Description of Research and related activities during the review period.

Background: When I interviewed for my position at MSU, I proposed a multi-level, cross-cutting program to address some of the biggest problems in plant sciences. Specifically, I wanted to focus on what I see as the "next revolution" in plant biology, in connecting the genotype, the environment and the phenotype with special emphasis on photosynthetic energy transduction. From my "start up" proposal sent to MSU in April, 2010:

> "My goal is to develop an aggressive, integrated program to understand the processes that limit and control energy capture by photosynthesis in both plants and algae through three parallel efforts, concurrently over a 5 year period: …1) answer some key fundamental research questions on the mechanism and regulation of photosynthesis; 2) "Establish a Photosynthetic Phenomics Center at MSU; 3) Develop and disseminate new phenotyping technologies to the world to enable new modes of research and to allow us to "see the unseen" (i.e. gather and analyze the crucial data on plant performance that is currently out of reach)."

I am happy to report that because of the tremendous support from MSU and the collaboration with my colleagues, we have been able to make great progress in all three of these ambitious goals. Indeed, in several cases, we have been able to move far beyond these original goals and start to tackle bigger challenges, such as directly impacting research on agriculture in the developing world. We were able to do this because we have opportunity to assemble an amazing team of students, scientists, researchers, engineers and entrepreneurs.

As detailed in the attached curriculum vitae, over the past 5 years, our work has resulted in 64 peer-reviewed publications (55 published or in press [1-55], 7 submitted [56-63]); over 45 invited talks (many as plenary or keynote addresses); the establishment of the MSU Center for Advanced Algal and Plant Phenotyping (CAAPP) and its series of new plant phenotyping platforms that are used not only at MSU but also around the world; 13 publically accessible and widely used software packages for plant phenotype analytics; the development of the PhotosynQ.org platform that aims to bring advanced plant phenotyping to the world; three patent applications [8, 9, 49] and 3 additional invention disclosures; one fully-independent and profitable spin-off company (Phenometrics, Inc.) as well two more spin-offs in progress to disseminate out other phenotyping platforms.

The work brought in substantial external funding, from over 30 externally-funded grants, from a range of agencies, including several programs at the U.S. Department of Energy, National Science Foundation, National Institutes of Health, U.S. Agency for International Development (USAID), the McKnight Foundation, ExxonMobil Corporation and VentureWell (Lemenson Foundation). In addition the CAAPP and the tools it has developed have been key in enabling other MSU research groups to obtain substantial external grant support (see below).

Brief highlights of selected accomplishments: *1) Fundamental mechanisms of photosynthesis.* Our basic research programs on the mechanisms and regulation of Photosynthesis led to important discoveries in several areas key to understanding how photosynthesis responds to environmental fluctuations, including: mechanisms by which photosynthesis regulates its energy budget by activating a molecular proton pump that stores energy in ATP [3-6, 18, 21, 25, 26, 32, 58]; The elusive reactive intermediate that determines the reaction mechanism of the Q-cycle, a process that accounts for a large fraction of the ATP in our ecosystem, with implications for how enzymes deal with reactive catalytic intermediates [12, 29, 47]; Important clues about how the chloroplast ATP synthase co-regulates the light and dark reactions of photosynthesis to optimize the balance between efficiency of photochemistry and the avoidance of photodamage; New mechanisms for the regulation of chloroplast energy storage activating ion transporters that alter the composition of the thylakoid proton motive force [2, 21, 23, 28]; An unexpected redox regulator of the chloroplast ATP synthase that tunes photosynthesis for function at low light [63]; The importance of the bulk of chloroplast-targeted genes in responding to fluctuating environmental conditions [58, 61]; A new "Achilles heel" of photosynthesis that appears to contribute to photodamage and loss of crop yield under field conditions and on which we propose several new lines of research that connect basic to applied research on improving the efficiency and robustness of photosynthesis [60].

2) "Establish a Photosynthetic Phenomics Center at MSU. We established the MSU Center for Advanced Algal and Plant Phenotyping (CAAPP) to develop and apply transformative phenotyping technologies to enable us to directly address the next big challenges in plant biology, to establish MSU as an international innovation center and "international point of destination" for phenotyping analysis. In its first three years, the Center has established key instrumentation platforms and associated analytical software and approaches that start to bridge the gaps in our knowledge from genes to phenotype and from the lab to the fields.

As of Sept, 2015, more than 24 MSU faculty and researchers, from 9 departments and programs have used CAAPP technologies and facilities including 14 different MSU AgBioResearch groups focusing on agricultural-relevant projects. CAAPP facilities have been used in an estimated 50 or more publications (both within and external to PRL), and its capabilities, direct involvement and preliminary data have contributed to more than 20 external grant proposals from MSU (over 14 were funded, totaling more than $46M, roughly $24M of that went to MSU).

3) Development and worldwide dissemination of new instrumentation and techniques. One of the big, "stretch goals" of my proposed work was to bring the tools we develop "to the world" to 1) enable researchers around the work to perform sophisticated scientific experiments; 2) use this data to gain new insights into the basic mechanisms of photosynthesis and its responses to the environment; and 3) use this data to improve agriculture, especially in the developing world. We developed the PhotosynQ platform (www.photosynq.org) to specifically address these issues, by bringing sophisticated phenotyping tools and analytics to farmers, researchers, extension agents and entrepreneurs, with the aim of enabling locally appropriate agricultural intelligence solutions. Using the PhotosynQ platform and tools, these communities will generate actionable data that can guide the management and breeding of plants to improve the productivity and sustainability of agriculture in their region. At the same time, the PhotosynQ platform enables the aggregation of regional data sets across the globe (on plant phenotypes, environmental parameters, outcomes), to produce global-level analytics capable of solving both global and local level problems. The PhotosynQ platform includes a sophisticated plant sensor, called the MultispeQ, that makes a series of useful plant and environmental measurements, yet is inexpensive, easy to use, wirelessly connected, expandable and reprogrammable and can be massively deployed anywhere in the world. In the first year of deployment, we have obtained approximately $1M in external funding, deployed 300 MultispeQ devices, engaged more than 980 members, supporting over 600 projects in 18 different countries, resulting in nearly 200,000 experimental points. From a pure scientific point of view, the results from our platforms have given us novel insights and basic understanding of photosynthetic responses to environmental changes, which we are pursuing in research proposed for the PRL renewal and other grants, as well as new crop status indicators, which form the bases of proposals to McKnight and Gates Foundations, ARPA-E etc.

b. Plans for research and related activities for the next five years (two pages).

This year is an exciting and pivotal time for nearly all aspects of my research program. Our efforts over the past 5 years have led to 1) the development of innovative tools that give us the opportunity to study plant phenotypes in transformative ways; 2) establishment of a center at MSU for development of new phenotyping tools; 2) key basic scientific observations that lead us to propose a new framework for understanding how photosynthesis responds (or, more importantly, sometimes fails to respond) to environmental challenges, with potential implications for both basic research and applications to the field; 3) demonstration that our PhotosynQ platform can be deployed around the world, even in developing countries, and obtain potentially actionable data on plant status, including early predictions of disease outbreaks, nutrient status and final crop yield.

In the next 5 years, I plan to build on these successes in several important directions:

1) Tackle some of the most critical (but previously intractable) basic questions about energy transduction in photosynthesis.

Why is photosynthesis so sensitive to rapidly fluctuating light? It is becoming clear that photosynthesis is highly sensitive to rapidly fluctuating environmental conditions, particularly light, and that this sensitivity probably represents a major limitation to crop and bioenergy yields. The mechanisms of this sensitivity are not yet understood, but our recent work strongly suggests that it reflects limitations in the rates of photosynthetic regulatory processes that result in either too low or excessive levels of the thylakoid proton motive force (a key intermediate in both photosynthetic energy transduction and feedback regulation). If our hypothesis is true, we will have not only identified an unexpected “Achilles heel” of photosynthesis, but also a way forward to detecting photosynthetic stress levels, with direct applications for crop monitoring and breeding.

Is photosynthesis too conservative? Over the past year, we have demonstrated both applied and basic applications for the PhotosynQ platform and the MultispeQ devices. *Is photosynthesis over-regulated or under-regulated?* Do plants lose productivity by dissipating more energy than they need to in order to avoid photodamage under rarely-seen fluctuating environmental conditions? NPQ and other regulatory processes act to protect photosynthetic organisms from photodamage, but at the cost of decreased photosynthetic efficiency. It has been proposed that photosynthesis is “over-regulated” and that increased energy conversion might be adjusting these controls under certain conditions. Until now, it has not been possible to directly test this fundamental question, but our new DEPI and PhotosynQ platform are allowing us to engage a broad community of researchers to assess the regulatory set points of a wide range of plants both under controlled conditions and around the world. Our preliminary data suggest that under many conditions photosynthesis is optimally regulated, but that deviations from this balance, particularly under environmental stresses, correlated strongly with photodamage and loss of crop yield (and biomass). If confirmed, these results could have profound impact on both our understanding of the importance of photosynthetic regulation as well as for practical applications for the detection of plant stress, predictions of yield etc.

What do all the chloroplast genes do? An astonishing finding from previous work was that systematically knocking out genes coding for chloroplast-targeted proteins resulted in only a small number of mutants with measurable photosynthetic phenotypes, in spite of the vast majority of these genes being well conserved. The development in the lab and CAAPP of a massive amount of background technologies, from the DEPI phenotyping platform to advanced visualization and statistical methods and software allowed us to show that under more natural-like conditions, the vast majority of chloroplast-targeted genes are, after all, critical for photosynthesis. The big questions we will address next are: how do we make sense of these wide range of effects? What are the basic mechanisms of these effects? What do all these genes do? How does this impact the concept of gene redundancy? We will approach these problems in highly collaborative way, involving a network of labs from PRL, MSU and around the world.

2) Disseminate these tools to the world in innovative ways to impact science at broader scales.

Towards establishing MSU as the center of innovation consortium that will result in a large, open-source database of photosynthetic phenotypes. (see more details in Section f.) We have already started this effort at MSU, by proposing to integrate our phenotyping platforms into existing MSU/AgBioResearch projects to enhance the capabilities of groups at MSU. For example, integration of PhotosynQ into these research projects will 1) empower AgBioResearch groups to collect high-throughput phenotyping data that will improve their understanding of plants' status in response to local conditions; 2) validate the PhotosynQ platform's capabilities in predicting yield and biotic and abiotic stresses; 3) lead to development of new phenotyping tools within the PhotosynQ platform; 4) expand and diversify use case's where PhotosynQ can provide potentially actionable results through plant breeding, crop protection, and crop management studies. Once this effort is established, we hope to expand the effort broadly.

Test if phenotyping tools can be applied to improve agriculture? The PhotosynQ platform also has potential practical applications to agriculture, particularly in the developing world, which not only has the greatest food needs, but also lacks the sophisticated plant monitoring and analytical tools needed to apply cutting edge approaches to agricultural improvement. This past year, we demonstrated that local communities in Africa and the U.S. can effectively use the platform to take high quality phenotype measurements. Most exciting, by analyzing results from multiple MultispeQ field trials in both Africa and the U.S., we were able to develop methods that give early estimates of crop yield and the onset of diseases. Intriguingly, the parameters developed to measure regulation balance (see above) were by far the best correlated with disease or crop yield, suggesting a strong relationship between photosynthetic regulation and sustainable energy capture and storage.

c. Internal and external leadership activities (1 page)

I feel I have played several important leadership roles in research, education and applied sciences both within MSU and internationally. I served on several high profile scientific panels, including the White House Office of Science and Technology Policy (2015) session on "Raising the Profile of Agriculture", scientific workshops (ARPA-E, NSF and PNNL), a DOE-sponsored panel on "The Efficiency of Photosynthesis" that led to a publication in Science (See Blankenship et al., 2011), several grant funding panels (DOE, NSF), external advisory panels for two DOE Energy Frontiers Research Centers. I have also been highly active on editorial boards, and in organizing key scientific meetings, including Chairing a prestigious Gordon Research Conference. I was also twice named as a MSU Global Fellow and currently serve as a mentor for the MSU Academy for Global Engagement. I was invited to give 7 Keynote and Plenary Lectures at international conferences. In 2010, I was given a Patriotic Employee award by the Washington State Air Force Reserves for my support of graduate student vets returning from Iraq, an effort that required changing university and departmental rules.

Leadership role in the critical "transformation" of the PRL. At the time I was recruited to MSU, PRL was under great pressure to alter its core research programs to better align with the energy-related focus of the Basic Energy Sciences programs at the U.S. Department of Energy. My view was (and still is) that PRL could effect this transition by addressing the genotype-to-phenotype problem related to energy capture, conversion and storage. Moreover, this approach could place us at the forefront of the phenotyping revolution in plant sciences. The reviewers and DOE program managers enthusiastically supported this research direction, thus contributing to renewals of the PRL grant, of which I lead an important subproject. I played a further role in shaping the PRL by serving on five faculty search committees, including chairing the successful searches for the new PRL Director, a junior faculty member focusing on synthetic biology, and the targeted hire of a Hannah Professor.

Phenotyping Innovation and Centers and dissemination of MSU technologies. As a part of our efforts to establish MSU as a national/international center for innovation in plant phenotyping, I founded and direct the Center for Advanced Algal and Plant Phenotyping. I feel it is a reflection of my leadership abilities that CAAPP integrates such diverse disciplines and expertise, from engineering, computation and computer science, product development, biophysics and spectroscopy, biology genetics, field research and outreach and that this group has been very productive in catalyzing innovation (producing several product-ready and scientifically useful platforms) and applying them to solve important scientific questions.

Broader impacts. We have led thee way in translating our research and technologies to directly impact science, agriculture and bioenergy efforts and science education on the ground. First, we developed a unique photobioreactor platform that allowed us to study the photosynthetic and growth responses of algae and cyanobacteria under simulate d environmental conditions. To make these tools available to the broader community, we licensed the technology and spun off a company, Phenometrics, Inc., and consequently the ePBR is the most widely-used research photobioreactor in the world, is used in the workflow at several of the largest algal bioenergy companies, and is cited in over 50 publications. We are even more excited by the growing impact of the PhotosynQ.org project (describe above), which is currently allowing us to directly impact international outreach and research, in particular in developing countries in Africa and Central America, which is leading to a new approach to both basic research and improvements to plant breeding and crop management. We are currently leading a new effort to make all CAAPP-developed technologies as widely used.

d. Educational and mentoring contributions, including classroom instruction, curriculum development, and individual mentoring of graduate and undergraduate students and postdoctoral fellows (1 page)

Classroom Instruction at MSU. While only 10% of my appointment is for teaching, I participate in both classroom and one-on-one graduate education. I teach in the graduate-level Plant Biochemistry course (BMB864), in which I cover the basics of photosynthesis. To prepare advanced students graduate students whose research involves photosynthesis and photosynthetic measurements, I developed a 3-credit interactive special topics course (BMB 960-Photosynthesis), which debuted in 2015, and directly addresses fundamental and current thinking in all areas of photosynthesis. A part of the course uses the PhotosynQ platform to enable students to make their own measurements, the interpretations of which are then discussed as a group and presented in a public poster session. The feedback on this course has been very favorable and I am pleased that the majority of the students who took the class are using the concepts, methods and tools directly in their on-going research.

Interdisciplinary training and catalyzed interactions. My lab is heavily involved in undergraduate and graduate student and post-doctoral teaching through hands-on research and development. The opportunity afforded by MSU and the Hannah funds has allowed us to bring together both from a wide range of disciplines and programs, including Biochemistry and Molecular Biology, Chemistry, Computer Science and Engineering, Crops and Soil Sciences, Electrical and Engineering Sciences, Forestry, Genetics and Cell Biology Horticulture, International Programs and Plant Biology. Having all these disciplines interact in the same space while working on common problems has truly facilitated communication, interactive learning and exchanges of ideas. In the past 5 years, my lab has mentored and supported 15 graduate students, 12 post-docs, 3 research assistant professors, 12 international visitors, and more than 40 undergraduates. (All undergraduates in the lab participate in research and/or development; no one is simply a “dishwasher”).

Outreach impact on education. My lab and the CAAPP are providing innovative educational tools to the MSU and international communities: 1) CAAPP has held a series of workshops on plant phenotyping that have been attended by participants across campus; 2) The PhotosynQ platform is particularly well suited for educational applications, potentially to teach both specific concepts and the scientific method. I use the platform in my Photosynthesis class (see above), but also distribute the devices freely to graduate students at many MSU labs as a research training tool. Several other formal classes currently use the platform at MSU (in Biological Sciences Program, College of Natural Science, Horticulture, and at KBS) as well as in other countries (Ukraine, Zambia, Ghana, The Netherlands).

e. What the funds were used for (1 page)

I feel very privileged to be a professor, and even more so to have access to endowment funds provided by the Hannah Professorship. I feel deeply obligated to use this position and these funds to "push the envelope" by pursuing science that would otherwise be out of reach, particularly highly innovative, high-risk/high impact and would benefit the broader community at MSU and beyond. In the following I give examples of how I applied the funds towards these broader aims.

Test risky, but bright ideas and obtain key preliminary studies for external funding. Our track record of success in translating these initially risky ideas to externally-funded project is very high, and nearly all of my externally funded grants have been enabled by these results. I briefly describe two examples of how the Hannah funds allowed us to rapidly take advantage of emerging opportunities by allowing us to apply resources for projects for which it would be difficult or impossible to obtain traditional funding. First, I have long dreamt that we could transform science and education by "bringing the lab to the world." However, without a clear demonstration of its feasibility, it would be almost impossible to get this "big idea" funded. I happened to meet Greg Austic, a singularly talented person with precisely the right skill set and a keen interest in open science. The Hannah funds allowed me to (essentially instantaneously) hire Greg, and set up the initial development leading to the establishment of the PhotosynQ project and nearly $1M in external funding.

In another example, during a conversation about a year ago with Professor Peter Ralph, a colleague from University of Sidney, Australia, we learned that the "Godzilla El Niño "predicted for late 2015 and 2016 was likely to induce a massive coral bleaching event around the world. Though tragic, this event could be a unique opportunity to study the phenomenon. Unfortunately, the existing field-deployable scientific tools have very limited capabilities, are very, require detailed knowledge to operate and unavailable to the vast majority of coral reef researchers around the world (especially in the remote regions). I used Hannah funds to very rapidly (within about two months) test new technology that allowed for production of miniature, very sensitive and robust of spectrophotometers, use this to build and test a new type of instrument, connect these to the PhotosynQ platform, manufacture test units and deploy them to collaborators in Australia and Hawaii. The preliminary results look very interesting and we plan in the next month to build and deploy up to 100 of these to community.

Reach out to experts and connect to new areas of research. For example, I funded travel and instrumentation support to engage photosynthesis expert Jeremy Harbinson from The Netherlands to develop a new method for measuring plant water use efficiency.

Build a research community. For example, I used funds to build web sites, organize workshops (with snacks and in some cases travel), set up a discussion room with free coffee open to all in the Plant Biology Building, etc. I also funded the dissemination (donations and loans) of PhotosynQ devices to various collaborators around the world, catalyzing a range of new projects and collaborations.

Network with potential donors and collaborators. These have been very successful, including funding travel for experts and potential collaborators for visits to my lab, as well as my travel to meet with funding agencies or to present at various meetings. Most recently, I used funds to attend the Plant and Animal Genome conference specifically to meet with representatives from the Gates Foundation and the DOE APRA-E program, resulting in invitations to submit two concept notes and a full proposal.

f. A description of plans for use of additional funding from the position for the next five years (1 page).

In the next period, I will use support to 1) establish our current work as a community resource; and 2) pursue new directions for basic research, innovative development, outreach and applications, initially towards fulfilling the research, educational and outreach directions set out in Section b. Some of these directions are clearly large in scope, “high risk/high return”, and involve building novel communities of researchers both at MSU and around the world. Some of these ideas do fit (at least initially) into traditional funding opportunities, and thus will require the generation of substantial preliminary results, building networks and developing larger grant proposals. In my view, this is precisely the kind of goal that endowment funds can be most usefully applied. Specifically, I plan to continue the kinds of approaches I have used in the past five years, but focusing more on taking advantage of the foundation we have established to address compelling scientific questions and applications.

For example, our major scientific goals can be summarized as “to understand the basic mechanisms of how plants work in their dynamic environments and use this knowledge to improve the efficiency and sustainability of agriculture.” A critical first step is to have the tools to acquire the massive amount of data and metadata needed to understand the complex interactions among genome, environments and phenome. In this context, I am really excited by our progress on both DEPI, PhotosynQ and analytical tools.

The next big steps are to: 1) deploy a network of these platforms (both PhotosynQ and DEPI to make a full phenotyping chain from field to lab) with key partners so we can obtain data sets that were previously unavailable; 2) accelerate the development of the big analytics to understand the data; 3) make the results available to the broader community to enable diverse research groups; and 4) develop agricultural management and agro-economic approaches to test if these tools can be effectively used to improve agriculture; 5) directly test the biophysical and genetic bases of the photosynthetic responses to environment that we observe in the field.

Obviously, my group cannot do all this alone! Indeed, we do not want to lose our focus on our core strengths. On the other hand, progress on our key scientific goals will be greatly enhanced by disseminating our platforms around the world. Thus, I am proposing to form the “MSU Pheno-Q consortium” to bring together groups from academia, national labs, industry and NGO/non-profits, to develop and apply novel phenotyping tools, analytics, educational platforms, needed to approach key scientific and agricultural issues.

Establishing such a consortium will require the investment made available by the Hannah funds to develop scientific networking, outreach, grant proposal development, innovation in phenotyping tools and analytics, and of course scientific insights.

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