Food & Agriculture

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Food & Agriculture focuses on the tools and technologies impacting how we feed the Earth's people and animals. Engineering biology provides unique means and opportunities to support growing populations with more and different types of food, address changes to food security, diet, and demand, and reduce the impact of climate change and urban growth in a sustainable manner. Increasing challenges from biotic and abiotic stresses also significantly impact agricultural productivity and health. Concepts include increasing yield and sustainable productivity, while reducing the consumption of resources, including land, water, fertilizers, and pesticides. Achieving these Aims and Objectives will help to meet increased demands for nutrient-rich foods and healthy food animals.

Societal Challenge 1: Produce more food for a growing global population.

- Science/Engineering Aim 1: Improve agricultural yields by increasing crop efficiency and production.
    - Engineering Biology Objective 1: Improve photosynthesis efficiency in crops and other food plants.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Edit genes in the photosynthetic pathway for improved properties, including stability, catalytic activity, and substrate specificity.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Improved efficiency of key enzyme(s) in the photosynthesis pathway.
        - Host and Consortia Engineering Achievement:
            - Introduce synthetic (heterologous or modified) enzymes/complexes/pathways to improve photosynthetic efficiency.
        - Data Integration, Modeling, and Automation Achievement:
            - Models for engineered photosynthesis pathway.
    - Engineering Biology Objective 2: Improve soil nutrients, water, and CO_2 use efficiency in crops and other food plants.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Gene and genome editing to modulate expression and properties of key proteins involved in transport, storage, mobilization, and usage.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Improve key protein properties in important pathways or associated regulatory/transcription factors that are directly or indirectly involved in transport, storage, mobilization, and usage.
        - Host and Consortia Engineering Achievement:
            - Increase or re-engineer microbiome and symbiotic interactions to introduce or enhance nitrogen fixation and nutrient mobilization.

- Science/Engineering Aim 2: Increase the availability and consistency of agricultural crop production by combating stressors and expanding consumable species.
    - Engineering Biology Objective 1: Maintain crop yield under abiotic stress.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Minimize change in crop development times expected under higher temperature by regulating plant hormones and developmental gene expression.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Introduce C4 pathways introduced into C3 organisms to maintain photosynthetic capacity with stress from temperature and temperature variation.
            - Improve efficiency of photosynthetic pathway components.
            - Reduce heat- and water-stress-response during critical reproductive periods, such as fruit and seed formation.
        - Host and Consortia Engineering Achievement:
            - Chloroplast engineering to improve/stabilize photosynthetic pathways.
            - Reduce transpiration rates due to increased temperatures.
        - Data Integration, Modeling, and Automation Achievement:
            - Modeling of crop response to complex environmental changes, including global climate change.
    - Engineering Biology Objective 2: Maintain crop yield under biotic stress.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Identify native insect and disease resistance traits (e.g., R genes) from non-crop species, or from non-domesticated “crop” species, and introduce to crop species.
            - Engineer durable resistance in crops from computationally-designed proteins modeled after natural resistances and improving therein.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Engineer novel insecticidal proteins with different mode-of-action or spectrum-of-control beyond those in use today.
        - Host and Consortia Engineering Achievement:
            - Introduce metabolic or signalling pathways that improve or reinforce plant defense response to insect or disease pressure.
    - Engineering Biology Objective 3: Accelerate domestication of wild plant species.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Insert desirable traits (encoded by multiple genes or processes) from wild species into modern crops, or from modern crops into edible wild species, to improve plant products such as fruit size and yield, while maintaining genetic diversity and better protection from biotic/abiotic stresses.

        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Improve expression and activity of “domestication” genes to (re)introduce into wild species to generate new crops, increasing the number and variety of regional sources for calories and protein.
        - Host and Consortia Engineering Achievement:
            - Add new pathways to improve oils, proteins, and vitamin sources in “alternative” or newly domesticated crop species.
- Science/Engineering Aim 3: Improve the production and yield of meat from livestock and fish.
    - Engineering Biology Objective 1: Increase food animal yield, such as increased litter size, faster reproduction, and faster development.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Modify animal/fish genomes to enhance production of growth hormones.
            - Delete genes/proteins that may restrict muscle mass (e.g., myostatin) which can also reduce fat content.
            - Modify fecundity genes to increase litter size.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Engineer synthetic proteins that promote growth hormone production.
        - Host and Consortia Engineering Achievement:
            - Introduce heterologous gene cassettes (inducible promoter-gene-terminator) into genome that encodes synthetic protein promoting growth hormone production.
        - Data Integration, Modeling, and Automation Achievement:
            - Model growth rate vs. hormone production/induction.
    - Engineering Biology Objective 2: Reduce infectious and non-infectious disease in food animals, including alternatives to antibiotics.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Modify animal genomes to auto-induce vaccination to common pathogens.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Develop synthetic peptides or proteins that protect animals from common viral and bacterial diseases.
        - Host and Consortia Engineering Achievement:
            - Introduce genes encoding synthetic peptides for disease resistance into genome of food animals to protect against common viral and bacterial disease.
        - Data Integration, Modeling, and Automation Achievement:
            - Improve modeling of disease transmission to predict optimal husbandry conditions for preventing disease.

    - Engineering Biology Objective 3: Engineer the rumen/livestock microbiome to improve digestion of feed for improved nutrient absorption and metabolism.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Introduce genes to increase or develop tunable populations of beneficial gut microbiota.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Develop enzymes that are efficient at breaking down complex carbohydrates at pH of cow rumen.
        - Host and Consortia Engineering Achievement:
            - Introduce novel or synthetic digestive enzymes/pathways to increase digestible fiber into most abundant microbiome species that aid in digestion or eliminate/inactivate anti-nutritive substances.
        - Data Integration, Modeling, and Automation Achievement:
            - Survey microbiome populations in cow rumen and identify most abundant species for manipulation.
            - Model microbiome establishment and interactions.
- Science/Engineering Aim 4: Enable and advance the production and availability of non-vertebrate animal food sources.
    - Engineering Biology Objective 1: Increase non-vertebrate yield, including faster reproduction and development.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Remove genes for non-essential functions from the perspective of engineering organisms as food (such as shell production, wing development).
            - Silence genes involved in dormancy or molting to increase development and reproductive cycle-time.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Develop synthetic anti-molting peptide that normally limits growth and reproductive cycle-time, to include in feed.
        - Host and Consortia Engineering Achievement:
            - Develop inducible system that increases the number of molts/year (especially at adult stage) to speed up development time and reach reproductive age more quickly.
            - Develop a system that allows crustacea to continuously molt by overexpressing steroid hormones.
    - Engineering Biology Objective 2: Increase non-vertebrate biomass.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Change or modulate hormonal pathways that limit growth by changing expression of pathway genes.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Design enzymes that degrade hormones to prevent development from larvae to adults (for insects food sources).

        - Host and Consortia Engineering Achievement:
            - Inducible system that allows tunable expression of proteins or full pathway to maximize growth rate or biomass accumulation.
            - Develop a system that allows crustacea to continuously molt by overexpressing steroid hormones.
- Science/Engineering Aim 5: Improve production of "clean meat". (Stephens et al., 2018)
    - Engineering Biology Objective 1: Increase the diversity, availability, and optimization of characterized and standardized cell lines used for clean meat.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Create cell line libraries (to include stem cells, myoblasts, etc.) with desired phenotypes, including taste, texture, and aroma.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Develop biosensors/reporters for cell lines that provide readouts for suboptimal performance or culture conditions to accelerate research and development.
            - Engineer synthetic pathways to render differentiation responsive to inexpensive triggers (e.g., a unique sugar, rather than a complex growth factor cocktail).
        - Host and Consortia Engineering Achievement:
            - Increase proliferation/division rate of cells to improve biomass accumulation rate.
            - Increase genetic stability of cells to maintain genetic integrity over generations.
            - Select for or engineer cells to exhibit higher propensity to differentiate down desired pathways (muscle, fat, etc.) and low propensity to pursue undesirable pathways (bone, tendon, etc.).
        - Data Integration, Modeling, and Automation Achievement:
            - Create database of cell line characteristics, including genomic, proteomic, and metabolomic data.
            - Establish shared dataset of metabolic parameters from a wide variety of cell lines under various growth conditions to facilitate systems biology approach to metabolic pathway engineering and modeling.
    - Engineering Biology Objective 2: Engineer renewable and alternative growth media to support cell growth and health.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Improve expression or specific activity of proteins in growth pathways in native organisms.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Maximize production of growth and maturation factors while minimizing impact on growth of hosts, i.e., on/off expression system development.

- Create multiple genes encoding various biosynthetic enzymes or constructing novel pathways to produce growth factors.
- Use rational design or directed evolution to engineer growth factor variants/mimics that are, for example, more stable, more potent, have higher binding affinity.
- Utilize small molecule screens or natural product screens to identify entirely new growth factor mimics.

■ Host and Consortia Engineering Achievement:
- Engineer yeast or other cost-effective hosts to produce growth factors and other small molecules useful in cell culture media.

■ Data Integration, Modeling, and Automation Achievement:
- Model maximum theoretical yield obtainable for growth factors produced in a variety of cost-effective hosts to enable educated host choices.
- Develop machine learning-informed algorithms for more sophisticated Design-of-Experiments to expand the explorable space for medium formulations with many variables.
- Incorporate empirical information from highly-parallelized microfluidics platforms to assess cell performance in novel formulations.
- Merge insights from spent media analysis with systems biology modeling of metabolic pathways to understand how to bias metabolism toward biomass and protein accumulation.

○ Engineering Biology Objective 3: Improve bioscaffolding materials and perfusion systems to grow larger, more complex, tastier, and thicker pieces of “meat”.

■ Biomolecule, Pathway, and Circuit Engineering Achievement:
- Create biodegradable and/or edible scaffold biomaterials from biomolecules.
- Evaluate a wide variety of native and modified biopolymers from the plant, fungal, and bacterial kingdoms for suitability to create tunable hydrogel scaffolds, specifically for properties like photoresponsiveness (photopolymerization, light-induced degradation, etc.) for fabricating more spatially defined scaffolds.
- Enzyme screening and engineering to make specific modifications to plant- or fungal-derived biopolymer scaffolds (for example, modified cellulose).

■ Host and Consortia Engineering Achievement:
- Engineer plants or other low-cost biomass platforms (such as fungal platforms) to express peptides that make scaffolds derived from them more amenable to animal cell attachment.
- Examine effects of growth conditions and strain selection on producing scaffolds with desirable properties from fungal hosts (such as mycelium or secreted proteins).

        - Engineer animal cells to produce enzymes and/or attachment molecules that enable a wider variety of scaffold materials or scaffold remodeling *in situ* to more closely mimic native extracellular matrix-cell interaction.
    - Data Integration, Modeling, and Automation Achievement:
        - Produce fluid dynamic models for *in silico* prediction of appropriate scaffold architecture, culture medium viscosity and flow rates, required nutrient and dissolved oxygen concentrations, among other properties for supporting thick tissue perfusion.
        - Develop empirically validated scaling factors for facilitating upscale from bench to production in tissue perfusion bioreactors.
- Science/Engineering Aim 6: Advance the quality of plant-based meat products and improve large-scale manufacturing capabilities.
    - Engineering Biology Objective 1: Diversify raw material supply chains and improve sensory performance ingredients for incorporation into plant-based meat.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Alter high-protein crops for even higher protein accumulation and/or bias toward accumulation of high-performing storage proteins for plant-based meat applications.
            - Alter lipid synthesis pathways of common oilseed crops to produce higher levels of high-value lipids that are traditionally scarce in plant sources (including saturated fats, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA)).
            - Edit crop plants for lower levels of secondary metabolites that negatively impact taste (such as saponins and other components of bitter or beany off-flavors).
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Identify new methods for storage and/or scavenging to improve shelf life of less-highly-refined fractions (for example, to slow oxidation and rancidity in plant flours with residual oil).
            - Identify plant-sourced homologs or synthetic mimics of proteins or small molecules determined to play critical roles in the taste of various types of meat.
        - Host and Consortia Engineering Achievement:
            - Perform thorough genetic, phenotypic, and compositional characterization of underutilized crops to identify promising candidates for novel sources of proteins, flavorings, or other functional ingredients.
            - Engineer promising specialty crop candidates for plant protein sources to achieve the same agronomic yield gains, robustness to pests, and abiotic stress, that are already standard in commodity crops.

- Explore capability of microbial fermentation to improve sensory and functional properties of plant proteins and other raw materials through, for example, enzyme secretion and selective metabolism of undesirable components.
- Engineer high-efficiency microbial production hosts to produce functional proteins or flavoring ingredients through synthetic biology and novel metabolic pathway introduction.

■ Data Integration, Modeling, and Automation Achievement:

- Capture and store agronomic data along with raw material characterization data to enhance predictive capacity for how growing conditions, soil, weather, etc., affect the end product.
- Develop better analytical tools for assessing/predicting functionality or performance of complex fractions of plant ingredients.
- Identify compositional signatures (for example, through mass spectrometry or capillary electrophoresis) that can be used as analytical tools to characterize nuanced performance characteristics of lots of raw materials.

○ Engineering Biology Objective 2: Improve large-scale manufacturing and texturization of plant-based meat.

■ Gene Editing, Synthesis, and Assembly Achievement:

- Edit crop plants for higher efficiency of fractionation into protein, starch, fiber, and oil components.

■ Biomolecule, Pathway, and Circuit Engineering Achievement:

- Develop new food processing enzymes (rationally designed or through directed evolution) that are optimized for plant-based substrates to improve raw ingredient functionalization (for example, hydrolysis or cross-linking of plant proteins to improve solubility, water-binding capacity, and gelling).
- Develop methods for microencapsulating ingredients like flavors and fats in edible ingredients such that they remain protected and stable during high-pressure processing.

■ Host and Consortia Engineering Achievement:

- Engineer crop plants for modified proteins that have natively improved functional properties for plant-based meat processing (such as solubility, cross-linking capability and fat-binding capacity).

■ Data Integration, Modeling, and Automation Achievement:

- Develop mechanistic models of plant protein denaturation, alignment, and crystallization within the context of high-shear processing methods like extrusion, to inform the process variables for a given composition of input materials.

- Science/Engineering Aim 7: Engineer microorganisms for nutrient production.
    - Engineering Biology Objective 1: Engineer hosts to produce safer food components (e.g., processing aids) and ingredients (e.g., vitamins).
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Modify vitamin biosynthetic pathways in native production hosts to increase yield or stability of provitamins.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Improve specificity and properties of enzymes involved in (pro)vitamin biosynthesis to increase yield.
        - Host and Consortia Engineering Achievement:
            - Introduce and optimize (pro)vitamin biosynthesis pathways from different sources into yeast, microalgae, and bacteria.
            - Introduce transporters to help increase production rates.
            - Reduce metabolic regulation and controls to increase production of (pro)vitamins.
        - Data Integration, Modeling, and Automation Achievement:
            - Computational tools for enzyme design and engineering.

Societal Challenge 2: Increase and improve the nutritional content and value of food.

- Science/Engineering Aim 1: Increase the nutrient content in agricultural crops.
    - Engineering Biology Objective 1: Improve the quantity and quality of seed proteins and proteins from vegetative plant tissues.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Increase expression of proteins with desired amino acid content by introducing engineered genetic parts (including promoters and peptide tags).
            - Modulate seed-specific pathway genes to enhance protein accumulation in seed without impacting germination.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Design novel proteins that incorporate important amino acids that can be expressed in seed or improve protein solubility.
            - *De novo*, model-based creation of proteins with high nutritional value.
        - Host and Consortia Engineering Achievement:
            - Introduce proteins of high nutritional value into plant tissue.
        - Data Integration, Modeling, and Automation Achievement:
            - Model protein and oil flux in the seed to ensure optimal accumulation.
            - Produce better models of important proteins to understand where protein quality can be improved.

- Engineering Biology Objective 2: Increase bioavailability of proteins through engineering structure, amino acid composition, and removing anti-nutritive factors.
  - Gene Editing, Synthesis, and Assembly Achievement:
    - Edit plant protein sequences to increase digestibility through changes to structure and amino acid content or reduce expression of anti-nutritive factors.
  - Biomolecule, Pathway, and Circuit Engineering Achievement:
    - Design new proteins to increase content of rare or needed amino acids and/or enhanced solubility.
    - Eliminate aspects of pathways that produce anti-nutritive factors that do not impact plant growth.
  - Host and Consortia Engineering Achievement:
    - Introduce or modulate pathways and feedback loops that play a role in protein degradation and amino acid scavenging.
- Engineering Biology Objective 3: Enable (increased) production of beneficial fatty acids and digestible fiber in staple crops.
  - Gene Editing, Synthesis, and Assembly Achievement:
    - Knockout genes/pathways that divert carbon away from fatty acid (FA) production in plants.
    - Reduce lignin biosynthesis in crops.
  - Biomolecule, Pathway, and Circuit Engineering Achievement:
    - Improve enzymatic properties of proteins involved in conversion of FAs to long-chain polyunsaturated fatty acids (LC-PUFAs) to increase production and accumulation in plants.
    - Develop more effective enzymes that can reduce lignin content in crops.
  - Host and Consortia Engineering Achievement:
    - Introduce pathways or novel enzymes from heterologous systems that are missing in plants to convert FAs into omega-3 or omega-6 LC-PUFAs.
    - Integrate and/or replace poorly perfoming or less desireable pathway enzymes.
    - Overexpress lignin-degradation enzyme(s) under an inducible promoter.

- Science/Engineering Aim 2: Improve the healthiness of agricultural crops by enabling the reduction and elimination of toxins.
  - Engineering Biology Objective 1: Engineer and improve crops and other agricultural plants to prevent accumulation of heavy metals. (Ali & Khan, 2018; Fan et al., 2018; Muthusaravanan et al., 2018; Nahar, Rahman, Nawani, Ghosh, & Mandal, 2017; Rai, Lee, Zhang, Tsang, & Kim, 2019)
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
      - Identify or generate regulators responsive to heavy metals.

        - Identify and remove, or modify specificity of, transporters involved in movement of heavy metals.
    - Host and Consortia Engineering Achievement:
        - Generate compartments or mechanisms for compartmentalization or sequestration and excretion of heavy metals.
    - Data Integration, Modeling, and Automation Achievement:
        - Protein modeling to identify putative sites for modification of transporter specificity, selectivity, and activity.
        - Automation in phenotyping.
- Engineering Biology Objective 2: Engineer and improve crops to enable reduction and/or elimination of toxins and allergens, such as gluten, peanut-allergen proteins, or other health-affecting factors. (Engagement Example: By engineering a reduction in the amount of asparagine in foods, such as potatoes, it is possible to decrease the formation of harmful acrylamides upon processing of those foods. See http://www.innatepotatoes.com for this example in action.)
    - Gene Editing, Synthesis, and Assembly Achievement:
        - Generate mutations that delete or modify allergenic proteins or protein domains (such as peanut protein or gluten).
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
        - Generate toxin specific sensors, reporters, and transcriptional regulators.
        - Modify metabolic pathways that generate anti-nutrients (such as phytate).
        - Modify endogenous biosynthetic pathways to metabolize or prevent production of toxins.
    - Host and Consortia Engineering Achievement:
        - Engineer mechanisms of sequestration and secretion.
        - Generate compartments, or mechanisms for compartmentalization or sequestration, and subsequent excretion of toxins.
    - Data Integration, Modeling, and Automation Achievement:
        - Protein modeling to identify putative sites for modification.
        - Flux analysis for modification of metabolic pathways.
        - Design and model signal perception and response systems for redirecting metabolism.
- Engineering Biology Objective 3: Improve food bio-processing to prevent and eliminate organic toxins (such as mycotoxins) in post-harvest environments.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
        - Identify and engineer enzymes for bioconversion of toxins into non-toxic, consumable degradation products.
    - Host and Consortia Engineering Achievement:
        - Generate microbial or cell-free systems to degrade or sequester toxins.

        - Data Integration, Modeling, and Automation Achievement:
            - Protein modeling to identify enzymes with specificity, selectivity and activity for targeting toxins.
- Science/Engineering Aim 3: Increase the nutrient content and value from animal food sources.
    - Engineering Biology Objective 1: Increase bioavailability of non-vertebrate proteins.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Identify and edit genes to reduce chitin content in insects, crustaceans, and molluscs to reduce allergenic potential.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Edit relevant proteins for structure and expression.
        - Host and Consortia Engineering Achievement:
            - Reduce processing pathways that prevent protein availability.
            - Enable inducible expression of chitinase in transgenic insects at time of death.
    - Engineering Biology Objective 2: Increase non-vertebrate nutrient content.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Introduce genes for relevant nutrients (such as B12) in non-vertebrate animals.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Engineer custom probiotics which produce relevant growth factors and micronutrients/vitamins.
        - Host and Consortia Engineering Achievement:
            - Host resilience optimized through genetically-determined pathogen resistance.

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