Cyborgian Material Design for Solar Fuel Production: *The Emerging Photosynthetic Biohybrid Systems*

Kelsey K. Sakimoto[1,2], Nikolay Kornienko[1,3], Peidong Yang[1,4,5,6,*]

[1] Department of Chemistry, University of California, Berkeley, California 94720, United States

[2] Current Address: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, Massachussetts 02138, United States; Department of Systems Biology, Harvard Medical School, Boston, Massachussetts 02115, United States

[3] Current Address: Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, United Kingdom

[4] Department of Materials Science and Engineering, University of California, Berkeley, California 94720, United States

[5] Kavli Energy Nanosciences Institute, Berkeley, California 94720, United States

[6] Materials Sciences Division, Lawrence Berkeley National Lab, Berkeley, California 94720, United States

* Corresponding Email: p_yang@berkeley.edu

Abstract:

Photosynthetic Biohybrid Systems (PBSs) combine the strengths of inorganic materials and biological catalysts by exploiting semiconductor broadband light absorption to capture solar energy and subsequently transform it into valuable CO_2-derived chemicals by taking advantage of the metabolic pathways in living organisms. In this work, we first traverse through a brief history of recent PBSs, demonstrating the modularity and diversity of possible architectures to rival and, in many cases, surpass the performance of chemistry or biology alone before envisioning the future of these hybrid systems, opportunities for improvement, and its role in a sustainable living here on earth, and beyond.

I. Chemical *vs.* Biological Strategies to Photosynthetic CO_2 Reduction

To meet the challenges of a growing, resource and energy hungry populace, humankind has embarked on an ambitious pursuit of a photosynthetic route to meet their needs. While biology, in a sense, has solved this problem, inefficiencies, particularly in terms of light harvesting, plague natural photosynthesis. As the solar-to-energy efficiencies of inorganic semiconductor photovoltaics now routinely top ~20% compared to the ~3% of the best photosynthetic organisms, a chemical/synthetic approach to solar energy absorption will clearly dominate the future.[1] But what of converting that solar energy into chemical bonds? In the realm of catalysis, namely the conversion of CO_2 and other small atmospheric molecules such as N_2 to complex organic molecules, chemistry (i.e. synthetic molecular and heterogeneous catalysts) and biology (i.e. enzymatic catalysts) offer two different approaches.

How does one reduce CO_2? Regardless of the approach, three things must typically occur: 1) electron transfer (ET) from catalyst to CO_2, 2) formation of C-C bonds, and 3) selection of a single (or a few) product(s). Though this task continues to confound chemists, the billion-year process of natural evolution has delivered biological approaches that remain difficult to mimic in their entirety. The lowest unoccupied molecular orbital (LUMO) of CO_2 consists of an antibonding π^* MO. Injection of an e^- into this MO serves to destabilize the linear O=C=O bond, facilitating CO_2 lysis and priming it for further reduction and hydrogenation.[2] However, transfer of a single e^- only serves to weaken the bond, producing a bent $CO_2^{\cdot -}$ radical anion. This comes at an energetic penalty, with the single e^- reduction potential at a massive -1.9 V vs. NHE (pH 7). Application of a strong nucleophilic reducing agent, a large electrochemical overpotential driving force, or high temperature thermal activation may overcome or bypass this significant activation energy.[3–5] However, such brute force methods often result in poor energetic efficiencies and limit their scale up for practical applications. Biology has taken an alternative approach to ease this energetic barrier. In tandem with a nucleophilic ET, enzymatic active sites such as those found within CO dehydrogenases (CODH) often feature a proximal electrophilic ligand to stabilize the anionic charge. In the Ni-Fe CODH found in anaerobic bacteria, a nucleophilic Ni site facilitates CO_2 reduction through a Ni-C bond, while the adjacent histidine site and hydroxyl group electrophilically stabilize the resulting negative charge, lowering the activation energy.[2] Additionally, the reaction proceeds through a two-e^- mechanism, eliminating the formation of high energy radicals. A neighboring FeS cluster, ubiquitous throughout biological redox catalysis for its ability to store and accumulate e^- for simultaneous charge transfer, achieves this feat.[2] With this insight, can we design a pared-down, synthetic analogue? Yes, and no. Synthetic catalysts, such as ionic liquid functionalized metal surfaces, are thought to incorporate CODH-like $CO_2^{\cdot -}$ ligand stabilization to lower the activation energy/overpotential, but still compare poorly to enzymatic counterparts.[6] And biomimetic molecular catalysts with active sites similar to their parent enzyme have revealed that nearly the entire enzyme is required to function at the same catalytic performance. In addition to the well-designed active site, most enzymes rely on their coordinating ligand shells of amino acid residues to affect electronic and structural influence on the actual active site.[7] Such factors effectively guide the reaction pathway through steric control and electronic stabilization of intermediates. Also, outer sphere ligand shells control mass transport to and from the active site, enhancing catalytic turnover rates.[8]

While inner-sphere CO_2-to-active site interactions remain important, that the catalytic action occurs not in an aqueous environment, but a locally hydrophobic one, is oft overlooked. Though H_2O operates as the H^+ source for biological CO_2 reduction, H_2O molecules act as a solutes rather than solvents within many proteins.[9] ET in these hydrophobic pockets can efficiently occur over distances much larger than what we observe in aqueous environments.[10] ET dynamics are often characterized by Marcus theory, which amongst other terms, pulls out a so called “reorganization energy” term related to the energy required to restructure the solvent around the e^- donor and acceptor site. In highly polar solvents such as H_2O, reorganizing the solvating dipole-coupled molecules slows down ET rates and lowers efficiency. This deceleration also grows exponentially with distance, thus necessitating immediate proximity of donor and acceptor. Organic solvents can mimic the non-polar environment of an enzyme, though their cost and toxicity remains prohibitive of large scale implementation.[11] Polymer based approaches offer a potential closer mimic of enzyme structures, though they remain unable to capture the full efficiency.[12]

In the formation of C-C bonds, local concentration of reactive C intermediates is the name of the game. Most heterogeneous materials that produce higher-order hydrocarbons bind intermediates very strongly to concentrate them on the surface and thus achieve neither high efficiency nor selectivity.[13,14] Tuning the local pH and supporting electrolyte (both of which affect CO_2 solubility) has advanced electrochemical CO_2 reduction to C_{2+} products.[15] However, even such approaches have not achieved the long carbon chain forming reactions of biology. Biology takes two approaches. The first is to increase the transient CO_2 concentration through carbonic anhydrases (CA). CA catalyze the interconversion of unreactive carbonate ions to $CO_{2.}$[16]. As the natural interconversion rate is low, CA ensure the local concentration of CO_2 remains elevated, enabling faster turnover frequencies and higher C-C bond formation rates. The second strategy employs stable, yet activated C intermediates. Chemical catalysis either requires binding/adsorption of an activated species to the active site (limiting turnover frequencies and requiring ultrafast C-C bond formation), or reactivation of a desorbed molecular species. In contrast, biosynthetic pathways often produce various acyl-CoA's as an activated C building block such as in the polyketide synthase pathways that produce long chain fatty acids.[17,18] By fixing CO_2 into a thioester, this reactive building block does not require reactivation nor must it remain bound to the active site for subsequent C-C bond formation. Similar long carbon chain forming chemistry exists in gas phase catalysis through the Fischer-Tropsch reaction, though control over selectivity remains loose.[19]

High selectivity is required for CO_2 reduction, and again, biology and chemistry offer significantly different approaches. The inherent problem lies in the energetic similarity of reduced CO_2 products and their intermediates.[20] Thus, competitive kinetics and minute changes in binding energies govern product distributions, typically affording a hodge-podge of simpler, less valuable products. In contrast, biology widely employs steric hinderance and electronic stabilization of select intermediates to guide reactions towards single products. The ligand environment surrounding an enzymatic active site dictates which chemical structures, and therefore which reactants and products, interact with the active site. As such, enzymes and biosynthetic pathways typically could produce a single product with 100% selectivity, even 100% enantiomeric selectivity.

II. Photosynthetic Biohybrid Systems (PBSs)

Since the myriad of strategies employed by biology remain an active field of investigation by seasoned biochemists (summarized in Table 1), it would be unreasonably hopeful to imagine we could currently capture all the performance capabilities of biological CO_2 reduction. A convenient shortcut would simply use the preassembled biosynthetic pathways, and link them with high efficiency non-biological light harvesting. Such an approach forms the basis of Photosynthetic Biohybrid Systems (PBSs) which combine high efficiency inorganic light harvesters with enzymatic catalysts and whole-cell organisms to effect CO_2 reduction at efficiencies approaching and exceeding that of natural photosynthesis alone, or chemical catalysis alone. The new challenge lies in selecting a compatible light harvesting system and biocatalyst, and the seamless integration of the disparate biotic and abiotic components. To date, a number of such systems have been demonstrated in the literature, offering several approaches to the PBS concept (Fig. 1).

The first forays into this field began modestly with examination of the interactions between inorganic nanostructures that would one day serve as light harvesters, and the bacteria whole cell catalysts capable of CO_2 reduction. Investigations of the microbial fuel cell bacteria *Shewanella oneidensis* and the CO_2 reducing acetate-producing *Sporomusa ovata* showed that Si nanowire arrays could form favorable interactions between nanostructure and cell.[21,22] Whereas most nanostructures had previously been used for antimicrobial purposes, this work served as a basis of new *pro*-microbial nanomaterials crucial for the new PBSs.

Building on this initial investigation, the first PBSs came in two forms: integrated and distributed. Integrated PBSs directly transfer e^- from the inorganic light harvester to the biological component in an apparent single step. As direct contact between bacterium and electrode are required, high surface area electrodes such as carbon cloths and nanowire arrays are highly desirable for high current densities. Distributed PBSs discretize the production of a molecular reducing equivalent such as H_2 or methyl viologen as a direct result of light harvesting and the reduction of CO_2 by a microbe capable of utilizing that molecular reducing equivalent. The work by Liu, et al. evoked an elegant, single step scheme[23] building off initial work for an abiotic solar water-splitting device.[24] Here, e^- derived from Si nanowire light absorbers are directly delivered to the acetogen *S. ovata* without the need of a mediating molecular reducing equivalent. The mechanism of this charge transfer still remains an active area of debate, with a number of competing mechanisms in contention.[25] In contrast, the work from Torella, *et al*. adopts a distributed approach in which a biocompatible water-splitting catalyst pair produced H_2 and O_2 from electrical energy (which may ultimately be derived from photovoltaic-based grid energy) that was subsequently consumed by an H_2-oxidizing CO_2 reducing bacterium (*Cupriavidus necator*, formerly *Ralstonia eutropha*).[26] This work demonstrated a highly flexible design, as the light harvesting photovoltaic, water-splitting electrocatalysts, and microorganism could in theory be easily substituted with new, better performing, or bespoke components as they become available. A similar concept was explored in Nichols, *et al.* in which photoelectrochemically generated H_2 was fed to a strain of methanogenic archaea, *Methanosarcina barkeri*.[27]

All three systems demonstrated the high selectivity of biosynthetic C-C bond forming chemistry, with *C. necator* producing isopropanol at ~90% of non-volatile reduced CO_2 products (minor formation of acetone and pyruvate).[26] The *M. barkeri* based system boasted a faradaic efficiency of ~86% for CO_2 to CH_4. The integrated *S. ovata* system fared better due to the lack of H_2 formation as a parasitic loss pathway, with ~90% Faradaic efficiency going towards the production of acetate. Though the kinetic performance of these initial proof-of-concept PBSs required optimization, their high product selectivity demonstrated the utility of biological CO_2 reduction combined with inorganic light harvesting.

An alternative approach was demonstrated in Sakimoto, *et al.* in which the microorganism facilitated not only CO_2 reduction, but the initial synthesis of the inorganic light harvester as well through a self-photosensitization mechanism.[28] The non-photosynthetic bacterium, *Moorella thermoacetica*, is capable of CO_2 reduction in a manner similar to *S. ovata*, generating acetate at nearly 100% selectivity. However, the introduction of Cd^{2+} triggers the bioprecipitation of CdS nanoparticles which may serve as light harvesters to render this non-photosynthetic organism newly photosynthetic with up to 84% quantum efficiency under monochromatic, low light conditions. This work demonstrated that the incredible synthetic power of biology may not only be leveraged to reduce CO_2, but to also prepare functional inorganic materials in a cost effective way under mild conditions to rival the energy and resource intensive traditional microfabrication route.

To demonstrate the full advantages of the PBS concept, the kinetic performance must be improved to surpass natural photosynthesis. To improve on the initial *C. necator* system, Liu, *et al.* employed a redesigned H_2 evolution catalyst that eliminated lingering biocompatibility issues of the previous design, namely Ni toxicity and the generation of reactive oxygen species (ROS).[29] Using a Co-P alloy, the 2nd generation system currently demonstrates calculated energy efficiencies of ~10% (when paired with an 18% Si-based photovoltaic), dwarfing the <3% typical of the best natural photosynthesizers. While the most efficient product of CO_2 reduction is biomass (with lesser efficiencies towards C_{3+} alcohols), metabolic engineering practices promises to guide the product selectivity to higher titers of a variety of compounds readily biosynthesized by this genetically tractable organism. Indeed, the knowledge developed by the metabolic engineering and synthetic biology community for glucose fermentation to high value commodity products may be facilely leveraged towards these CO_2 reducing PBSs.

III. The Frontiers of PBSs

As biological systems have evolved to yield higher complexity and greater functionality, so to may PBSs evolve. Recent work by Sakimoto, *et al.* have demonstrated a second generation design of the *M. thermoacetica*-CdS PBS in which CO_2 reduction is paired with photocatalytic O_2 evolution.[30] While the O_2 sensitive CdS inorganic light absorber is unable to carry out stable water oxidation, pairing this system in tandem with a TiO_2 based co-photocatalyst is able to achieve net oxygenic photosynthesis. This work marks the first step in an evolutionary line of PBSs, an emergent intertwined evolution of chemistry and biology that may yield more complex hybrid organisms. As natural evolution has traversed from singled cell prokaryotes all the way to multi-cellular eukaryotes, so too may PBSs evolve higher complexity and functionality (Fig. 2). Additional photocatalysts and microorganisms may evolve PBSs to incorporate tandem and sequential reactions, as well as peripheral features such as sensing and regulatory mechanisms. Divisions of these components by semi-permeable membranes likens them to eukaryotic and multi-cellular organisms. This vision of a cyborgian evolution – biology augmented with inorganic materials – may bring the PBS concept to full fruition, selectively combining the best of both worlds.

For integrated PBSs, the mechanism of charge transfer between inorganic and biological interfaces remains mysterious. Work by Kornienko, *et al.* has employed time resolved spectroscopic techniques to follow the ET dynamics within the *M. thermoacetica*-CdS system.[31] Their work has revealed that the direct transfer mechanism is dependent on hydrogenase expression levels within *M. thermoacetica*, and occurs at relatively quick time scales. While the details are still under exploration, the ability to use conventional spectroscopic techniques such as transient absorption spectroscopy and time-resolved infrared spectroscopy open up the possibility of deeply probing the nature of this unique biotic-abiotic interface.

Improvements in performance must run the age old gauntlet of optimization, informed by future experimental and theoretical work. Of particular practical bottlenecks are the volumetric productivity (amount of product produced per volume) which is limited by the bulky nature of biological entities. Additionally, the susceptibility of biological systems to oxidative damage seems incompatible with high production rates, and will require clever scale-up strategies such as high surface area electrodes. From an engineering perspective, separation and downstream processing of bio-derived products may be informed by similar difficulties encountered by the fermentation industry.[32]

Beyond CO_2 reduction, the PBS architecture holds promise for a number of other chemical transformations, amongst which the next most pressing is N_2 fixation. Nitrogen is a crucial component of most biomolecules, necessary as an agricultural fertilizer, a precursor to pharmaceuticals/upgraded chemicals, and a possible next generation carbon-neutral fuel. An NREL based research team has developed a significant body of work interfacing semiconductor quantum dot light harvesters with a wide variety of oxidoreductases, including hydrogenase, $NADP^+$ reductase, and most recently nitrogenase.[33–35] As progress continues on CO_2 reduction, the future of PBSs will seek to expand the scope of photosynthetic chemistry, and position itself as a comprehensive technology for a sustainable future.

As PBSs position themselves to supplant traditional chemical routes to Earth's terrestrial chemical and material needs, we turn an eye towards their possible implementation to meet extra-terrestrial needs as well (Fig. 3). Though much of Earth's chemical industry has been formulated around the assumption of large spaces to build chemical factories and non-cyclical waste stream processing, living in space building off-world permanent space colonies require a different way of thinking. Limited volume constraints and the high $/mass ratio payloads destined for space necessitate high efficiency routes towards chemical synthesis. In addition, the confined quarters and delicate life support systems call for highly safe technologies devoid of hazardous chemicals and high temperatures and pressures. That biological catalysts require nothing more than simple inorganic salts and carbon sources at mild temperatures to power their growth, self-replication, and self-repair mechanisms, facilitates a benign synthetic route compared to traditional preparation of chemical catalysts. Finally, long term space habitation dictates that no mass may be lost, i.e. all waste must be recycled and reused using solar energy as the only input. PBSs satisfy such stringent requirements, requiring neither toxic chemicals nor extreme reaction conditions. They also are highly tolerant of mixed input streams, making them ideal for waste recycling systems. Though their efficiencies already outpace many other synthetic routes, further improvements will steadily move this new hybrid technology towards implementation both here at home, to Mars, and beyond.

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Table 1 Summary Comparison of Chemical and Biological Routes to Photosynthesis

	Chemical	Biological
Light Harvesting	~18-20% energy efficiency	<3% energy efficiency
Activation Energy	Large (sequential e^- transfer, highly polar environment)	Small (multi-e^- transfer, intermediate stabilizing ligands, local hydrophobicity,↑CO_2 concentration)
Transport to/from Active Site	Diffusion	Mediated
CO_2 Reduction Products	Mostly C_1 (CO, CH_4, formic acid…)	Mostly C_{2+} (organic acids, alcohols, aromatics, polymers…)
Selectivity	Poor (electronically controlled)	Near 100% (sterically controlled)
Preparation	Traditional Synthesis	Self-replicating

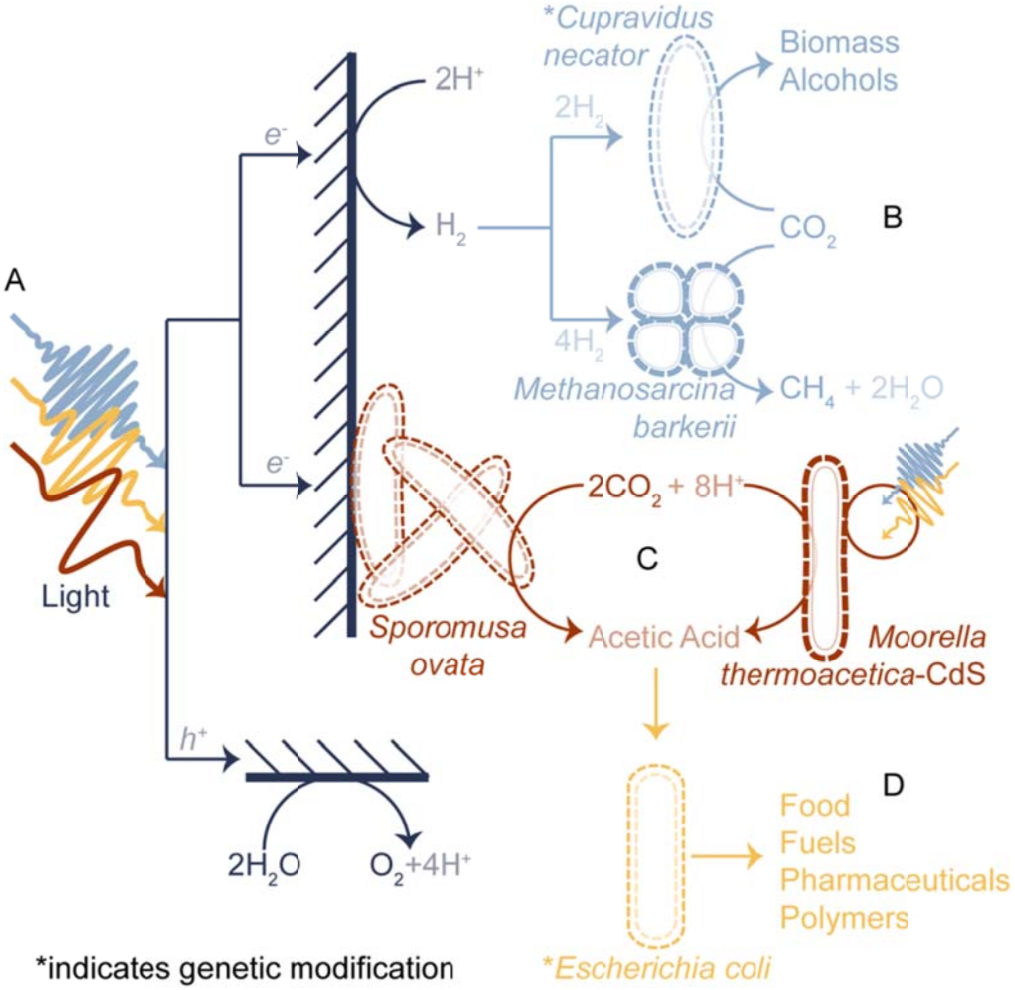


Figure 1 Overview of Different PBS Architectures. Utilizing *e*$^-$ derived from a semiconductor light harvester (A), PBSs channel reducing equivalents to generate H_2 (B) to feed CO_2 reducing microorganisms. These *e*$^-$ may also go directly to the bacterium (C) to generate reduced CO_2 products, such as acetic acid. This acetic acid may then be fed to genetically engineered organisms (D) to upgrade to a wide range of products.

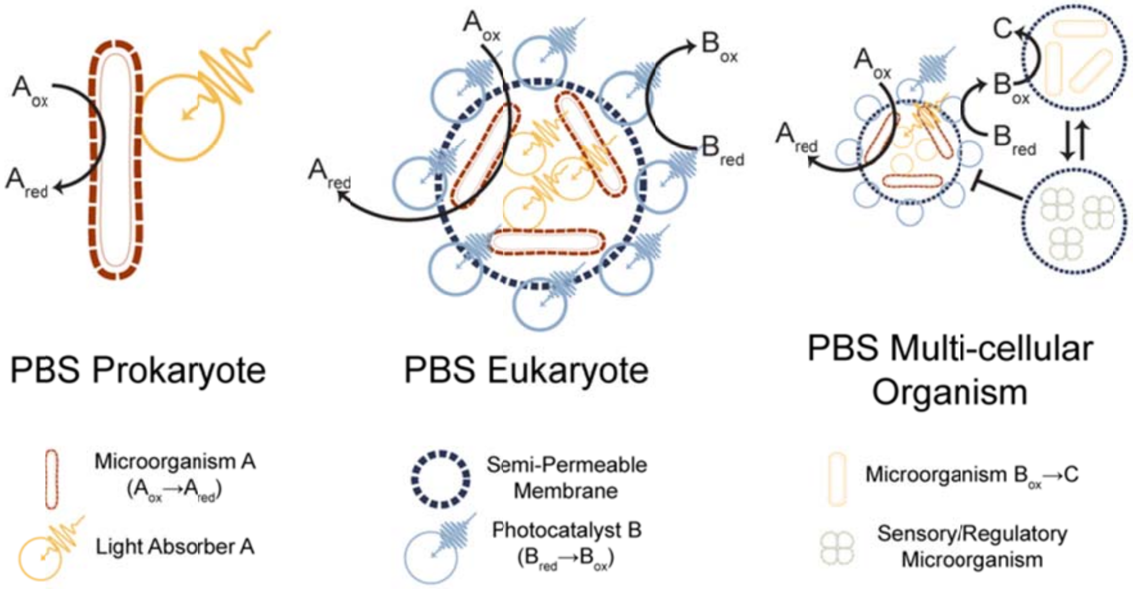


Figure 2 Conceptual Designs of PBS Evolution. Additional light absorbers/photocatalysts to PBSs may extend their functionality, such as concurrent tandem reactions. Encapsulation of these PBSs by semipermeable membranes, in the manner similar to eukaryotes, and pairing with other PBSs may lead to complex, interdependent multi-cellular PBSs.

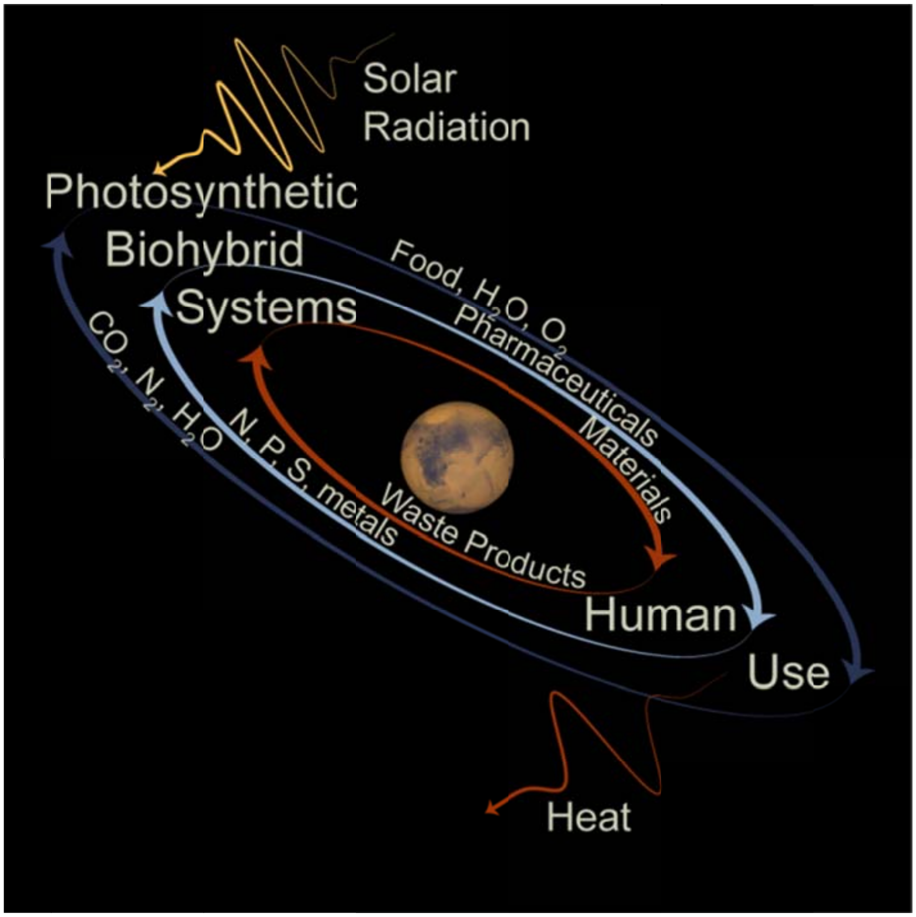
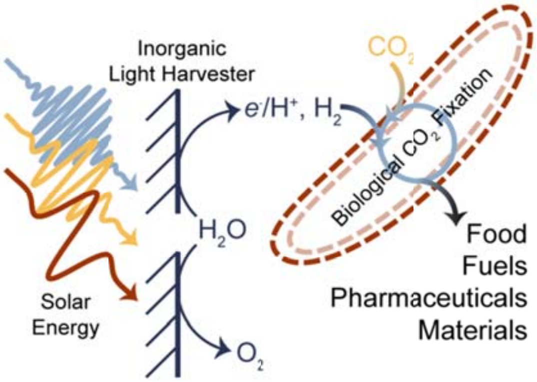


Figure 3 Closed Material Loop Concept for PBSs for Future Space Missions. PBSs have the potential to supply all the requirements for human habitation in space, using only solar energy to recycle waste products back into useful goods. NASA's Goddard Space Flight Center Scientific Visualization Studio.


Inorganic Light Harvester
CO$_2$
e^-/H$^+$, H$_2$
Biological CO$_2$ Fixation
H$_2$O
Solar Energy
O$_2$
Food
Fuels
Pharmaceuticals
Materials