BIOGRAPHICAL SKETCH

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NAME: Schloss, Patrick

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POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Cornell University, Ithaca, NY	BS	05/1997	Agricultural and Biological Engineering
Cornell University, Ithaca, NY	PHD	12/2001	Biological and Environmental Engineering
University of Wisconsin, Madison, WI	Postdoctoral Fellow	05/2006	Microbial ecology

A. Personal Statement

My research group is broadly interested in beneficial and pathogenic host-microbiome interactions with the goal of improving our understanding of how the microbiome can be used to reach translational outcomes in the prevention, detection, and treatment of colorectal cancer, Crohn's disease, and *Clostridium difficile* infection. To address these questions we test traditional ecological theory in the microbial context using a systems biology approach. Specifically, my laboratory specializes in using animal models and studies involving human subjects to understand how biological diversity affects community function using a variety of culture-independent genomics techniques including sequencing 16S rRNA gene fragments, metagenomics, and metatranscriptomics. To support these efforts, we also develop and applying bioinformatic tools to facilitate our analysis. This has made us leaders in the field of host-microbiome research. The combination of wet and dry laboratory approaches within my research group and the past oversight of numerous federally-funded projects makes it an ideal environment to conduct the proposed research. My h-index is 37 and our microbiome-focused research spanning 77 publications has been cited more than 14,000 times.

B. Positions and Honors

Positions and Employment

1997 - 2002 Graduate Research Assistant, Dept of Biological and Environmental Engineering, Cornell University, Ithaca, NY
2002 - 2006 Associate Researcher, Dept of Plant Pathology, U of Wisconsin, Madison
2006 - 2009 Assistant Professor, Dept of Microbiology, U of Massachusetts, Amherst
2009 - 2016 Associate Faculty, Center for Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor
2009 - 2013 Assistant Professor, Dept of Microbiology & Immunology, U of Michigan, Ann Arbor
2012 - 2013 Assistant Professor, Dept of Civil & Environmental Engineering, U of Michigan, Ann Arbor
2013 - 2017 Associate Professor, Dept of Microbiology & Immunology, U of Michigan, Ann Arbor
2013 - 2015 Associate Professor, Dept of Civil and Environmental Engineering, U of Michigan, Ann Arbor
2014 - 2017 Editor, Applied & Environmental Microbiology, Washington, DC
2017 - Chair of American Society for Microbiology Journals Board, Washington, DC
2017 - Professor, Dept of Microbiology & Immunology, U of Michigan, Ann Arbor

Other Experience and Professional Memberships

2004 - Member, American Society for Microbiology
2005 - 2010 Member, International Society for Microbial Ecology

Honors

2003	Soil Biology Postdoctoral Fellow, United States Department of Agriculture
2003	University of Wisconsin Teaching Fellowship, Howard Hughes Medical Institute
2008	Chancellor's Junior Faculty Fellow, University of Massachusetts
2013	Distinguished Alumnus, University of Wisconsin Department of Bacteriology
2014	League of Research Excellence, University of Michigan Medical School
2016	Frederick Novy Collegiate Professorship in Microbiome Research
2016	Elected to American Academy for Microbiology

C. Contribution to Science

1. A critical aspect of the scientific method is the ability to reproduce the research performed by others so that the field can correct itself as well as build upon previous work and methods to move forward. My lab's efforts in this area have included implementing these materials in our own research, carrying out meta-analyses to validate and synthesize the work of others, and developing instructional materials to disseminate best practices for insuring that microbiome research is reproducible. Believing that the best way to lead is through our own example, in each of the manuscripts published by the Schloss lab since 2014, our lab has posted the code and literate programming documents for each of our papers to a GitHub repository to insure transparency to better demonstrate the methods behind each of the numbers and figures in our papers. This has led to numerous other research groups being able to build off of our own research. As the Chair of the American Society for Microbiology Journals Board, I am committed to developing protocols to improve the reproducibility of the research reported in our society's journals. To make it easier for others to develop the skills to implement these methods that focus on transparency, automation, version control, and literate programming, we have leveraged funding from an NIH grant to develop instructional materials that others can use to implement the practices used in our lab in their own research. This effort builds upon a tradition in other areas of our laboratory known for producing an open source software package, mothur, which has formalized much microbiome research making it more reproducible. Finally, we believe that carrying out meta-analyses to validate previous efforts and synthesize their results is a powerful method for demonstrating reproducibility. We recently demonstrated the benefit of this approach by tackling the important question of whether there are reproducible microbiome-based biomarkers for human obesity.

    a. Schloss PD. Riffomonas: Instructional materials for reproducible microbiome research. http://riffomonas.org
    b. Schloss PD. Preprinting Microbiology. MBio. 2017 May 23;8(3). e00438-17. PMID: 28536284; PMCID: PMC5442452
    c. Sze MA, Schloss PD. Looking for a Signal in the Noise: Revisiting Obesity and the Microbiome. MBio. 2016 Aug 23;7(4). e01018-16. PubMed PMID: 27555308; PubMed Central PMCID: PMC4999546

2. Whether changes in the microbiome induce tumorigenesis or does the microbiome change as a result of tumorigenesis is the heart of our research into the role of the microbiome in colorectal cancer. Our studies in this area have been significant because they demonstrated an experimental framework for establishing causation in microbiome research. Attesting to the significance of this approach, one reviewer commented, "This is one of the best experimental models I have read of the effect of microbiota on disease progression". We used 16S rRNA gene sequencing to identify changes in the microbiome in a murine model of colon cancer. We then demonstrated that altering the gut community with antibiotics suppressed tumor formation. Finally, when we transferred the original tumor-associated microbiome into germ free mice and applied the tumorigenesis-inducing treatment, we observed an increase in the number and size of tumors. Overall, our results point to the microbiome as a necessary component to the process of tumorigenesis. As we state in the paper, the microbiome interacts with the immune system to "create an increasingly inflammatory environment that generated a self-reinforcing pathogenic cascade between the gut microbiome and the host ultimately leading to the development of cancer." The first wave of microbiome research has been limited to the characterization of the composition of the microbiome under a variety of conditions. This study is significant because it moves beyond this threshold and delves into designing experiments that manipulate the communities to test predictions about the role of the

microbiome. Furthermore, it demonstrates an extreme level of rigor that my lab is working at to understand the role of the microbiome in health and disease.

a. Zackular JP, Baxter NT, Iverson KD, Sadler WD, Petrosino JF, Chen GY, Schloss PD. The gut microbiome modulates colon tumorigenesis. MBio. 2013 Nov 5;4(6):e00692-13. PubMed PMID: 24194538; PubMed Central PMCID: PMC3892781.

b. Zackular JP, Rogers MA, Ruffin MT 4th, Schloss PD. The human gut microbiome as a screening tool for colorectal cancer. Cancer Prev Res (Phila). 2014 Nov;7(11):1112-21. PubMed PMID: 25104642; PubMed Central PMCID: PMC4221363.

c. Zackular JP, Baxter NT, Chen GH, Schloss PD. Manipulation of the gut microbiota reveals role in colon tumorigenesis. *mSphere*. 2015 Nov;1(1):e00001-15. PubMed PMID: 27303681; PubMed Central PMCID: PMC4863627.

d. Baxter NT, Ruffin MT IV, Rogers MAM, Schloss PD. Microbiota-based model improves the sensitivity of fecal immunochemical test for detecting colonic lesions. *Genome Medicine*. 2016: Apr;8:37. PubMed PMID: 27056827; PubMed Central PMCID: PMC4823848.

3. Sequencing 16S rRNA genes and clustering those sequences into operational taxonomic units (OTUs) is the primary analysis method that underlies most microbiome research projects. When I began developing software to analyzing 16S rRNA gene sequences, researchers either assigned sequences to OTUs manually or they used private scripts. Our tool, DOTUR, automated and standardized the process and made the source code publicly available. DOTUR has gone on to be cited 1,650 times since it was published in 2005 (Web of Science, 5/22/2015). Noticing that a growing number of tools were being published without providing their source code, we resolved to create a fully open source software package that any researcher could use to perform a broader set of analyses. The result was mothur. In the five years since it was published, mothur has been cited more than 4,600 times, while the closest competitor, QIIME (published at approximately the same time) has been cited 4,500 times. We are able to keep mothur relevant through regular feature releases and by publishing articles that describe and test new algorithms. The long list of co-authors attests to our mission of serving the research community. While the first three authors wrote the source code, the rest provided documentation and a diverse array of use cases. We are frequently commended for supporting the diverse community of researchers who frequently have limited bioinformatics skills. We are proud of the broad adoption of mothur by users across the microbiome field and around the world. The citations alone are a measure of the significance of this paper. More importantly, mothur has resulted in the standardization of methods and increased the bioinformatics literacy within the field. Sequencing of 16S rRNA genes will continue to be part of microbiome research and mothur will remain a significant part of that effort.

a. Schloss PD, Westcott SL, Ryabin T, Hall JR, Hartmann M, Hollister EB, Lesniewski RA, Oakley BB, Parks DH, Robinson CJ, Sahl JW, Stres B, Thallinger GG, Van Horn DJ, Weber CF. Introducing mothur: open-source, platform-independent, community-supported software for describing and comparing microbial communities. Appl Environ Microbiol. 2009 Dec;75(23):7537-41. PubMed PMID: 19801464; PubMed Central PMCID: PMC2786419.

b. Schloss PD, Westcott SL. Assessing and improving methods used in operational taxonomic unit-based approaches for 16S rRNA gene sequence analysis. Appl Environ Microbiol. 2011 May;77(10):3219-26. PubMed PMID: 21421784; PubMed Central PMCID: PMC3126452.

c. Kozich JJ, Westcott SL, Baxter NT, Highlander SK, Schloss PD. Development of a dual-index sequencing strategy and curation pipeline for analyzing amplicon sequence data on the MiSeq Illumina sequencing platform. Appl Environ Microbiol. 2013 Sep;79(17):5112-20. PubMed PMID: 23793624; PubMed Central PMCID: PMC3753973.

4. Primary succession is the process by which populations of organisms colonize a habitat without the influence of organisms that previously inhabited the environment. Examples include the conversion of volcanic lava flows to forests or the colonization of the sterile gut of an infant. Whether assembly of these communities is a product of neutral or deterministic processes is a matter of significant debate in the literature. This is also a question of significant biomedical interest as colonization of the gut of pre-term infants can lead to necrotizing entercolitis and it impacts how communities reassemble after an antibiotic

perturbation. With this in mind, we colonized germ-free mice with a murine gut microbiome and tracked the succession of the populations. To better understand the mechanisms that were involved in colonization, we used generalized Lotka-Volterra dynamic models to quantify the intrinsic growth rates of each population and the types of interactions between the populations. While this manuscript was significant because it was the first to apply this type of modeling to a microbial community, its true significance was due to our use of a systems biology approach to understanding the ecology of individual populations. We know that very few bacteria are readily cultured in the laboratory. Even if they could be grown in the laboratory it would be under artificial conditions on nutrient-rich media with idealized conditions. This would make it difficult to truly understand the in vivo growth and ecology of these populations. Through our modeling, we were able to demonstrate that a lack of mutualistic interactions between the bacterial populations in the murine microbiome led to a stable and reproducible gut microbiome. We are currently expanding this work to understand how perturbations to the system through the use of antibiotics, diet manipulations, and exogenous populations, affect the interactions within the community.

a. Schloss PD, Schubert AM, Zackular JP, Iverson KD, Young VB, Petrosino JF. Stabilization of the murine gut microbiome following weaning. Gut Microbes. 2012 Jul-Aug;3(4):383-93. PubMed PMID: 22688727; PubMed Central PMCID: PMC3463496.
b. Schloss PD, Iverson KD, Petrosino JF, Schloss SJ. The dynamics of a family's gut microbiota reveal variations on a theme. Microbiome. 2014;2:25. PubMed PMID: 25061514; PubMed Central PMCID: PMC4109379.
c. Marino S, Baxter NT, Huffnagle GB, Petrosino JF, Schloss PD. Mathematical modeling of primary succession of murine intestinal microbiota. Proc Natl Acad Sci U S A. 2014 Jan 7;111(1):439-44. PubMed PMID: 24367073; PubMed Central PMCID: PMC3890833.
d. Baxter NT, Wan JJ, Schubert AM, Jenior ML, Myers P, Schloss PD. Intra- and inter-individual variations mask interspecies variation in the microbiota of sympatric peromyscus populations. Appl Environ Microbiol. 2015 Jan;81(1):396-404. PubMed PMID: 25362056; PubMed Central PMCID: PMC4272734.

5. My research group participated in the first phase of the Human Microbiome Project (HMP) as a member of the Data Analysis Working Group. We developed the data curation pipeline that was used to process the data that was ultimately used in publications from the first phase of the project. This series of papers has symbolic significance indicating my overall service to the community of microbiome researchers. Several dozen papers were published from the HMP in the initial phase that were based on a single time point, including several involving my lab. The HMP has since released data collected from additional time points. The final dataset included sampling 300 individuals at up to 18 body sites on two or three occasions. In Ding & Schloss (2014), we asked whether there were enterotypes, or more broadly, community types, that could be identified at the 18 body sites across the body. Previous analyses were limited to single time points and were unable to quantify the stability of community types through time. To address these questions, we characterized the stability of the community types at each body site, identified associations between the community types found at each body site, and quantified the association between each community type and the subjects' metadata. Overall, we showed that the interpersonal variation of the microbiome sampled from healthy individuals is considerable and that we still do not understand which factors drive differences in the structure of the microbiome. This study was significant because it demonstrated that "healthy" does not represent matching some ideal microbiome composition. Furthermore, it established a framework to connect clinical data with community types that will prove useful in developing diagnostics and assessing risks for developing diseases.

a. A framework for human microbiome research. Nature. 2012 Jun 13;486(7402):215-21. PubMed PMID: 22699610; PubMed Central PMCID: PMC3377744.
b. Structure, function and diversity of the healthy human microbiome. Nature. 2012 Jun 13;486(7402):207-14. PubMed PMID: 22699609; PubMed Central PMCID: PMC3564958.
c. Ding T, Schloss PD. Dynamics and associations of microbial community types across the human body. Nature. 2014 May 15;509(7500):357-60. PubMed PMID: 24739969; PubMed Central PMCID: PMC4139711.

6. The standard microbiome analysis will determine whether the communities from healthy and diseased individuals have the same diversity or composition. By analogy, these studies are similar to genome-wide association studies that seek to identify single alleles that can be associated with the disease. Just as geneticists sought out the gene responsible for Huntington's Disease, there are microbiome researchers searching for the "obesity bug". It is far more likely that the microbiome involvement for many diseases is analogous to polygenic traits. Geneticists are also looking for the combination of alleles that result in diabetes and so microbiome researchers need to seek out the consortia within the broader microbiome that is responsible for colon cancer. Another difficulty with the standard microbiome study is that they rarely incorporate clinical data; even if the clinical data are reported it only serves a descriptive role and is not incorporated into the overall analysis. In this study we overcame these limitations to identify the subsets of microbiome found in patients' microbiomes that were associated with *Clostridium difficile* colonization. *C. difficile* infections have emerged as the leading nosocomial infection in the US. Through animal models and epidemiological studies, it has been determined that antibiotic perturbations alter the composition of the gut microbiome to allow colonization by *C. difficile*. We sequenced the microbiome of individuals with and without diarrhea and used their microbiome and clinical data to identify collections of bacteria and clinical data that were associated with *C. difficile* infection. This was a significant result demonstrating that incorporating the microbiome into diagnostic and risk models improve models based on clinical data alone. In subsequent work in my laboratory, we are using similar approaches to identify individuals with early-stage colon cancer. We are also addressing these results using animal models of *C. difficile* infection. For the first time, it appears possible to use the microbiome to assess risk of disease.

    a. Reeves AE, Theriot CM, Bergin IL, Huffnagle GB, Schloss PD, Young VB. The interplay between microbiome dynamics and pathogen dynamics in a murine model of Clostridium difficile Infection. Gut Microbes. 2011 May-Jun;2(3):145-58. PubMed PMID: 21804357; PubMed Central PMCID: PMC3225775.
    b. Schubert AM, Rogers MA, Ring C, Mogle J, Petrosino JP, Young VB, Aronoff DM, Schloss PD. Microbiome data distinguish patients with Clostridium difficile infection and non-*C. difficile*-associated diarrhea from healthy controls. MBio. 2014 May 6;5(3):e01021-14. PubMed PMID: 24803517; PubMed Central PMCID: PMC4010826.
    c. Schubert AM, Sinani H, Schloss PD. 2015. Antibiotic-induced alterations of the murine gut microbiota and subsequent effects on colonization resistance against *Clostridium difficile*. mBio. 6: e00974-15. PubMed PMID: 26173701; PubMed Central PMCID: PMC4502226.

Additional publications:
http://www.ncbi.nlm.nih.gov/sites/myncbi/patrick.schloss.1/bibliography/45109108/public

D. Research Support

Ongoing Research Support

2016/03/01-2021/02/28
U01 AI124255-01, National Institute of Allergy and Infectious Diseases (NIAID)
Young, Vincent B (contact-PI) & Schloss, Patrick David (multi-PI)
Systems biology of *Clostridium difficile* infection
Model the infection and severity of Clostridium difficile in hospital and long-term care facilities
Role: dual-PI

2015/09/01-2017/08/31
R25GM116149-01, National Institute of General Medical Sciences (NIGMS)
Schloss, Patrick David (PI)
Development of reproducible informatics skills among microbiome researchers
Developing instructional materials to improve reproducible informatics skills among microbiome researchers
Role: PI

Completed Research Support

2010/09/27-2014/06/30
R01 HG005975-03, National Human Genome Research Institute (NHGRI)
Schloss, Patrick David (PI)
Identifying population-level variation in cross-sectional and longitudinal HMP studies
Develop the mothur software package to accommodate the rapidly changing sequencing technologies and enable human microbiome research.
Role: PI

2012/02/01-2016/01/31
R01 GM099514-01, National Institute of General Medical Sciences (NIGMS)
Schloss, Patrick David (PI)
Diversity and stability relationships in the murine microbiome
Characterize the succession of the gut microbiota in colonized germ-free mice and following antibiotic perturbations.
Role: PI