ANNA LEA SCHOULTIES NAFF was born on a small farm in Northern Kentucky, November 29, 1920. Her early education and that of a younger brother began at Dale Grade School and continued through Cold Spring High where her favorite subject was mathematics. She was the salutatorian for her high school class. After finishing high school Anna worked during the summers and studied at Eastern Kentucky University for two years. She worked at Williamson Heater, Cincinnati for a year before transferring to the University of Kentucky's Department of Home Economics. Her graduation in 1944 was "with DISTINCTION". Receipt of a Haggin Fellowship enabled Anna to take up undergraduate and graduate work in Chemistry. She received a Master of Science in 1946 and her thesis was published in 1947.

Anna married Benton Naff in December 1946 in Portland, Oregon. She taught chemistry at the University of Kentucky 1946-47 and at Oregon State University 1947-50. While her husband was located at Bowling Green State University, Ohio, Anna attended the University of Michigan Ann Arbor and earned a Master of Arts Degree in Library Science. At that time (1953) she began research with the Owens Illinois Glass Company exploring the properties of epoxy resins and silicones. Her investigations resulted in an important practical contribution,--the invention of an organic ink for use on glass; patent issued 1958.

The family moved from Ohio in 1955. Anna continued research but in an academic environment. She assisted her husband in the acquisition of grants and produced a number of chemical research publications (1955-63). From the Fall of 1964 to the end of the summer of 1965 when her husband was on a Sabbatical, Anna served as a Cataloger in the Main Library at Brown University. A year later she went back to library work, first at the National Bureau of Standards and then at the National Institutes of Health. The work in Acquisition and Cataloging areas provided significant professional advancement and she continued to work at N.I.H. until near the end of her career. Anna died September 21, 1973.

The Department of Chemistry at the University of Kentucky organizes an annual Symposium on Chemistry and Molecular Biology.

This Symposium was established in honor of Anna S. Naff, a University of Kentucky graduate, through the generous support of Dr. Benton Naff of the N.I.H. The Symposium has an interdisciplinary character and is attended by students and faculty from Chemistry, Biochemistry, Biology, Pharmacy, Engineering, Medicine. Agriculture and Symposium features renowned experts from around the world, including Nobel prize-winning scientists, and is attended by faculty and students from colleges and universities in Kentucky and the contiguous States.

The Mechanobiology of the Genome

NAFFsymposium

Annual

April 4, 2025

Healthy Kentucky Research Building

College of Arts and Sciences

### Schedule

 $8:\!\!30_{\!\scriptscriptstyle AM}$  Registration and Welcome

Ryan Cheng, Ph.D.

# 9:00<sub>AM</sub> Dr. Dennis E. Discher From curvature sensing and rupture to chromosome loss

The nuclear membrane reassembles around chromosomes after cell division. Two types of filamentous 'lamin' proteins localize to the membrane-chromosome interface, and exhibit different sensitivities to nuclear deformation. One type is more ancient and is always expressed but depletes at sites of high curvature. The other lamin accumulates when the nucleus is stressed and helps modulate differentiation but also prevents nuclear rupture. Tissue profiling supports the in vitro findings, and tumor profiling shows similar trends for mutations including chromosome losses that drive cancer. Our methods and insights are helping to clarify roles for nuclear rupture and/or division errors in chromosome loss.

### 10:30 Dr. Andrew Stephens

# Interphase based changes from G1 to G2 in actin and nuclear mechanics dictate nuclear integrity

The structural integrity of the nucleus and genome protection are dependent on nuclear mechanical elements of chromatin and lamins to resist the antagonistic forces of the actin cytoskeleton. Failure of the nucleus to resist antagonistic forces cause abnormal nuclear shape and blebbing, rupture, and cellular dysfunction found in many human diseases and cancers. As the nucleus grows during the interphase cell cycle the amount and composition of the chromatin and lamins changes, which could affect nuclear blebbing. To determine the effect of G1, S, and G2 interphase stages on nuclear blebbing and integrity, we tracked cells using Fluorescent Ubiquitin Cell Cycle Indicator (FUCCI) and labeling of S phase nuclei using bromodeoxyuridine (BrdU). Static population images show that nuclear blebs are present at equal levels as the total population in G1, S, and G2 for wild type and perturbations known to increase nuclear blebbing. Time lapse imaging reveals that nuclear blebs form predominantly in G1 and then persist into S and G2.

Measurements ofactin-based nuclear confinement reveal G1 nuclei are under greater confinement and have more focal adhesion density than late S/G2 nuclei. We applied artificial confinement to determine if actin confinement underlies nuclear blebbing and rupture. Upon increased artificial confinement, G2 nuclei lost nuclear integrity more frequently and under less confinement than G1 nuclei, suggesting G2 nuclei are weaker than G1 nuclei. Single nucleus micromanipulation force measurements confirm that G1 nuclei are stronger than G2 nuclei which showed both a decreased chromatin-based short extension rigidity and decreased lamin-based strain stiffening at long extension. We show novel findings of drastic changes in both nuclear and actin mechanics throughout the interphase stages of the cell cycle that drastically impact nuclear shape and integrity.

#### 11:30<sub>AM</sub> Coffee Break

12:00 Poster Session

### 2:30<sub>PM</sub> Dr. John Marko

## Self-organization of DNA-protein complexes and chromosomes

The chromosomes of all cells are based on tremendously long DNA molecules, with folding, geometry and toplogy regulated and dynamic throughout the cell cycle. Our group uses biophysical, cell-biological and mathematical approaches to study individual protein-DNA interactions and the structure and dynamics of whole chromosomes. I will discuss the surprising kinetics we have discovered for individual protein-DNA interactions, and the potential role of active ATP-powered "loop extrusion" processes in the folding, individualization and segregation of chromosomes, with particular attention to eukaryote mitosis.

3:30 Presentation of poster

4:00<sub>PM</sub> Close of the 50th Naff Symposium

### Speakers

#### Dennis E. Discher, Ph.D.

Robert D. Bent Professor

Director, Physical Sciences Oncology Center/Project at University of Pennsylvania



The Discher lab has sought to identify and elucidate some soft matter concepts across cell, molecular and tissue biology. They also have, occasionally, used biological approaches to inject some biological insights into soft matter science and engineering. Early discoveries included matrix elasticity effects on stem cell maturation and differentiation (Cell 2006), mechanosensing by a cell's nucleus (Science 2013), and properties scaling of amphiphilic polymer assemblies for nano-delivery (Science 2002). Current

efforts focus on physics-driven evolution of mutations (Cell 2016) and engineering of macrophages to attack solid tumors (Nat BME 2023). The latter followed molecularly detailed studies of 'foreign' versus 'self' recognition (Science 2013). Dozens of trainees have secured positions in academia or industry around the world. Discher has been elected to the US National Academy of Medicine, the US National Academy of Engineering, and the American Association for the Advancement of Science, and he serves on Editorial Boards of Science, Molecular Biology of the Cell, and PNAS Nexus among other journals.

#### Andrew Stephens, Ph.D.

Assistant Professor, Department of Biology University of Massachusetts Amherst



Prof. Andrew Stephens was born and raised in Kansas City, Missouri. He received his undergraduate degree from the University of Missouri, Kansas City and studied dynein processivity in single molecule assays. Stephens completed his Ph.D. at the University of North Carolina Chapel Hill in Dr. Kerry Bloom's lab where he studied the pericentromeric chromatin spring's essential role in yeast mitosis. He continued as a Post Doc in Dr. John Marko's lab at the University of Northwestern to adapt micromanipulation force

measurements to single nuclei and study the importance of chromatin mechanics in controlling abnormal nuclear morphology which is present in many human diseases. He is now an Assistant Professor at the University of Massachusetts Amherst. The Stephens Lab was started in 2020 and uses a combination of nuclear force measurements and cell biology to determine the mechanical force balance between the nucleus and the cytoskeleton which controls nuclear shape, integrity, and function.

#### John F. Marko, Ph.D.

Professor, Department of Physics & Astronomy and Molecular Biosciences Northwestern University



John Marko is a professor of Physics & Astronomy and Molecular Biosciences at Northwestern University in Evanston, Illinois. He graduated from the University of Alberta, Edmonton with a B.Sc. in physics in 1984, then received his Ph.D. in physics from Massachusetts Institute of Technology in 1989. Prof. Marko's research interests include biological physics, statistical mechanics and theoretical soft matter physics applied to problems of self-organization in molecular and cell biology. The Marko lab uses biophysical methods, with

particular emphasis on micromanipulation of single DNA molecules and single chromosomes, to study the internal structure of chromosomes in vivo, and to study chromosome-organizing proteins and DNA topoisomerases in vitro. They also develop mathematical models relevant to these types of experiments. Projects in progress involve combining fluorescence microscopy and force microscopy in experiments on DNA-protein complexes and whole chromosomes, and in-vivo studies of coupling of chromosome dynamics to gene expression.