BIOGRAPHICAL SKETCH

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NAME: **Goldstein, Robert Patrick (Bob)**

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

POSITION TITLE: James L. Peacock III Distinguished 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	Completion Date	FIELD OF STUDY
Union College, Schenectady, NY	BS	6/1988	Biology
University of Texas, Austin, TX	PhD	12/1992	Developmental Biology
MRC Laboratory of Molecular Biol., Cambridge UK	Postdoc	8/1996	Cell Biology
University of California, Berkeley, CA	Postdoc	4/1999	Evolution & Development

A. Personal Statement

We seek to understand cell biological mechanisms of animal development, a topic of study for which *C. elegans* is especially well suited. We have used cell manipulation, live imaging of subcellular dynamics, biophysical measurements, and the identification and study of key proteins to make contributions toward answering fundamental questions: how cells change shape, how cells change positions, how cells become polarized, and how cells divide in specific orientations. And we have worked to develop new methods for *C. elegans* to advance our goals and to facilitate progress by the field. We have used *Drosophila* and *Xenopus* to test the extent to which phenomena we discover in worms extend more generally.

We have also worked to develop tardigrades (also known as water bears) as a new model system for studying the evolution of developmental mechanisms and for investigating how biological materials can survive extremes.

14 postdocs have trained in the lab (nine are now in faculty positions, one is in industry, and three are currently in the lab, one of whom will start a faculty position this summer) as well as 18 graduate students (including four currently in the lab, one in a faculty position, two currently in postdocs, a scientific editor, two professional scientists in industry, and two working in professional microscopy careers).

B. Positions, Scientific Appointments, and Honors

Positions

1999-present	UNC Chapel Hill Biology Department faculty, Member of Lineberger Comprehensive Cancer Center and Curriculum in Genetics and Molecular Biology
1996-1999	University of California, Berkeley, Miller Institute Research Fellow, Dept of Molecular and Cell Biology, laboratory of David Weisblat
1992-1996	Postdoctoral Fellow, MRC Laboratory of Molecular Biology, Cambridge, England, laboratory of John White 1992-1993, independent 1993-1996
1988-1992	PhD, University of Texas at Austin, laboratory of Gary Freeman

Positions, Professional Service to the Field: Editorial

2019-present	Editorial Board, *Developmental Cell*
2011-present	Associate Editor, *Genetics*
2011-present	Editorial Board, *PLoS One*
2007-2015	Editorial Board, *Developmental Dynamics*
2007-present	Member, *Faculty of 1000*, Morphogenesis & Cell Biology Section
2005-2015	Board of Reviewing Editors, *Molecular Biology of the Cell*
2004-2021	Editorial Board, *BMC Developmental Biology*
1999-present	Editorial Board, *Development*

Positions, Professional Service to the Field: Grant panels

2015, 2011, 2004	NIH study section DEV-1
2006, 2005	NIH study section NCF
2004	NIH study section CHHD-C
2004-present	NSF Developmental Mechanisms and Evo/Devo Panels (four times)

Positions: Other Professional Service to the Field

2023	ASCB Nominating Committee
2022-present	Pew Scholars National Advisory Committee
2021-present	ASCB K99/MOSAIC Program mentoring to foster diversity, equity and inclusion
2021-present	*C. elegans* Community Mentor Match Program mentoring to foster diversity, equity and inclusion
2020	Chair, ASCB Nominating Committee
2019, 2018, 2017	ASCB Capitol Hill Day meetings with members of Congress and their staff
2018, 2009	Program Committee, ASCB Annual Meeting
2017-2019	ASCB Council
2017	Co-editor, Seminars in Cell & Developmental Biology issue on Cellular Mechanisms of Morphogenesis
2017, 2016	Co-Organizer, ASCB subgroup meeting on Emerging Model Systems
2016-present	Advisory Board, *Caenorhabditis* Genetics Center
2016-present	MBL Embryology Summer Course Faculty, *C. elegans* and tardigrade module
2016	ASCB Minisymposium Co-Chair, Multicellular Interactions, Tissues, and Development
2015, 2014	MBL Physiology Summer Course Faculty
2014	Co-Organizer, ASCB subgroup meeting on Cell Biology of Morphogenesis
2012	Co-Organizer, Santa Cruz Developmental Biology Meeting
2011	External Reviewer, Duke Developmental & Stem Cell Biology Training Program

Positions: Outreach and Community Service

2016-present	Leading a program I designed bringing workshops to public elementary school teachers to build DIY microscopes for their schools
2006-present	Faculty mentor in UNC's Carolina Covenant program for students from low-income backgrounds

Honors

2022	Keynote Speaker, Gordon Conference: Adhesion Across Scales: From Molecules to Morphogenesis
2022	Symposium Speaker, ASCB/EMBO Annual CellBio Meeting
2018	Chapman Family Teaching Award at UNC Chapel Hill
2016	James L. Peacock III Distinguished Professor
2008	Elected Life Fellow of Clare Hall, Cambridge University
2007	Guggenheim Fellow
2007	Visiting Fellow, Clare Hall, Cambridge University
2005	Hettleman Prize for Artistic and Scholarly Achievement, UNC Chapel Hill
2000-2002	March of Dimes Basil O'Connor Scholar
2000-2004	Pew Scholar

C. Contributions to Science

1. Cellular mechanisms of morphogenesis *in vivo*. Half of the lab currently works on understanding mechanisms of cell shape change driving morphogenesis. Our work has helped to establish *C. elegans* gastrulation as a useful model for dissecting cellular mechanisms of morphogenesis. We found that apical constriction drives internalization of the endoderm precursors in *C. elegans* gastrulation, and we have been working on understanding the subcellular mechanisms that lie at the heart of driving the relevant cell shape

changes. We have used *Drosophila* and *Xenopus* at times to determine the extent to which what we discover in *C. elegans* is true more generally, and specifically in neural tube formation, which also involves apical constriction.

Roh-Johnson M, Shemer G, Higgins CD, McClellan JH, Werts AD, Tulu US, Gao L, Betzig E, Kiehart DP, and B Goldstein. (2012) Triggering a Cell Shape Change by Exploiting Pre-Existing Actomyosin Contractions. *Science* 335:1232-1235. PMC3298882

Marston DJ, Higgins CD, Peters KA, Cupp TD, Dickinson DJ, Pani AM, Moore RP, Cox AH, Kiehart DP, and Goldstein B (2016). MRCK-1 drives apical constriction in *C. elegans* by linking developmental patterning to force generation. *Current Biology* 26:2079-2089. PMC4996705

Slabodnick MM, Tintori SC, Prakash M, Zhang P, Higgins CD, Chen AH, Cupp TD, Wong T, Bowie E, Jug F, Goldstein B (2023). Zyxin contributes to coupling between cell junctions and contractile actomyosin networks during apical constriction. *PLoS Genetics* 19(3): e1010319.

Zhang P, Medwig-Kinney TN, Goldstein B (2023). Architecture of the cortical actomyosin network driving apical constriction in C. elegans. *Journal of Cell Biology* 222(9):e202302102.

2. Developing tardigrades as a new animal model system. I began studying tardigrades (also known as water bears) as a side project soon after setting up my lab at UNC in 1999. My initial goal was to explore whether tardigrades could be useful as a new model for studying the evolution of developmental patterning mechanisms. This goal was sparked by the then-recent discovery that *C. elegans* and *Drosophila* are much more closely related to each other than previously expected, both being members of the Ecdysozoa. I postulated that phyla closely related to these two animals could become valuable lab models, if organisms with a set of useful characteristics for study in the lab could be found. We have developed methods for studying gene function as well as genomic tools for this system. We have been using this system to study how developmental mechanisms evolve, and we reported on evidence that the compact body plan of tardigrades evolved by loss of a large body region, corresponding to the entire thorax and nearly the entire abdomen of *Drosophila*. We are also using these organisms to understand how biological materials can be made to survive some remarkable environmental extremes. We identified tardigrade genes required for surviving desiccation, and we found that some proteins encoded by these genes are also sufficient to promote the viability of other organisms. Our recent work on tardigrades has identified additional, potent desiccoprotectants as well as unexpected responses that contribute to radiation tolerance.

Gabriel WN, McNuff R, Patel SK, Gregory TR, Jeck WR, Jones CD, and B Goldstein (2007). The Tardigrade *Hypsibius dujardini*, a New Model for Studying the Evolution of Development. *Developmental Biology* 312:545-559. PMID:17996863

Smith FW, Boothby TC, Giovannini I, Rebecchi L, Jockusch EL, and B Goldstein (2016). The compact body plan of tardigrades evolved by the loss of a large body region. *Current Biology* 26:224-229. PMID:26776737

Boothby TC, Tapia H, Brozena AH, Piszkiewicz S, Smith AE, Giovanninni I, Rebecchi L, Pielak GJ, Koshland D, and B Goldstein (2017). Tardigrades use intrinsically disordered proteins to survive desiccation. *Molecular Cell* 65:975-984. PMC5987194

Clark-Hachtel CM, Hibshman JD, De Buysscher T, Goldstein B. Tardigrades dramatically upregulate DNA repair pathway genes in response to ionizing radiation. *bioRxiv* 2023.09.07.556677 doi.org/10.1101/2023.09.07.556677

3. Development and use of CRISPR-based genome editing methods and other methods for *C. elegans*. To advance our efforts to use *C. elegans* to study cell biological mechanisms in development, we sought to insert fluorescent tags into genes at their endogenous loci, allowing 100% of a protein population to be tagged and its function in tagged form to be assessed *in vivo*. We did this by adapting Cas9/CRISPR-based methods to trigger homologous recombination in *C. elegans*. This work together with work from other *C. elegans* labs, and later streamlining of the methods, have revolutionized *C. elegans* genome engineering, making it possible to make essentially any genome edit, and rapidly—typically in 2-3 weeks from conceiving of an edit to having the worms in hand. We use AddGene to share our plasmids openly with the field. To our knowledge, most *C. elegans* labs doing CRISPR-based genome engineering are using our methods among their essential gene editing methods (to date, AddGene has distributed 1,789 samples on our behalf). We have made use of these methods to assess best protein fluorophores for use in *in vivo* experiments. We developed methods for generating transgenes that can evade long-problematic germline silencing issues in

C. elegans. We also developed methods for single-cell, single-molecule biochemistry (Dickinson et al., 2017). All of these methods advance our own research goals and also accelerate research by others.

Dickinson DJ, JD Ward, DJ Reiner, and B Goldstein (2013). Engineering the *Caenorhabditis elegans* genome using Cas9-triggered homologous recombination. *Nature Methods* 10:1028-1034. PMC3905680

Dickinson DJ, AM Pani, JK Heppert, CD Higgins, and B Goldstein (2015). Streamlined Genome Engineering with a Self-Excising Drug Selection Cassette. *Genetics* 200:1035-49. PMC4574250

Dickinson DJ and B Goldstein (2016). CRISPR-based Methods for *C. elegans* Genome Engineering. *Genetics* 202:885-901. PMC4788126

Heppert JK, Dickinson DJ, Pani AM, Higgins CD, Steward A, Ahringer J, Kuhn JR, and B Goldstein (2016). Comparative assessment of fluorescent proteins for *in vivo* imaging in an animal model system. *Molecular Biology of the Cell*, 27:3385-3394. PMC5221575

4. Cell polarization orchestrated by intercellular signaling. I discovered *C. elegans* endoderm induction as a graduate student. My work helped develop *C. elegans* into a system in which isolated cells manipulated *in vitro* could be used to study cell-cell interactions. I made use of methods for primary culture of embryonic cells (developed by Lois Edgar) to discover some fundamental developmental phenomena including endoderm induction, and (using *C. elegans*) that cell-cell interactions can orient mitotic spindles. We continue to use cell manipulations together with modern tools to study the mechanistic bases for these phenomena. We found that Wnt signals can function as positional cues as cells become polarized, that Wnts can freely diffuse long distances, and we found a role for TPR-GoLoco proteins (LGN homologs) in mitotic spindle orientation by a cell-cell signal.

Goldstein B (1992). Induction of gut in *Caenorhabditis elegans* embryos. *Nature* 357: 255-257. PMID:1589023

Goldstein B, H Takeshita, K Mizumoto, and H Sawa (2006) Wnt Signals Can Function as Positional Cues in Establishing Cell Polarity. *Developmental Cell* 10: 391-396. PMC2221774

Heppert JK, Pani AM, Roberts AM, Dickinson DJ, and B Goldstein (2018). A CRISPR tagging-based screen reveals localized players in Wnt-directed asymmetric cell division. *Genetics* 208:1147-1164. PMC5844328

Pani AM and B Goldstein (2018). Direct visualization of a native Wnt in vivo reveals that a long-range Wnt gradient forms by extracellular dispersal. *eLife* 7:e38325. PMC6143344

5. Cell and embryo polarity. As a postdoc I discovered that the antero-posterior axis of *C. elegans* is specified by the fertilizing sperm. This finding revealed that the unfertilized egg of *C. elegans* has no developmentally relevant asymmetries, and this and further work demonstrated that the sperm brings in components that orchestrate polarized cortical flow. We have made use of this system to study how mitotic spindles become positioned asymmetrically in cells before stem cell-like divisions. We found that the spindle checkpoint serves a second role in addition to timing anaphase: it also times when the spindle shifts asymmetrically, by mechanisms that are not yet well understood. We used genome-scale approaches to identify transcripts that become enriched asymmetrically in daughter cells of the first cell division and of later divisions. More recently we developed an approach for biochemical analysis of protein complexes from single cells, and we used it to identify important, rapid regulation of Par protein complexes that enables anterior Par complexes to move with cortical flow.

Goldstein B and SN Hird (1996). Specification of the anteroposterior axis in *Caenorhabditis elegans*. *Development* 122: 1467-1474. PMID:8625834

Labbé J-C, E McCarthy, and B Goldstein (2004) The forces that position a mitotic spindle asymmetrically are tethered until after the time of spindle assembly. *Journal of Cell Biology* 167: 245-256. PMC2172534

Tintori SC, Osborne Nishimura E, Golden P, Lieb JD, and Goldstein B (2016). A transcriptional lineage of the early C. elegans embryo. *Developmental Cell*, 38:430-444. PMC4999266

Dickinson DJ, Schwaeger F, Pintard L, Gotta M, and B Goldstein (2017). A Single-Cell Biochemistry Approach Reveals PAR Complex Dynamics during Cell Polarization. *Developmental Cell* 42:416-434. PMC5575849

Link to NCBI My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40275253/?sort=date&direction=descending

D. Research Support

Active

NIH R35 GM134838 (PI: Goldstein) 1/1/20 - 12/31/24 Annual direct costs: $250,000
C. elegans gastrulation: A model for understanding apical constriction mechanisms
This is a MIRA grant and hence lacks Specific Aims. The project is using *C. elegans* gastrulation as a model for studying how cells change shape and internalize in embryos. The project also develops methods useful to these goals and to *C. elegans* researchers more generally.

NSF IOS 2028860 (PI: Goldstein) 8/15/20 - 7/31/25 Annual direct costs: $166,417
Using Tardigrades and Other Animals to Investigate Adaptations to Extreme Stresses
This grant was an Accomplishment-Based Renewal, awarded “for an investigator who has made significant contributions, over a number of years, in the area of research addressed by the proposal”. The project uses tardigrades and other extremotolerant animals as models for understanding the mechanisms by which animals can survive extremes and to understand the evolutionary origins of animal protectants. The project also uses an outreach project developed by the PI to build smartphone-based microscopes in public elementary schools with teachers in low-income parts of North Carolina, and to assess predicted outcomes of this outreach.

Pending

none