BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Luque, Antoni

eRA COMMONS USER NAME (credential, e.g., agency login): a_luque

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. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE (if applicable) | END DATE MM/YYYY | FIELD OF STUDY |
|---|---------------------------|---------------------|----------------------------------|
| University of Barcelona, Barcelona, Not Applicable, N/A | BS | 08/2006 | Physics |
| University of Barcelona, Barcelona, Not Applicable, N/A | MS | 08/2007 | Biophysics |
| Universitat de Barcelona, Barcelona, Not Applicable, N/A | PHD | 06/2011 | Physical Virology |
| New York University, New York, NY | Postdoctoral Fellow | 10/2014 | Chromatin multiscale modeling |

A. Personal Statement

I am an Associate Professor of Biology, and my research is focused on the physical properties and evolution of viral capsids. I have an interdisciplinary background in biophysics, with training in thermodynamics and statistical mechanistic, molecular coarse-graining, and predictive modeling. My interdisciplinary understanding of science has been shaped and expanded as I navigated different departments and cultures throughout my career, including Departments in Physics, Chemistry, Mathematics and Statistics, and Biology. The R21 technology development proposal presented here crystalizes my interest in using my accumulated knowledge over 15 years of basic research to take a leap toward applied science to have a more immediate impact on society. The proposed innovations rely strongly on integrating core elements of my research, including the generalized geometrical theory of viral capsids, classical nucleation theory of viral capsids, virus structural bioinformatics, and multiscale molecular modeling of capsids. My publications in this section capture some of the newest ideas and methods behind this proposal. My publications in the Contributions to Science section emphasize some longer-term foundational aspects. I also want to highlight recent funded projects that provide evidence of my ability to lead, collaborate, and deliver on research proposals. In particular, the NSF 1951678 award, which is now concluding, and I led as sole PI, focused on the "Characterization and prediction of viral capsid geometries," setting the stage for this proposal, including nine peer-reviewed publications. In the project, GBMF 9871, I am working in a multi-PI team to discover new viruses of bacteria, which has facilitated me to explore new methods to test my predictions, which I am adapting here to investigate the new system in this proposal. In summary, I have the expertise, leadership, and discipline to carry out the proposed research project. Ongoing and recently completed project that I would like to highlight include:

Ongoing and recently completed projects that I want to highlight:

GBMF 9871 – Gordon and Betty Moore Foundation Rohwer (PI), Role: co-PI 01/11/21 – 31/12/2024 Perpetual viral origins

NSF 1951678 Luque (PI) 01/09/2020 – 30/08/2024 Characterization and prediction of viral capsid geometries

- 1. Brown C, Agarwal A, Luque A. pyCapsid: identifying dominant dynamics and quasi-rigid mechanical units in protein shells. Bioinformatics. 2024 Jan 2;40(1) PubMed Central PMCID: PMC10786678.
- Lee DY, Bartels C, McNair K, Edwards RA, Swairjo MA, Luque A. Predicting the capsid architecture of phages from metagenomic data. Comput Struct Biotechnol J. 2022;20:721-732. PubMed Central PMCID: PMC8814770.
- 3. Luque A, Benler S, Lee DY, Brown C, White S. The Missing Tailed Phages: Prediction of Small Capsid Candidates. Microorganisms. 2020 Dec 8;8(12) PubMed Central PMCID: PMC7762592.
- 4. Twarock R, Luque A. Structural puzzles in virology solved with an overarching icosahedral design principle. Nat Commun. 2019 Sep 27;10(1):4414. PubMed Central PMCID: PMC6765026.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

| 2023 - | Associate Professor, University of Miami, Department of Biology, Coral Gables, Florida |
|---------------|--|
| 2021 - | Recurrent reviewer panelist at the Mathematical Biology program, National Science Foundation |
| 2021 - 2023 | Associate Professor, San Diego State University, Department of Mathematics & Statistics, San Diego, California |
| 2020 - | Recurrent reviewer panelist at the Division of Molecular Cell Biology, National Science Foundation |
| 2015 - 2021 | Assistant Professor, San Diego State University, Department of Mathematics & Statistics, San Diego, CA |
| 2012 - 2014 | Postdoc, New York University, Department of Chemistry, New York, NY |
| <u>Honors</u> | |
| 2007 - 2010 | PhD Research Fellowship, Government of Catalonia, Spain |
| 2020 | Student Research Mentor Hall of Fame, San Diego State University |
| 2019 | Outstanding Faculty Award from the College of Sciences, San Diego State University |
| 2019 | Outstanding Faculty Award from the Department of Physics, San Diego State University |
| 2018 | Faculty Innovation and Leadership Award, California State University |

- 2017 Outstanding Faculty Award from the Department of Physics, San Diego State University
- 2017 Center for Teaching and Learning Academy Award, San Diego State University
- 2012 PhD Thesis Clausetre de Doctors Honors Award, Universitat de Barcelona
- 2011 PhD Thesis Honor Award, Government of Catalonia, Spain
- 2007 Extraordinary Master Thesis Award in Biophysics, Universitat de Barcelona

C. Contribution to Science

1. I have contributed to 30 scientific publications, including high-impact journals ranging from generalist journals like Nature and PNAS to specialized ones like Nucleic Acids Research and Bioinformatics. My early career publications, associated with my Master's and PhD research and under the supervision of Dr. David Reguera at the Universitat de Barcelona, focused on theoretical physical models to investigate the structure, mechanical properties, and self-assembly of viral capsids. That is when I had my first opportunity to contribute to the geometrical theory of viral capsids, expanding it to describe the landscape of geometrically possible and physically favorable elongated capsids. An important follow-up work, in collaboration with atomic force microscopy experiments, demonstrated that mechanical pre-stress reinforces the capsids of elongated shells like phage phi29 to sustain the internal pressures associated with the packing of its genome at quasi-crystalline densities, building up more than 50 atmospheres. In collaboration with cryo-electron microscopy experiments, I also revealed the molecular reinforcement of other capsids, like phage T7. Additionally, combining the

classical nucleation theory of viral capsids with coarse-grained simulations, I identified a new physical mechanism involved in the last steps of viral capsid assembly, which favors mechanically stressed capsids instead of the most ideally relaxed molecular configurations. Overall, my initial work on the structure, mechanical properties, and self-assembly of viral capsids yielded eight publications, including three key ones highlighted below.

- Luque A, Reguera D. Theoretical Studies on Assembly, Physical Stability and Dynamics of Viruses. Subcellular Biochemistry [Internet] Dordrecht: Springer Netherlands; 2013. Chapter Chapter 19553-595p. Available from: https://link.springer.com/10.1007/978-94-007-6552-8_19 DOI: 10.1007/978-94-007-6552-8_19
- b. Luque A, Reguera D, Morozov A, Rudnick J, Bruinsma R. Physics of shell assembly: Line tension, hole implosion, and closure catastrophe. The Journal of Chemical Physics. 2012 May 14; 136(18):-. Available from: https://pubs.aip.org/jcp/article/136/18/184507/190580/Physics-of-shell-assembly-Line-tension-hole DOI: 10.1063/1.4712304
- c. Carrasco C, Luque A, Hernando-Pérez M, Miranda R, Carrascosa JL, Serena PA, de Ridder M, Raman A, Gómez-Herrero J, Schaap IA, Reguera D, de Pablo PJ. Built-in mechanical stress in viral shells. Biophys J. 2011 Feb 16;100(4):1100-8. PubMed Central PMCID: PMC3037554.
- d. Luque A, Zandi R, Reguera D. Optimal architectures of elongated viruses. Proc Natl Acad Sci U S A. 2010 Mar 23;107(12):5323-8. PubMed Central PMCID: PMC2851771.
- 2. In my postdoc, I moved to the Department of Chemistry at New York University to investigate chromatin under the supervision of Dr. Tamar Schlick, using multiscale molecular modeling that combined all-atom molecular dynamics to advanced Monte-Carlo sampling methods and continuum electrostatics methods like the Poisson-Boltzmann equation. This allowed me to investigate how posttranslational modifications in linker histones can regulate the compaction of chromatin. I also identified a thermodynamic relationship between the concentration of linker histones and the linker DNA length between nucleosomes. At the end of my postdoc, I proposed a new multiscale framework to incorporate Hi-C data with molecular simulations as part of a summative review. Overall, I contributed to three publications on the chromatin field, as highlighted below.
 - Luque A, Ozer G, Schlick T. Correlation among DNA Linker Length, Linker Histone Concentration, and Histone Tails in Chromatin. Biophysical Journal. 2016 June; 110(11):2309-2319. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0006349516302193 DOI: 10.1016/j.bpj.2016.04.024
 - b. Ozer G, Luque A, Schlick T. The chromatin fiber: multiscale problems and approaches. Current Opinion in Structural Biology. 2015 April; 31:124-139. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0959440X15000548 DOI: 10.1016/j.sbi.2015.04.002
 - Luque A, Collepardo-Guevara R, Grigoryev S, Schlick T. Dynamic condensation of linker histone C-terminal domain regulates chromatin structure. Nucleic Acids Res. 2014 Jul;42(12):7553-60. PubMed Central PMCID: PMC4081093.
- 3. Based on my PhD and postdoc, as an independent researcher, I had envisioned focusing on investigating viruses that store their genome in the form of chromatin, like the human papillomavirus. However, the rapid emergence of next-generation sequencing applied to study uncultured viruses changed my focus because I became fascinated with the possibility of exploring the physical properties of uncultured viruses across environmental conditions. I joined the Viral Information Institute at San Diego State University (SDSU) as an Assistant Professor of Mathematics and Statistics because researchers at SDSU had pioneered the field of viral metagenomics and allowed me to expand on my skills in dynamical systems, statistical learning, and bioinformatics, contributing to a variety of problems in viral ecology regarding the conditions associated with the switch between the lytic and latent lifestyle of viruses in the environment. I contributed to 10 publications on viral ecology, including the three key publications highlighted below.

- Luque A, Silveira CB. Quantification of Lysogeny Caused by Phage Coinfections in Microbial Communities from Biophysical Principles. mSystems. 2020 Sep 15;5(5) PubMed Central PMCID: PMC7498681.
- b. Joiner KL, Baljon A, Barr J, Rohwer F, Luque A. Impact of bacteria motility in the encounter rates with bacteriophage in mucus. Sci Rep. 2019 Nov 11;9(1):16427. PubMed Central PMCID: PMC6848219.
- c. Knowles B, Silveira CB, Bailey BA, Barott K, Cantu VA, Cobián-Güemes AG, Coutinho FH, Dinsdale EA, Felts B, Furby KA, George EE, Green KT, Gregoracci GB, Haas AF, Haggerty JM, Hester ER, Hisakawa N, Kelly LW, Lim YW, Little M, Luque A, McDole-Somera T, McNair K, de Oliveira LS, Quistad SD, Robinett NL, Sala E, Salamon P, Sanchez SE, Sandin S, Silva GG, Smith J, Sullivan C, Thompson C, Vermeij MJ, Youle M, Young C, Zgliczynski B, Brainard R, Edwards RA, Nulton J, Thompson F, Rohwer F. Lytic to temperate switching of viral communities. Nature. 2016 Mar 24;531(7595):466-70. PubMed PMID: 26982729.
- 4. Finally, as I transitioned from Assistant professor to Associate professor, I was able to start integrating my early molecular research on capsids and genomes with my latest work on viral ecology to further expand on my interest in the evolution and diversity of capsids. This led to a key publication that showed how the finite number of geometrical tiles compatible with icosahedral capsids explains the limited number of conserved capsid protein folds observed in the virosphere. Building on the conserved HK97-fold, I combined theoretical biophysical, machine learning, and bioinformatics to find evidence of viral genomes encoding small capsids that had not been isolated among tailed phages, representing a milestone in physical virology on how to search for new structural properties in capsids among uncultured viruses. I am currently invested in developing new computational coarse-grained methods and experimental collaborations to further characterize the stability and assembly conditions of capsids of uncultured viruses for biotechnological applications. The following four publications capture our most relevant recent contributions in exploring the evolution and diversity of capsids.
 - Brown C, Agarwal A, Luque A. pyCapsid: identifying dominant dynamics and quasi-rigid mechanical units in protein shells. Bioinformatics. 2024 Jan 2;40(1) PubMed Central PMCID: PMC10786678.
 - Lee DY, Bartels C, McNair K, Edwards RA, Swairjo MA, Luque A. Predicting the capsid architecture of phages from metagenomic data. Comput Struct Biotechnol J. 2022;20:721-732. PubMed Central PMCID: PMC8814770.
 - c. Luque A, Benler S, Lee DY, Brown C, White S. The Missing Tailed Phages: Prediction of Small Capsid Candidates. Microorganisms. 2020 Dec 8;8(12) PubMed Central PMCID: PMC7762592.
 - d. Twarock R, Luque A. Structural puzzles in virology solved with an overarching icosahedral design principle. Nat Commun. 2019 Sep 27;10(1):4414. PubMed Central PMCID: PMC6765026.

<u>Complete List of Published Work in My Bibliography:</u> https://www.ncbi.nlm.nih.gov/myncbi/antoni.lugue santolaria.2/bibliography/public/