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Questions

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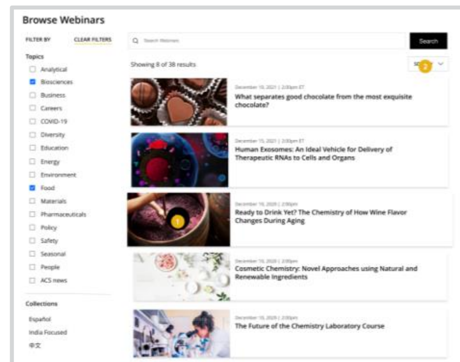

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A Career Planning Tool For Chemical Scientists

ACS Chemistry for Life®

ChemIDP is an Individual Development Plan designed specifically for graduate students and postdoctoral scholars in the chemical sciences. Through immersive, self-paced activities, users explore potential careers, determine specific skills needed for success, and develop plans to achieve professional goals. **ChemIDP** tracks user progress and input, providing tips and strategies to complete goals and guide career exploration.

https://chemidp.acs.org

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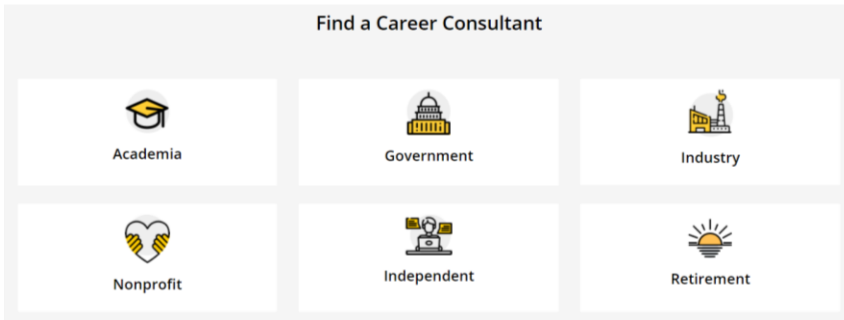
Career Consultant Directory



- ACS Member-exclusive program that allows you to arrange a one-on-one appointment with a certified ACS Career Consultant.
- Consultants provide personalized career advice to ACS Members.
- Browse our Career Consultant roster and request your one-on-one appointment today!

www.acs.org/careerconsulting

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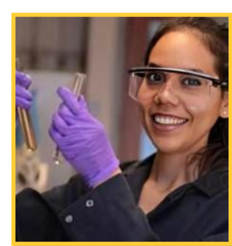
ACS Bridge Program

Are you thinking of Grad School?

If you are a student from a group underrepresented in the chemical sciences, we want to empower you to get your graduate degree!

The ACS Bridge Program offers:

- **A FREE common application that will highlight your achievements to participating Bridge Departments**
- **Resources to help write competitive grad school applications and connect you with mentors, students, and industry partners!**



Learn more and apply at www.acs.org/bridge

Email us at bridge@acs.org

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ACS Scholar Adunoluwa Obisesan

BS, Massachusetts Institute of Technology, June 2021
(Chemical-biological Engineering, Computer Science & Molecular Biology)

"The ACS Scholars Program provided me with monetary support as well as a valuable network of peers and mentors who have transformed my life and will help me in my future endeavors. The program enabled me to achieve more than I could have ever dreamed. Thank you so much!"

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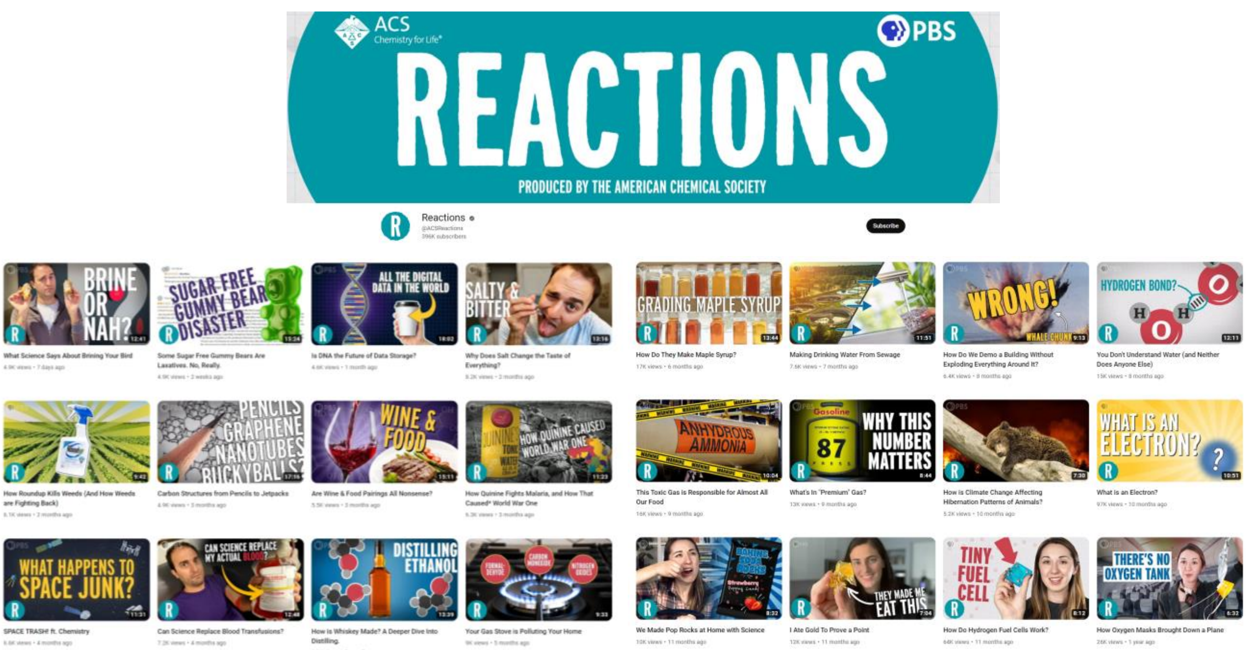

https://www.youtube.com/c/ACSReactions/videos

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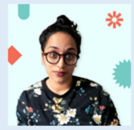
Looking for a new science podcast to listen to?

TINY MATTERS

Check out Tiny Matters, from the **American Chemical Society.**

Sam Jones, PhD
Science Writer & Exec Producer



Deboki Chakravarti, PhD
Science Writer & Co-Host

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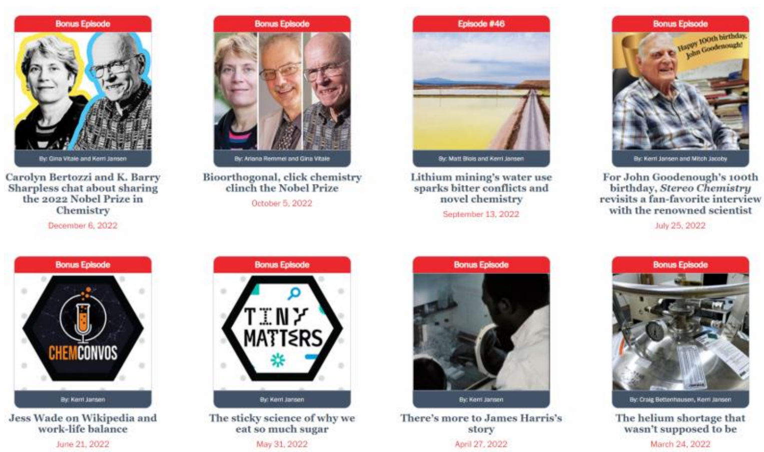
c&en's STEREO CHEMISTRY



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ACS Industry Member Programs

- **ACS Industry Matters**

  ACS member only content with exclusive insights from industry leaders to help you succeed in your career. #ACSIndustryMatters

  Preview Content: acs.org/indnl

- **ACS Innovation Hub LinkedIn Group**

  Connect, collaborate and stay informed about the trends leading chemical innovation.

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ACS on Campus is the American Chemical Society's initiative dedicated to helping students advance their education and careers.

ACS ON CAMPUS

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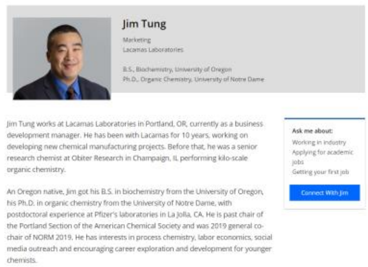
ACS Career Resources

ACS Chemistry for Life®

Virtual Office Hours	Personal Career Consultations	LinkedIn Learning
		
https://www.acs.org/careerconsulting.html	https://www.acs.org/careerconsulting.html	https://www.acs.org/linkedInlearning

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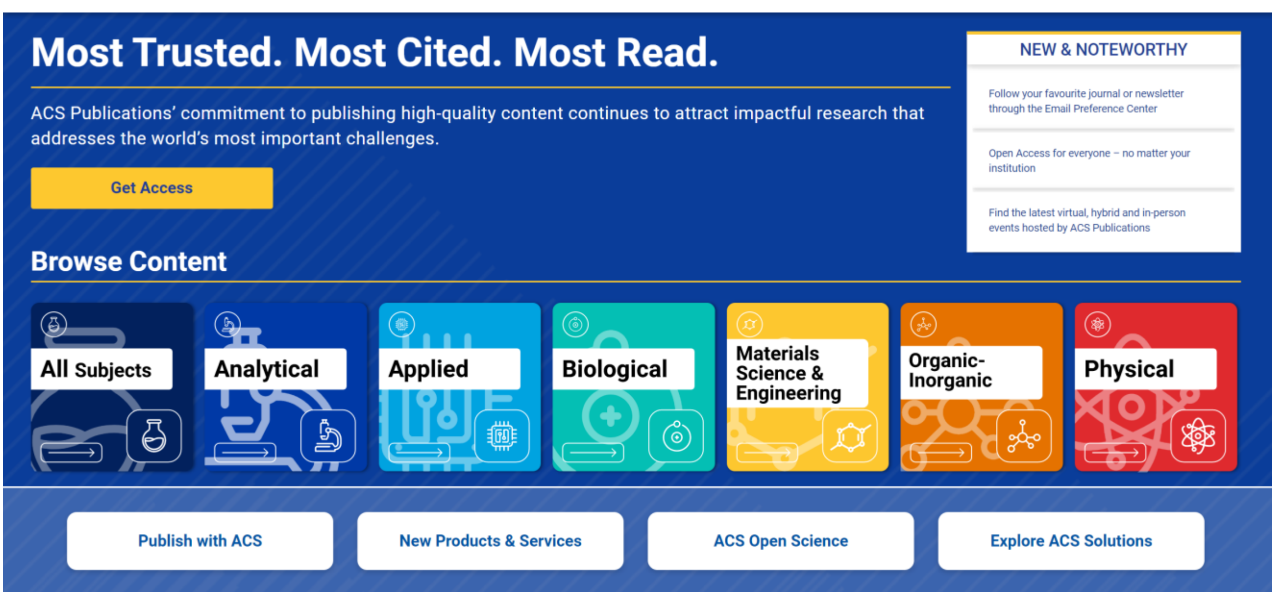
ACS Publications
Most Trusted. Most Cited. Most Read.



https://pubs.acs.org

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ACS Advocacy

See your influence in action!

ACS Chemistry for Life®

The impact and results of **ACS member advocacy** outreach and efforts by the numbers!

2439+	1739+	49	2000
Members participated In Act4Chemistry	ACS Advocacy Workshops participants or enrollees	Years of Public Policy Fellows	Letters sent to Congress
Get Involved	Enroll in a workshop	Become a Fellow	Take Action

American Chemical Society https://www.acs.org/policy 17

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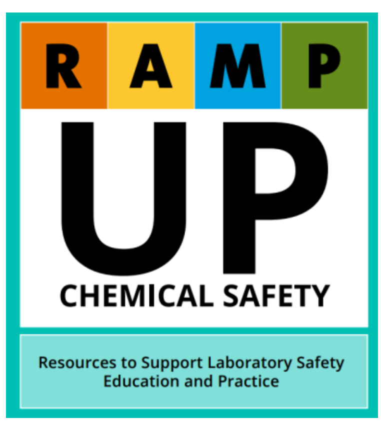
ACS Technical Division Chemical Health & Safety (CHAS)

ACS Committee Chemical Safety

A complete listing of ACS Safety Programs and Resources



Download it for free in the “Projects & Announcements” Section! www.acs.org/ccs

ACS Chemistry for Life® ACS Institute Learn. Develop. Excel. Lab Safety American Chemical Society 18

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ACS OFFICE OF DEIR

Advancing ACS' Core Value of Diversity, Equity, Inclusion and Respect

Resources

Inclusivity Style Guide
Designed to help staff and members use language and images that respect diversity in all its forms.

ACS Webinars on Diversity
Covering diversity and inclusion at the workplace

ACS Publications DEIR Hub
See what ACS Publications is doing for fostering inclusivity in scholarly publishing

ACS Volunteer and ACS Meetings Code of Conduct
Fostering a positive and welcoming environment for attendees, volunteers and staff.

C&EN Trailblazers
C&EN highlights scientists from different backgrounds who are making an impact in chemistry.

NEW! Download DEIR Educational Resources
Download this educational guide for additional recommendations on videos, articles, books, podcasts, and more on diversity, inclusion, and related topics.

Quick Guide: Inclusion Moments
Learn more about what Inclusion Moments are and see ideas to host them during your meetings.

Quick Guide: How to host inclusive in-person events
Recommendations and best practices to ensure that your events can accommodate everyone.

Diversity, Equity, Inclusion, and Respect
**Adapted from definitions from the Ford Foundation Center for Social Justice:

Equity**
Seeks to ensure fair treatment, equality of opportunity, and fairness in access to information and resources for all. We believe this is only possible in an environment built on respect and dignity. Equity requires the identification and elimination of barriers that have prevented the full participation of some groups.

Diversity**
The representation of varied identities and differences (race, ethnicity, gender, disability, sexual orientation, gender identity, national origin, tribe, caste, socio-economic status, thinking and communication styles, etc.), collectively and as individuals. ACS seeks to proactively engage, understand, and draw on a variety of perspectives.

Inclusion**
Builds a culture of belonging by actively inviting the contribution and participation of all people. Every person's voice adds value, and ACS strives to create balance in the face of power differences. In addition, no one person can or should be called upon to represent an entire community.

Respect
Ensures that each person is treated with professionalism, integrity, and ethics underpinning all interpersonal interactions.

https://www.acs.org/diversity

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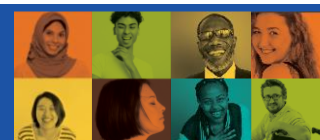
www.acs.org/membership



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Introductory set of complimentary benefits.

$0	Community Associate

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ACS Webinars

Thursday, March 7, 2024| 2-3pm ET

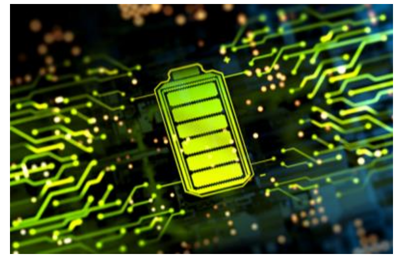
The Art of Self-Reinvention

Co-produced with the ACS Women Chemists Committee

Wednesday, March 13, 2024| 11am-12:30pm ET

Fungal Foes: Understanding the Challenges and Exploring New Treatment Options

Co-produced with the ACS Publications



Thursday, March 14, 2024| 1pm-2:15pm ET

Powering the Future: The Latest Battery Technologies

Co-produced with the Science History Institute

Register for Free

Browse the Upcoming Schedule at www.acs.org/acswebinars

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Say hello in the questions window!

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Sustainable Biomanufacturing at Scale:
Fermentation of Animal-Free Dairy Proteins

SUNIL SUKUMARAN, PhD
Chief Technology Officer, Perfect Day Inc.

LAURA MCCONNELL, PhD
Science Fellow, Regulatory Scientific Affairs, Bayer and Deputy Editor, ACS Agricultural Science and Technology

This ACS Webinar® is co-produced with the ACS Committee on Science.

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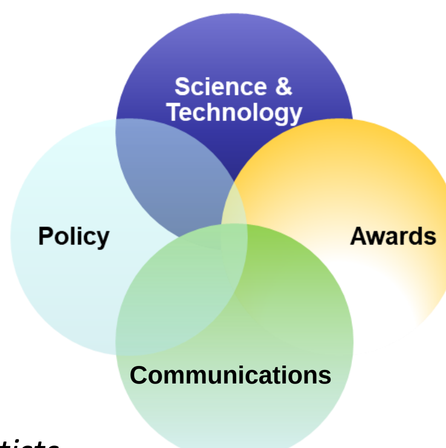
ACS Committee on Science (COMSCI)

ACS Chemistry for Life®

Mission:

- *Identify and promote new frontiers of chemistry*
- *Examine scientific basis & formulate public policies related to chemical sciences*
- *Recognize outstanding chemical scientists*



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Webinars

January 2024

Frontier Fridays: Sorbent-based Direct Air Capture of CO_2 at Scale

Watch Now →

Symposia at Fall ACS Meeting

Scaling New Heights of Chemistry Education with Artificial Intelligence Tools
Organized by: Robert Pribush, Judith Benham, Tom Holme, Mary Carroll

Elevating Atmospheric Chemistry Measurements and Modeling with Artificial Intelligence
Organized by: Carl Picconatto, Jeff Arnold, and Mary Carroll

Policy Statements

- ✓ Energy
- ✓ Sustainability
- ✓ Hydraulic Fracturing
- ✓ Forensic Science

Awards

- National Medal of Science
- National Medal of Technology and Innovation
- Dreyfus Award in the Chemical Sciences

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Sustainable Biomanufacturing at Scale: Fermentation of Animal-Free Dairy Proteins

PERFECT DAY

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THE FUTURE IS BRIGHT
Perfect Day is working tirelessly towards our kinder, greener mission, and we’ve already passed key milestones in our journey
PERFECT DAY, INC · CONFIDENTIAL

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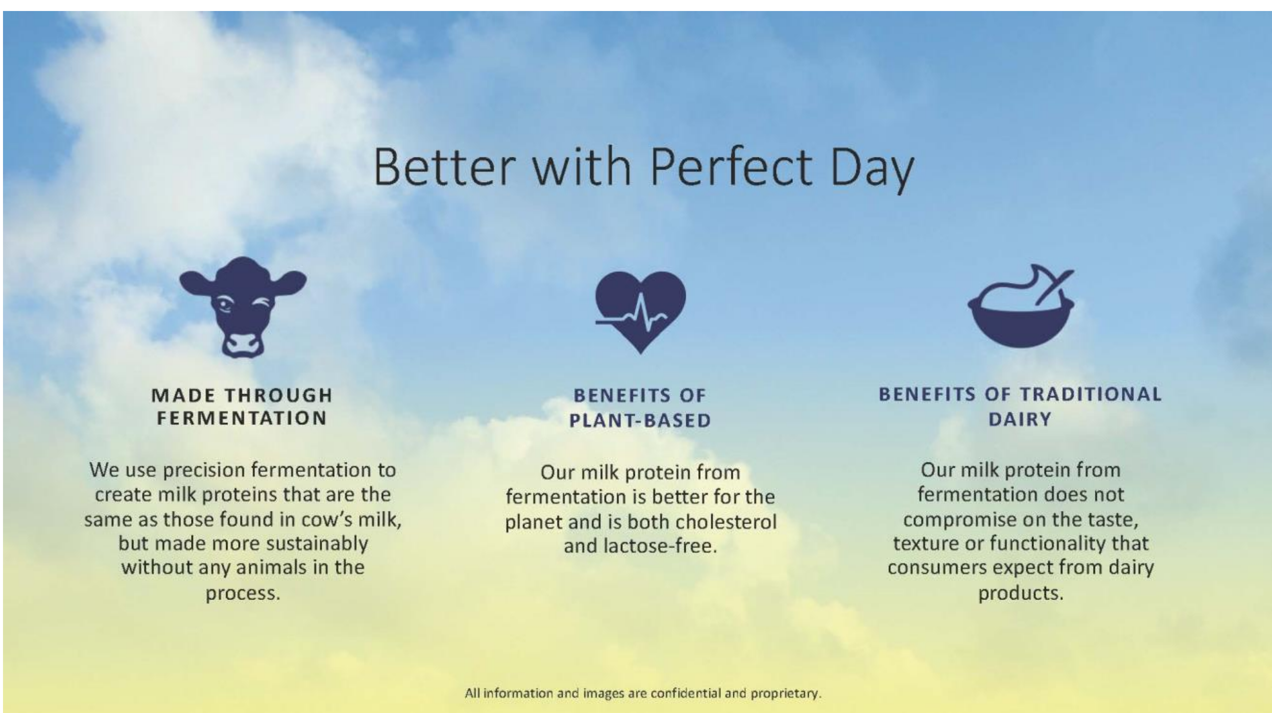
Better with Perfect Day
MADE THROUGH FERMENTATION
We use precision fermentation to create milk proteins that are the same as those found in cow’s milk, but made more sustainably without any animals in the process.
BENEFITS OF PLANT-BASED
Our milk protein from fermentation is better for the planet and is both cholesterol and lactose-free.
BENEFITS OF TRADITIONAL DAIRY
Our milk protein from fermentation does not compromise on the taste, texture or functionality that consumers expect from dairy products.
All information and images are confidential and proprietary.

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MICROFLORA
Like stories from books, genes can be digitized. We introduce a digital copy of the genetic sequence behind bovine whey protein production to our microflora, giving this tiny organism this ability to produce pure protein. No animal inputs are needed for this process.

MEDIA
We feed our microflora raw materials essential for growth (e.g., sugars, vitamins, minerals).

FERMENTATION
Now, our flora can use fermentation to convert plant sugars into milk proteins that are nutritionally equivalent to those that come from cows.

FILTRATION & SPRAY DRYING
The protein is separated from the flora and dried into a powder.

PURE PROTEIN POWDER
The result is a pure protein powder, free of flora, that fits seamlessly into product applications.

NO-COMPROMISE PRODUCTS
Because it's the same protein food makers are already familiar with, it can be used to make all kinds of delicious, dairy products from fermentation.

29

Our Impact

An ISO-conformant, third-party reviewed life cycle assessment of our process found that if just 5% of the dairy products on US shelves today used our animal-free protein, in a year we'd save:

Enough water to **fill 1.4 million Olympic swimming pools**, thanks to an up to 99% reduction in water use*

Equivalent to the **emissions from 140K round trip flights between SFO & JFK**, thanks to an up to 97% reduction in GHG emissions*

Enough energy to **power Washington D.C. for 6 years**, **thanks to an up to 60% reduction in energy consumption***

*Compared to whey protein found in traditional milk. Data from ISO-certified, third-party-validated report.

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We're bringing higher quality, sustainable protein to the category.

Protein Source	BCAA (g/100g powder)	Function	Animal Free	Lactose Free	Soy Free	GHG Emissions (per 100g protein)
Dairy (WPI)	20	★★★	✗	✗	✓	9.50
Pea	11	★☆☆	✓	✓	✓	0.44
Oat	7	★★☆	✓	✓	✓	2.70
Almond	N/A	★☆☆	✓	✓	✓	0.26
Soy	9	★★☆	✓	✓	✗	1.98
Perfect Day	23	★★★	✓	✓	✓	**0.29**

Acronyms: WPI (whey protein isolate), BCAA (branched-chain amino acids), GHG (greenhouse gas)

Sources:
1. BCAA (g/100g powder): Gorissen et al., 2008, "Protein content and amino acid composition of commercially available plant-based protein isolates", https://doi.org/10.1007%2Fs00726-018-2640-5
2. GHG Emissions per 100g Protein (Poore & Nemecek, 2018); "Plant Proteins: Assessing Their Nutritional Quality and Effects on Health and Physical Function," Hertzler, Lieblein-Boff, Weiler, Allgeier; Gras Notice for Partilly Defatted Almond Protein Flour, Blue Diamond.

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The below brands, and many more, are now in over 5K grocery stores around the globe

BEL GROUP
Cream Cheese

NICK'S
Ice Cream

BORED COW
Milk

MYPROTEIN
Sports Nutrition

GRAETER'S
Ice Cream

RENEWAL MILL
Bakery Mix

STRIVE
Milk

Natreve
Sports Nutrition

Partners in Testing

Nestlé

NESTLE
~~Milk~~

STARBUCKS
Barista Milk + Ice Cream

MARS
Chocolate

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Global Footprint

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The State of Our Industry

Opportunities	Challenges
High consumer demand for sustainable products	Scale required to meet demand outpacing available infrastructure
Global market for products and cross-border appeal	Geographic expansion requires varied regulatory approval processes
Government interest is high and potential funding available	Requires proactive policy engagement by existing leaders
Path to price parity is proven and achievable	Largely price intolerant during period of scale-up
Common sustainability goal drives deep collaboration	Requires pushback against narrative of disruption as success

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Growing Consumer Demand

Research shows **90 million consumers** will be interested in precision fermentation food and beverages when they understand its benefits

	Ready		Easily convinced		Convinced with benefits		Unconvinced		Currently out of reach		Total across groups in each age cohort
Gen Z (18-25)	14%	4,440,553	19%	6,379,001	14%	4,439,579	39%	12,625,547	15%	4,896,658	100%
Millennials (26-41)	27%	18,911,267	15%	10,050,526	13%	8,887,815	27%	18,672,987	18%	12,331,595	100%
Gen X (42-57)	16%	10,074,889	8%	4,830,936	14%	9,015,227	37%	23,099,536	25%	15,697,681	100%
Boomers (58-73)	3%	1,899,418	6%	3,698,010	14%	7,919,066	45%	25,960,005	32%	18,299,525	100%
Total in each segment	**35,326,127**		**24,958,473**		**30,261,687**		**80,358,074**		**51,225,459**		

Total addressable market today

90,546,287 willing to buy TODAY

Data from The Hartman Group for Perfect Day & Cargill

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We've built our business to meet demand and scale our impact through partnerships…

PERFECT DAY & nthBio by PERFECT DAY

Enable Impact

Our B2B ingredients business partners with companies big and small who want to use our protein as a no-compromise ingredient, allowing us to green and transform existing supply chains by working with some of the largest, and most mission-aligned, food companies in the world.

Accelerate Impact

*n*th Bio offers our expertise and technology services—from the earliest stages of molecular development to commercial-scale manufacturing, and the many steps in-between— to companies who share our mission, empowering them to extend the impact of precision fermentation into new areas of the food system and beyond

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…and address the challenges & technology gaps the industry continues to face.

Volumes & scale-up
DSP
Global regulatory frameworks

Linear development
Lost agility - IP ownership
Limited capacity & capability
Lack of SME integration

Capital intensity & price
Breadth of expression systems
Screening tool requirements

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ZOOMING IN

nthBio™

BY PERFECT DAY

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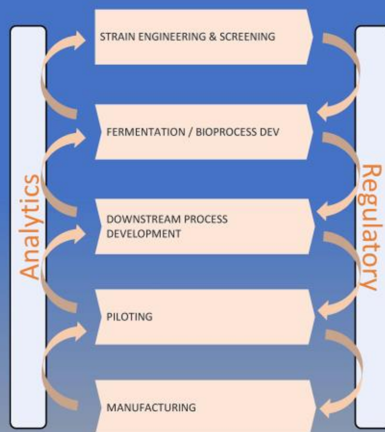
OUR END-TO-END SOLUTION



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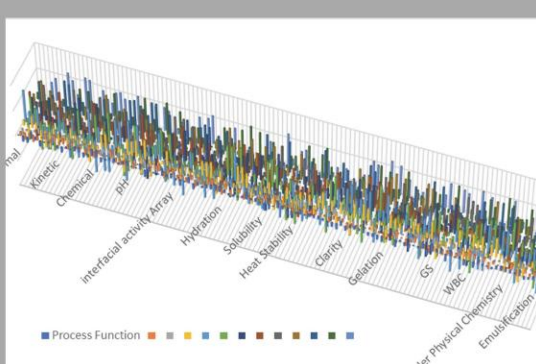
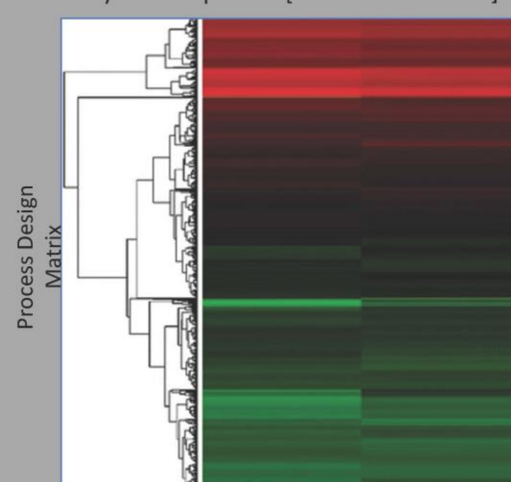
Our Protein

Evaluating Physical Properties vs. Process



We measure well over 400 physical properties for changes relative to WPI, or other control metrics, in response to changes in process [Host, Design, Media, Fermentation PD, Separations, Food Formulations, Application, Site-Specific-Metrics…]

Physical Properties [Relative to control]



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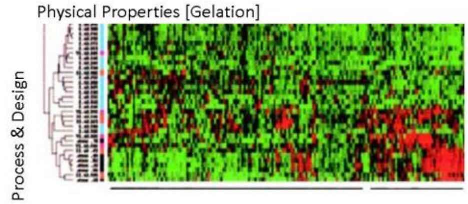
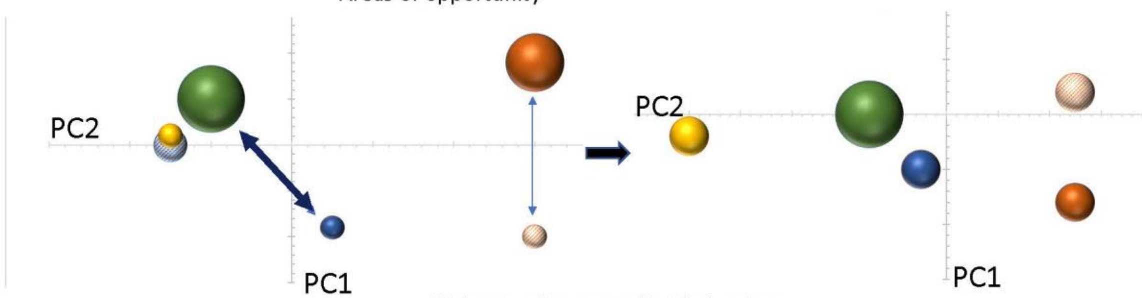
Identifying the Process Functions that matter for Quality and Regulatory Specification





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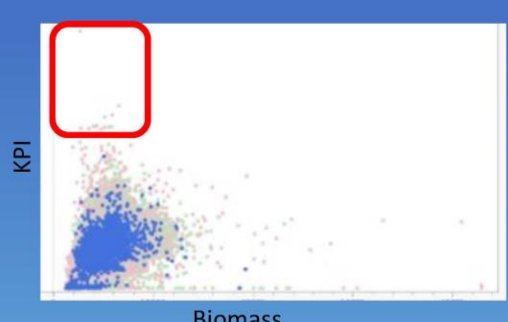
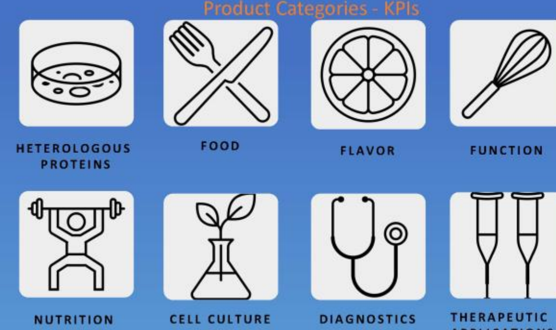
NthBio Platform - uHTS Screening

Screening Improvements	Strain Backgrounds	Diversity Inputs
KPI – Productivity/Titer Product & Strain Stability New Product Feasibility Quality/PTM modifications Scalability Production Strain Banking	Filamentous Fungi (Many) Yeast (some) Bacteria (Some)	Targeted Product Libraries Targeted GOF Libraries Mutagenesis – whole org and targeted Evolution Selections



Product Categories - KPIs



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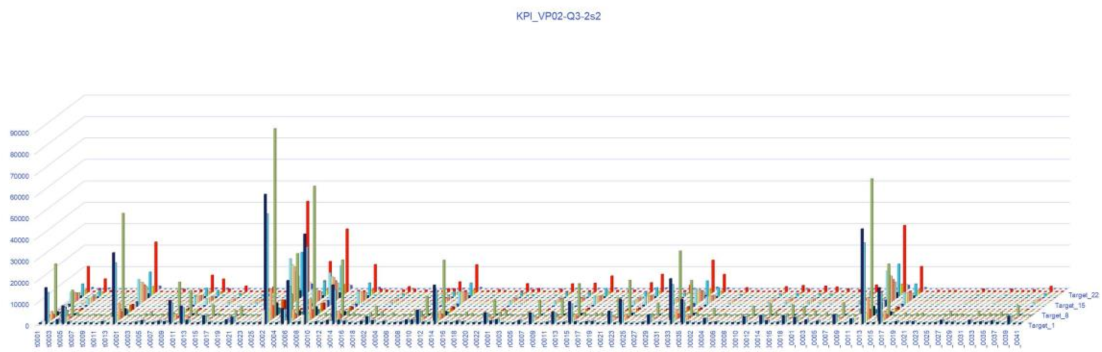
Analysis of Hits



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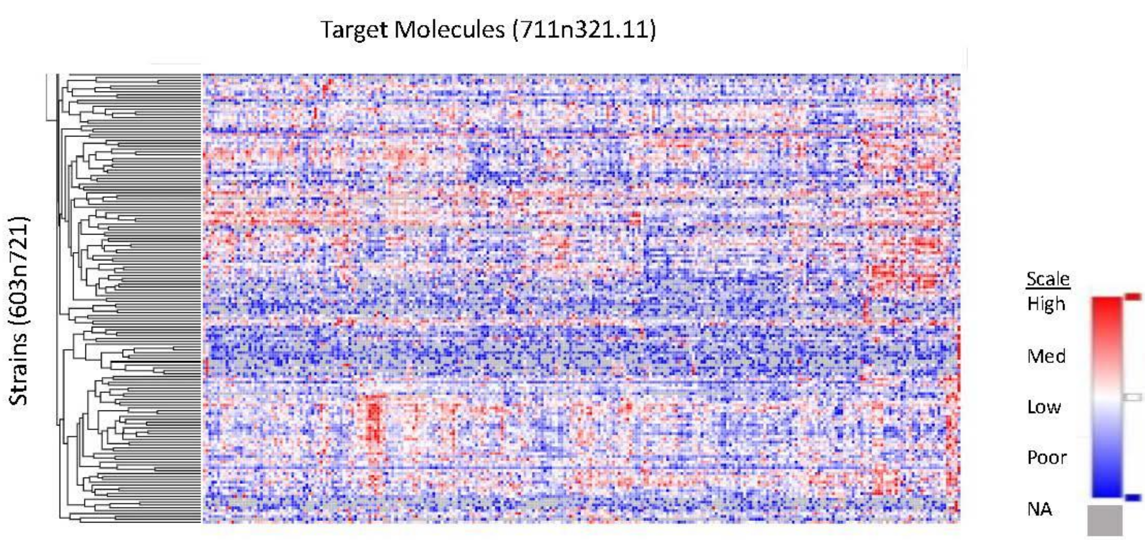
Large Scale Analysis - Strains vs. Product Expression



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Improving recombinant protein production through genome-scale metabolic modeling (GSMM)

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WHAT IS FLUX???

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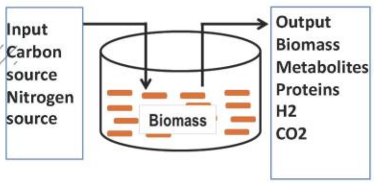
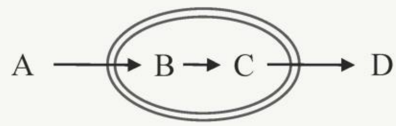
Why should we carry out metabolic flux analysis

- To quantify the carbon flux distribution
- To understand the complex interplay between energy metabolism, carbon fixation, and assimilation pathways
- Connects genomics with metabolism

Flux balance analysis



Theory: Pseudo steady state Approximation



$$\frac{dB}{dt} = 0$$

$$\frac{dC}{dt} = 0$$

$$\frac{dA}{dt} = -ve$$

$$\frac{dD}{dt} = +ve$$

$$v = flux\ (rate\ of\ reaction) = \frac{mmole\ of\ substrate\ consumed\ or\ Product\ formed}{g\ biomass * hour}$$

 3

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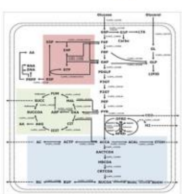


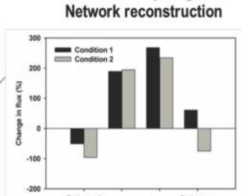
Clostridium sporogenes
Network reconstruction

$$\begin{bmatrix} S_{1,1} & \cdots & S_{1,n} \\ \vdots & \vdots & \vdots \\ S_{m,1} & \cdots & S_{m,n} \end{bmatrix} \begin{bmatrix} v_1 \\ \vdots \\ v_n \end{bmatrix} = \begin{bmatrix} \frac{dM_1}{dt} \\ \vdots \\ \frac{dM_m}{dt} \end{bmatrix}$$

$$S \cdot v = 0$$

Mathematical representation of network : Mass balance equations

Experimentation under different substrate combinations



Up and down regulation of pathway

Defining the measurable fluxes and constrains

$$v_{e1} = k_1 \qquad lb_1 \le v_1 \le ub_1$$
$$v_{e2} = k_2 \qquad lb_2 \le v_2 \le ub_2$$
$$\vdots \qquad \qquad \vdots$$
$$v_{ex} = k_x \qquad lb_n \le v_n \le ub_n$$

Optimization

Objective function
= max $V_{biomass/butanol}$

Small scale metabolic network

- Understanding of substrate dependant product modulation
- Simulation of Phenotypic Traits Depends on the Medium Conditions
- Prediction of targets for high alcohol titers

No. of Reactions	152
No. of Metabolites	206

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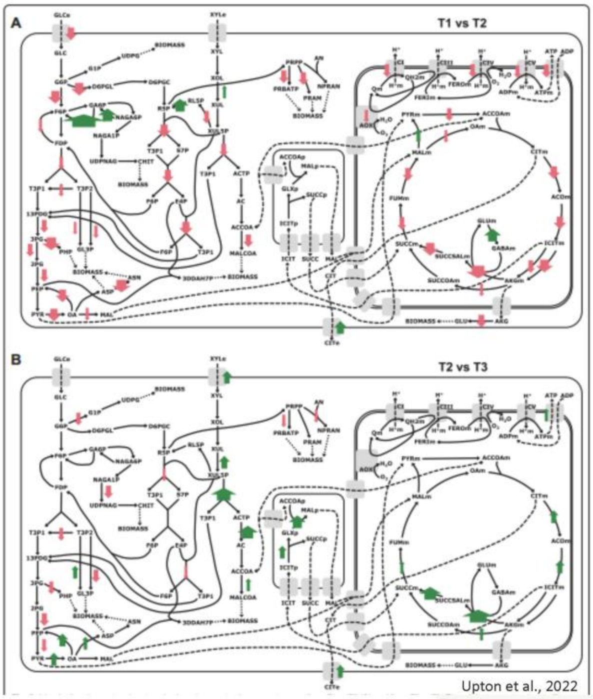

Integration of *A. niger* transcriptomic profile with metabolic model identifies potential targets to optimise citric acid production from lignocellulosic hydrolysate

Prediction of targets for higher citric acid titers

T1: Glucose consumption phase before the onset of citric acid production and phosphate-limited growth.

T2: Glucose consumption phase , citric acid producing, phosphate-limited growth.

T3: Xylose consumption phase after glucose was fully consumed. Citric acid producing and phosphate-limited growth.

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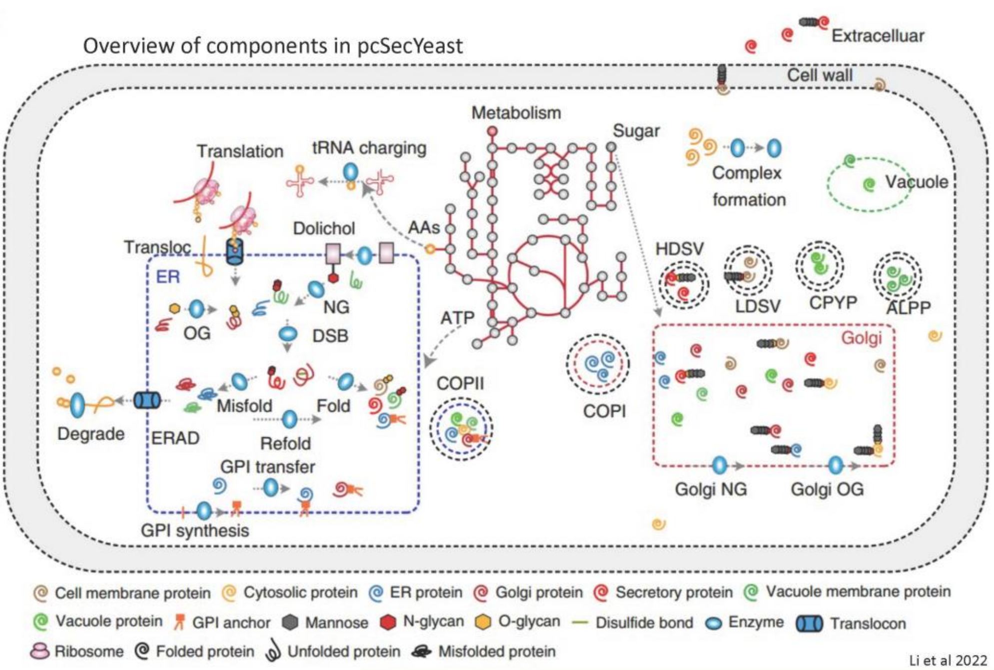
pcSecYeast : Simulate and explain phenotypes caused by limited secretory capacity



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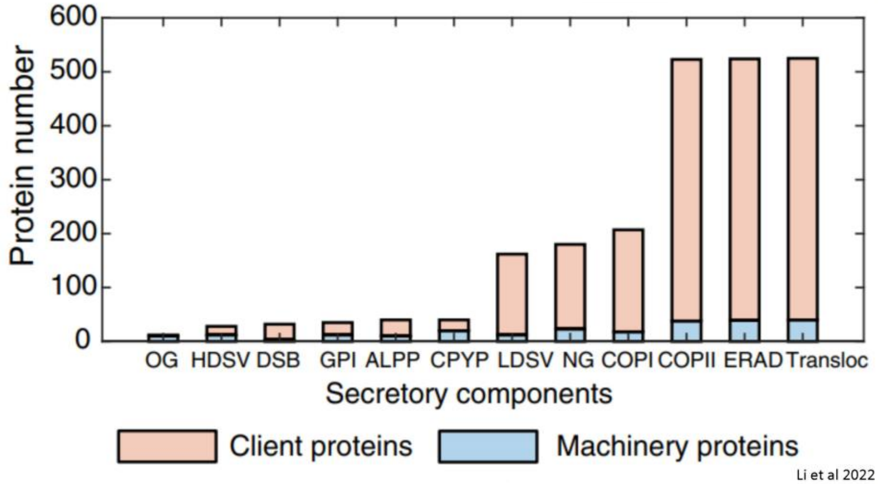
Subsystems in the secretory pathway and the protein number in each subsystem



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1. OG : O-glycosylation
2. HDSV : high-density secretory vesicles
3. DSB : disulfide bond formation
4. GPI : glycosylphosphatidylinositol
5. ALPP: alkaline phosphatase pathway
6. CPYP: carboxypeptidase Y pathway
7. LDSV: low-density secretory vesicles
8. NG: N-glycosylation
9. COPI: Coat Protein Complex I
10. COPII: Coat Protein Complex II
11. ERAD: ER-associated degradation
12. Transloc: translocation

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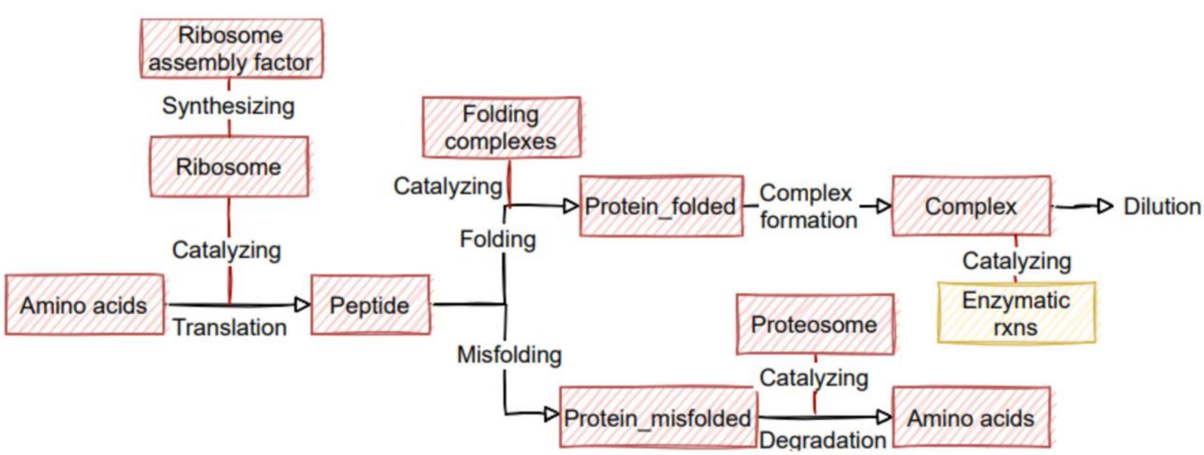
Flowchart of the protein related process in the pcSecYeast.



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GEM Yeast8

- ✓ Reactions for production of post-translational modification precursors
- ✓ Reactions catalyzed by isozymes were also split into multiple identical reactions with various isozymes. This step was performed to facilitate later kcat match and enzyme constraining step
- ✓ Translation initiation, elongation, and termination reactions added for each protein (total 1639)
- ✓ Protein translocation pathways added : co-translational translocation, post-translational translocation, and post-translational translocation-tail-targeting

Co-translational translocation
1. signal peptide recognition
2. ER receptor biding to peptide-SRPC
3. binding of peptide -SRPC-SRC to the translocator (Sec61C)
4. binding of peptide -SRPC-SRC to the translocator (Ssh1C)
5. signal peptidase
6. export the signal peptide out of ER for degradation

Post-translational translocation
1. exit the ribosome
2. bind to the cytosolic chaperone
3. Translocation
4. pulling of nascent protein

*The coefficient of ATP in step 4 was set as length/40, since the ATP molecule bound to the chaperone Kar2, is assumed to be hydrolyzed to ADP for every 40 amino acids that pass through the translocon pore

Post-translational translocation-tail targeting
1. load the TA proteins
2. bind to Get3
3. bind to ER receptor

Reactions for complex formation for enzymes used in either of these pathways are added to the model.

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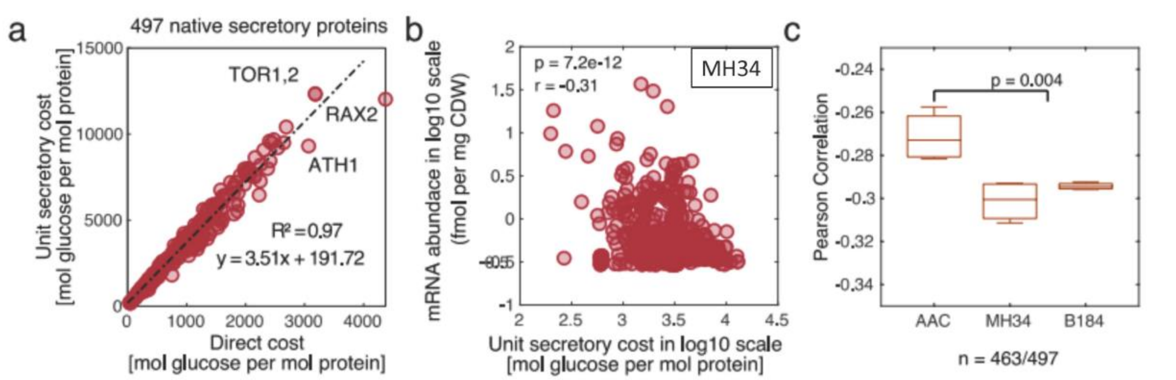
Direct cost vs unit secretory cost



Direct cost : Includes the energetic cost for synthesis, modification and secretion of this protein
Unit secretory cost : Direct cost + cost for the corresponding increased fraction of the catalytic machineries in these processes caused by the increase of this protein

Total no of proteins : 1639
Metabolic proteins : 1156
Secretory proteins : 483

$$\text{Secretory cost}_i = \text{unit secretory cost}_i \cdot [E_i] = \text{unit secretory cost}_i \cdot \frac{V_{\text{glc,total}}}{k_{\text{cat},i} \cdot \frac{[S]}{[S]+K_{M,i}}}$$

AAC: low yield α-amylase strain
MH34 and B184: high yield α-amylase strain

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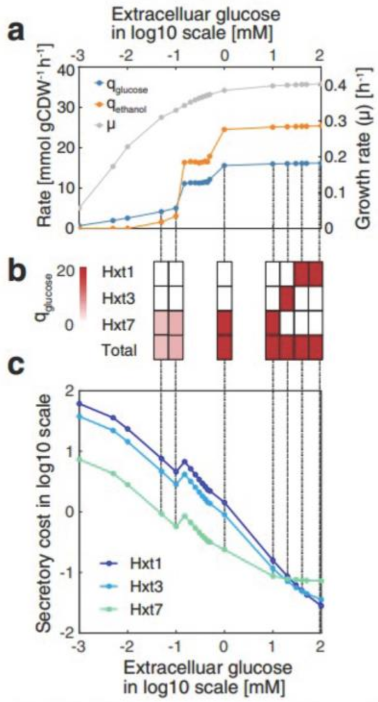

Simulated physiological response of *S. cerevisiae* as a function of the extracellular glucose concentration

Hxt 1 and Hxt 3: Low affinity transporters : Low unit secretory cost

Hxt 7: High affinity transporters : High unit secretory cost

Glucose limitation phase
Hxt 7

High Glucose concentration
Hxt 1 and Hxt 3

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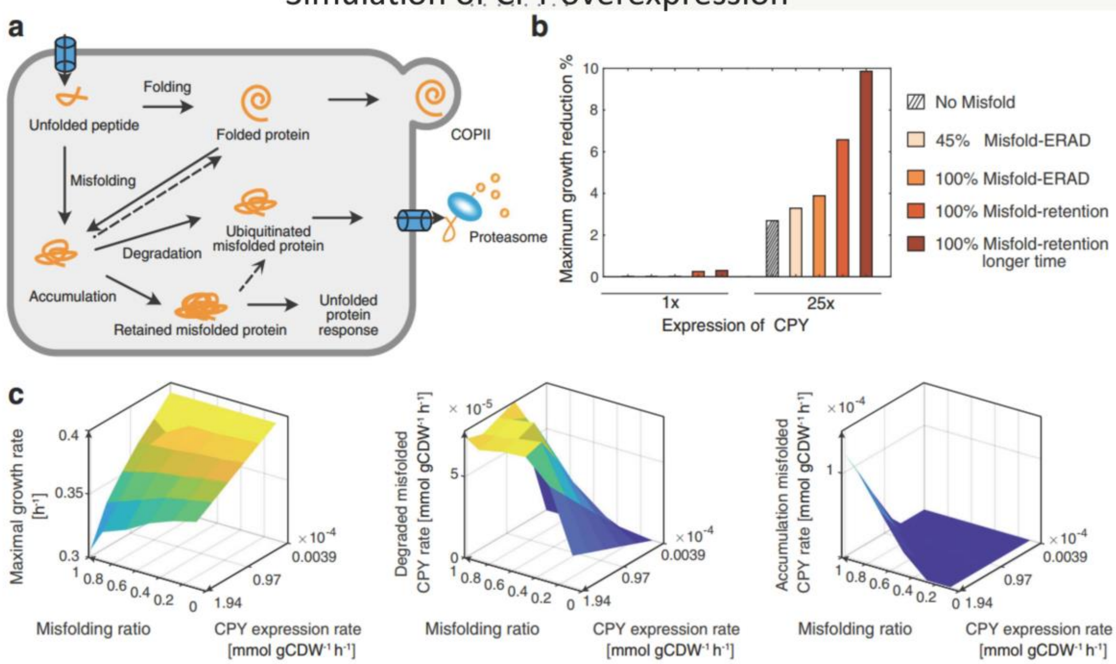
Simulation of CPY overexpression



Simulations for various CPY expression levels and misfolding ratios with the constraint for retro-translocation enzymes

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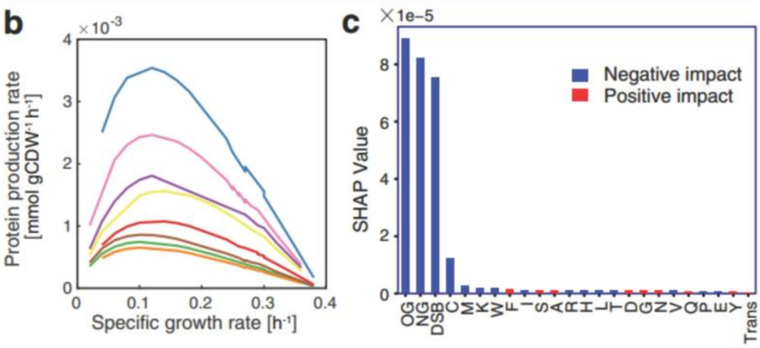
Protein	abbr.	DSB	NG	OG	GPI	Length
Insulin precursor	IP	3	0	0	0	53
Human granulocyte colony stimulating factor	hGCSF	2	0	1	0	174
Hemoglobin	Hemoglobin	0	0	0	0	299
β-glucosidase	BGL	0	0	0	0	421
α-amylase	α-amylase	4	1	0	0	478
Acid phosphatase	PHO	8	9	0	0	435
Human serum albumin	HSA	17	1	0	0	585
Human transferin	HTF	19	0	1	0	679



Overview of protein features for eight recombinant proteins produced by *S. cerevisiae*

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Need of the hour ?

- Scale down models ?
- In-depth appreciation of stage specific Physiology
- A relevant mathematical model with relevant constraints put in place
- Alternate feed-stock
- Recycling resources

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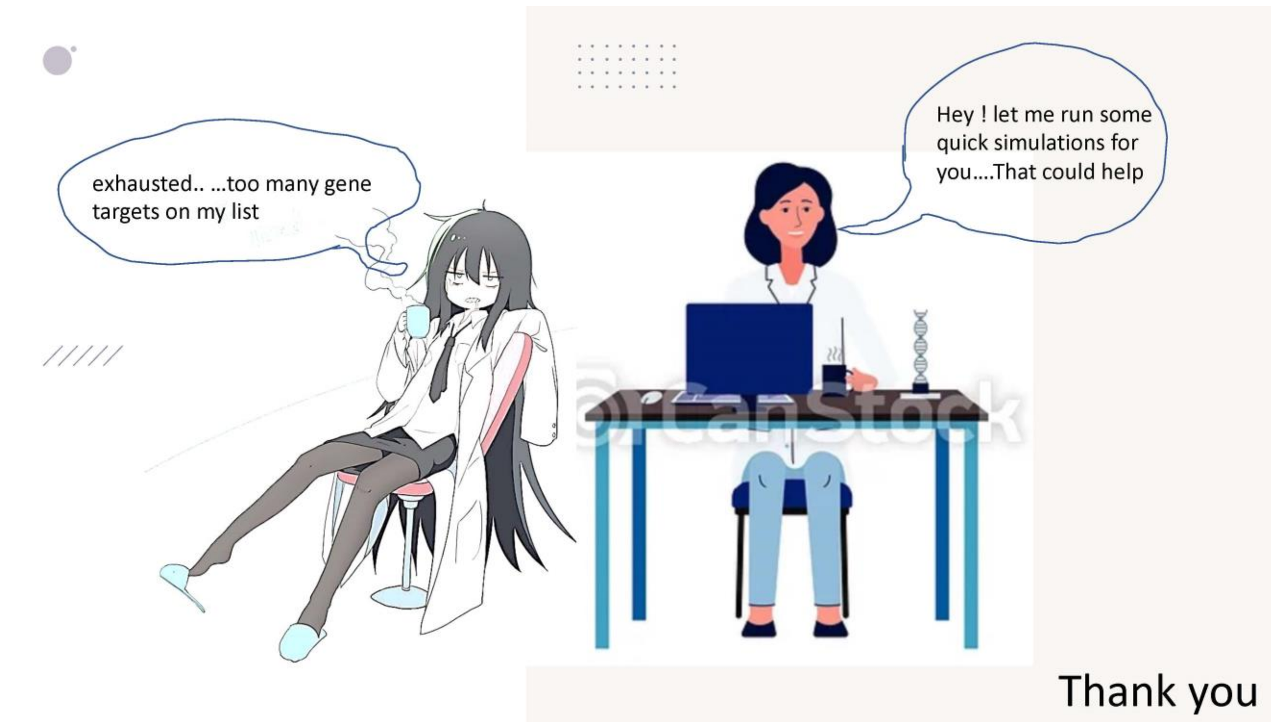
exhausted.. ...too many gene targets on my list
Hey ! let me run some quick simulations for you....That could help
Thank you

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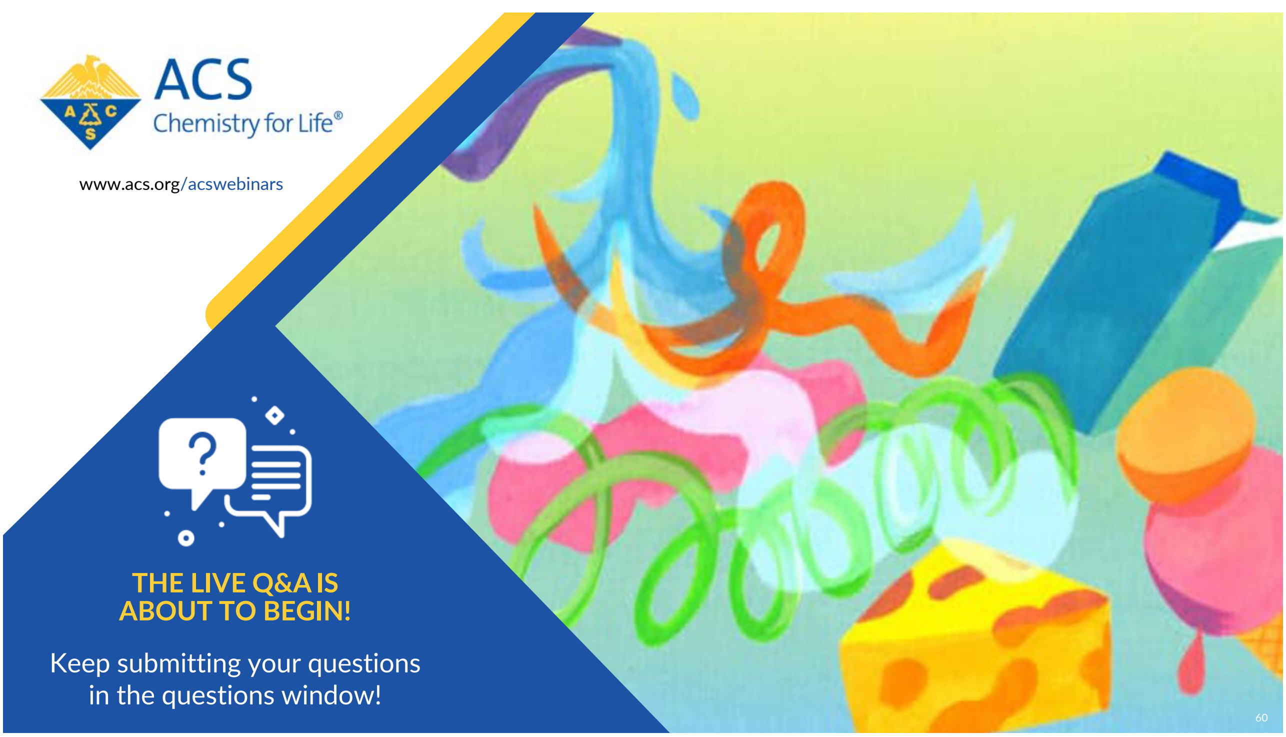
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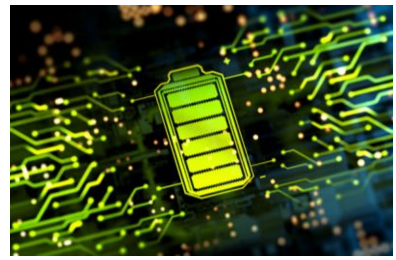

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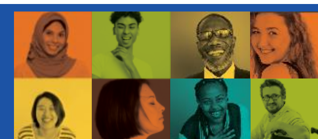

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