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: **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 *(if applicable)*	Completion Date MM/YYYY	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 found in worms extend more generally. We have also worked to develop water bears (tardigrades) as a new model system for studying the evolution of developmental mechanisms and for understanding how biological materials can survive extremes. 10 postdocs have trained in the lab (four currently in the lab, four in faculty positions, and two in second postdocs) as well as 13 graduate students (including three currently in the lab, one currently in a postdoc, a science writer, a scientific editor, three working in professional microscopy-related careers, one pursuing a career in research in a lab animal residency at Johns Hopkins University, and two working in scientific outreach and education careers).

B. Positions and Honors

Positions

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

Positions: Editorial

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

Editorial Board, *PLoS One*	2011-present

Positions: Grant panels

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

Positions: Professional Service

Program Committee, ASCB Annual Meeting	2009
Co-Organizer, Santa Cruz Developmental Biology Meeting	2012
Co-Organizer, ASCB subgroup meeting on Cell Biology of Morphogenesis	2014
MBL Physiology Course Summer Faculty	2014, 2015
ASCB Minisymposium Co-Chair, Multicellular Interactions, Tissues, and Development	2016
Co-Organizer, ASCB subgroup meeting on Emerging Model Systems	2016
ASCB Council	2017-2019

Honors

Pew Scholar	2000-2004
March of Dimes Basil O'Connor Scholar	2000-2002
Hettleman Prize for Artistic and Scholarly Achievement, UNC Chapel Hill	2005
Guggenheim Fellow	2007
Visiting Fellow, Clare Hall, Cambridge University	2007
Elected Life Fellow of Clare Hall, Cambridge University	2008

C. Contribution to Science

1. Cellular mechanisms of morphogenesis *in vivo*. Most 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.

Lee J-Y, DJ Marston, T Walston, J Hardin, A Halberstadt, and B Goldstein (2006) Wnt/Frizzled Signaling Controls *C. elegans* Gastrulation by Activating Actomyosin Contractility. ***Current Biology*** 16: 1986-1997. PMC2989422

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

Martin AC and B Goldstein (2014). Apical constriction: themes and variations on a cellular mechanism driving morphogenesis. ***Development*** 141:1987-98. PMC2875788

Sullivan-Brown J, Tandon P, Bird KE, Dickinson DJ, Tintori SC, Heppert JK, Meserve JH, Trogden KP, Orlowski SK, Conlon FL, and Goldstein B (2016). Identifying regulators of morphogenesis common to vertebrate neural tube closure and *C. elegans* gastrulation. ***Genetics*** 202:123-139.

2. Developing water bears as a new animal model system. I began studying water bears (tardigrades) as a side project soon after setting up my lab at UNC in 1999. My initial goal was to explore whether tardigrades could be a useful 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 orhanisms 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. Recently, we began a new project studying how these animals can survive remarkable environmental extremes. We have identified water bear genes required for surviving desiccation, and we found that certain of these genes are also sufficient to promote the viability of desiccated unicellular organisms (bacteria and yeast).

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

Tenlen JR, S McCaskill, and B Goldstein (2013). RNA interference can be used to disrupt gene function in tardigrades. ***Development Genes and Evolution*** 223:171-181. PMC3600081

Boothby TC, JR Tenlen, FW Smith, JR Wang, KA Patanella, E Osborne Nishimura, SC Tintori, Q Li, CD Jones, M Yandell, DN Messina, J Glasscock, and B Goldstein (2015). Evidence for extensive horizontal gene transfer from the draft genome of a tardigrade. ***PNAS*** 112:15976-15981. and follow-up letter PNAS 113(22):E3058-61.

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.

3. Development and streamlining of CRISPR-based genome editing 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 our recent streamlining of the methods, have revolutionized *C. elegans* genome engineering, making it possible to make essentially any genome edit 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; as of Jan 1 2016, AddGene had distributed 818 samples on our behalf in the previous 26 months. We made use of these methods to assess best protein fluorophores for use in *in vivo* experiments, and we will soon submit one more *C. elegans* methods manuscript, on new methods we developed for generating transgenes for *C. elegans* that can evade long-problematic germline silencing issues. These methods advance our research goals and 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.

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***, in press.

4. Cell-cell interactions. My early work helped develop *C. elegans* as 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 that the endoderm of *C. elegans* is induced by an early cell-cell interaction, and I discovered that cell-cell interactions can orient mitotic spindles. We continue to use this system to study the mechanistic bases for these phenomena. We found more recently that Wnt signals can function as positional cues as cells become polarized, 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 (1995). Cell contacts orient some cell division axes in the early *C. elegans* embryo. ***Journal of Cell Biology*** 129: 1071-1080. PMC2120481

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

Werts AD, M Roh-Johnson, and B Goldstein (2011). Dynamic localization of *C. elegans* TPR-GoLoco proteins mediates mitotic spindle orientation by extrinsic signaling. ***Development*** 138:4411-4422. PMC3177311

5. Cell and embryo polarity. I began to study how the first cell of the *C. elegans* embryo (the 1-cell stage) becomes polarized by discovering that the fertilizing sperm brings in components that polarize the embryo. This finding revealed that the unfertilized egg of *C. elegans* has no developmentally relevant asymmetries. We have made use of this system more recently 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. Recently we have collaborated on identifying transcripts that become enriched asymmetrically in the two daughter cells resulting from this cell division.

Goldstein B and SN Hird (1996). Specification of the anteroposterior axis in *C. 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

McCarthy Campbell EK, AD Werts, and B Goldstein (2009) A Cell Cycle Timer for Asymmetric Spindle Positioning. ***PLoS Biology*** 7(4):e88. PMC2671557

Osborne Nishimura E, Zhang JC, Werts AD, Goldstein B, and Lieb JD (2015). Asymmetric Transcript Discovery by RNA-seq in *C. elegans* Blastomeres Identifies *neg-1*, a Gene Important for Anterior Morphogenesis. ***PLoS Genetics*** 11(4): e1005117. PMC4395330

Link to NCBI My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/robert.goldstein.1/bibliography/40275253/public/?sort=date&direction=descending

D. Research Support

Active

NIH R01 GM083071 Goldstein (PI) 6/1/08 - 8/31/20
Mechanisms of *C. elegans* Gastrulation
This project uses *C. elegans* gastrulation as a model for cellular and molecular mechanisms of morphogenesis, taking advantage of the ability to combine methods of genetics, molecular biology, cell biology, advanced microscopy and cell manipulation.

NSF IOS 1557432 Goldstein (PI) 6/15/16 - 5/31/20
Using Water Bears to Investigate Adaptations to Extreme Stresses
The long-term goal of this work is to contribute to understanding the mechanisms by which animals and animal tissues can survive extremes.

Completed in last 3 years

NSF IOS 1257320 Goldstein (PI) 7/1/13 - 6/30/16
Uncovering the Origins of Arthropod Body Plan Patterning
In this project, we developed a little-studied animal system—tardigrades—used as an outgroup to address how modular, segmented body forms and appendages diversified among ancestors of the arthropods, using genomics, gene expression analysis, and reverse genetic methods. A tardigrade genome project is being completed and used to generate a publicly shared database.