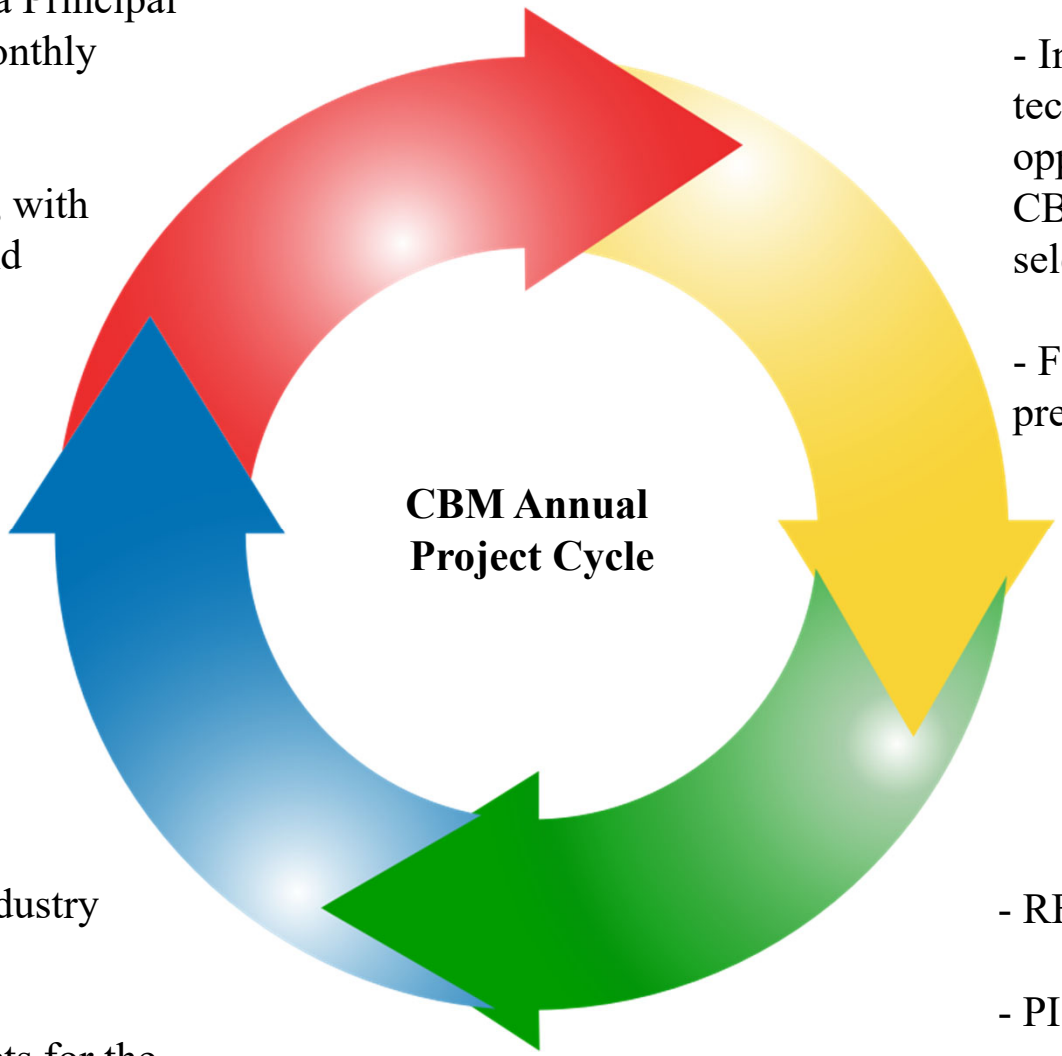
- Old projects conclude, with external publications and presentations

April

- Spring Meeting of the Industry Advisory Board

- Industry members identify technical gaps, needs and opportunities for next round of CBM projects -RFP topics selected

- Final project reports from previous year projects



November

- Fall Meeting of the Industry Advisory Board

- Funding of new projects for the coming year

July

- RFP sent to faculty

- PIs prepare and submit proposals

- Summer ‘supergroup’ meetings to foster intergroup collaboration

Student Recruiting & Training Opportunities

CBM Career Opportunity Showcase

- Industry members speak with current students and postdocs, profiling their company and describing job opportunities and career paths.
- Profiles and presentations from current employees highlighting different career paths
- Q&A with the students to address questions and concerns

CBM Mentorship Circles

- Mentors from different CBM member companies meet with graduate students and postdocs to discuss career choices, job search, resume building, soft skills and other career-related topics of interest to the mentees

Increasing the Value of Academic Collaboration

- ***FAST!*** - Projects executed swiftly under an umbrella membership agreement

- ***No Administrative Costs*** – Administrative costs for the center are paid by NSF. Membership fees go directly to project support.

- ***No Overhead Fees*** – Projects funded within the center are not charged overhead – roughly doubling 'buying power'

- ***Cost Sharing*** – Joint funding of projects with like-minded industry members stretches dollars.

- ***Recruiting***– Get to know potential new employees as you work together with them over the course of the project

- ***Targeted Funding*** – Address your organization's key emerging problems/opportunities

CBM
Center for Bioanalytic Metrology

Win - Win

CBM Center for Bioanalytic Metrology

Industry
- problem solving
- networking with faculty & peers
- pipeline to new hires
- continuous learning

Students
- jobs
- insights on industry
- understanding impact of research

Faculty
- understanding current needs
- jobs for students
- access to materials/workflows

Science
- improved measurement tools and techniques
- Efficient solutions by matching problems with solution providers
- sharing resources and information for more effective problem solving

Regular Membership
- $60k per calendar year
- Contact Chris Welch at cwelch6@nd.edu