George D. Bittner, CV

September 2024

A. *PERSONAL DATA*

Full Name:	George Davis Bittner
Place and Date of Birth:	August 17, 1941; New York, NY
Marital Status:	Married (Dr. Cathy Yang, MD, PhD)
Children:	Jack, Lucie
Current Home Address:	2812 Pearce Road, Austin, Texas 78730 (512) 346-4392
Current Office Address:	Patterson Laboratories, Room 321 Department of Neuroscience University of Texas Austin, TX 78712-1064 (512) 923-3735 (cell). preferred # to call (512) 471-6971 (Lab) email: bittner@austin.utexas.edu web site https://sites.cns.utexas.edu/bittnerlab

B. *EDUCATION*

9/56- 6/59	Robert E Lee High School, Jacksonville, FL ranked 1/838 Valedictorian
9/59 - 6/62	Duke University, Durham, NC; A.B., Chemistry, 9/62 . Magna Cum Laude
9/62 - 12/66	Stanford Medical School, Palo Alto, CA; 5 year MD/PhD program. Withdrew in good standing (sixth in class) 12/66 via leave of absence in December of fifth year to devote full time to research,
6/64 - 8/67	Stanford University; Ph.D., Neurological Sciences, 1967; Supervising Professor: Dr. Donald Kennedy, Chairman, Biological Sciences, FDA Commissioner, President of Stanford University, Chief Editor of *Science and Scientific Americsan*
11/67 - 6/69	NIH Postdoctoral fellowship with Dr. Jose Segundo, Department of Anatomy/Cell Biology, UCLA, Los Angeles, CA

C. *PROFESSIONAL EXPERIENCE*

CEO CertiChem 5/00 – 5/22, CEO PlastiPure 5/00 – 6/08, CSO PlastiPure 7/08 – 5/22
Professor, Department of Neuroscience, 9/2013 - present
Professor, Neurobiology Section, School of Biology, 9/98 – 8/2013
Professor, Dept. of Zoology, University of Texas, Austin, TX, 9/82 – 8/98
Adjunct Professor, College of Pharmacy, University of Texas, Austin, TX, 9/87 – 5/05
Associate Professor, Department of Zoology, University of Texas, 9/74 - 8/82
Assistant Professor, Department of Zoology, University of Texas, 9/69 - 8/74
Adjunct Professor, Dept. of Physiology and Biophysics, University of Texas Medical Branch, Galveston, TX, 3/96 - present
Visiting Associate Professor, Department of Physiology, University of Texas Medical School, San Antonio, TX, 9/77 - 8/78
Visiting Associate Professor, Department of Anatomy, Case-Western Reserve University Medical School, Cleveland, OH, 8/75 - 1/76
NIH Postdoctoral Fellow, Dr. Jose Segundo, Department of Anatomy, UCLA, 11/67 - 6/69
NIH Predoctoral Fellow, Dr. Donald Kennedy, Biological Sciences, Stanford University, 1965 - 67
Research Assistant, Dr. Keith Killam, Department of Pharmacology, Stanford University, 1962 - 63

D. *UNIVERSITY ADMINISTRATIVE RESPONSIBILITIES (since 1985)*
Biology Graduate Advisor, 1982 - 1990
Program Director, Neurobiology Training Grant, 1985 - 1991
Program Director, Electron Microscope Applications to NIH, NSF, 1985 - 1986
Organizing Director, Institute for Neuroscience, 1985 - 1986
Member, Executive Committee, Institute for Neuroscience, 1986 - 1994
Member, Executive Committee, Institute for Biotechnology, 1988 - 1995
Natural Science Promotion Committee (2002-2004; Chair, 2003-2004)
Natural Sciences Courses and Curricula committee (2003-2005)
CNS Scholarship Committee (2002-present)
University of Texas Libraries Committee (8/2014-2019); Chair 2017-2018
Student Conduct Hearing Officer (9/2016-2020)
Reviewer of 2-5 URF proposals yearly (2018 present)
CNS FRA committee 2019-present

E. *PROFESSIONAL SOCIETIES* Past and present*

Society for Neuroscience*
A.A.A.S. (Elected Fellow)*
Society for Neurochemistry
American Chemical Society*
Neurotrauma Society
Society for Cell Biology
Society for Developmental Neurobiology
Endocrine Society*

F. *PROFESSIONAL AND PUBLIC SERVICE (Since 1985)*
Member, NINCDS Review Committee for Program Project Grants, 1986 - 1987
Member, Advisory Committee for Basic Neuroscience Research, Air Force Office of Sponsored Research, 1987 - 1988
Vice President, Central Texas Biotechnology Consortium, 1986 - 1989
Member, Neuroscience Review Committee for Veteran Administration Grants, 1990
Treasurer, Society for Neuroscience (Austin Chapter), 1985 - 1996
Member, Biotechnology Committee, Austin Chamber of Commerce, 1987 - 1994
Member, NSF and Howard Hughes Panels for Predoctoral Fellowships in Neurobiology, 1993 - 1995
Chair, Neuroscience Panel for Howard Hughes and NSF Predoctoral Fellowships, 1996Editorial Review Board, Neural Regeneration Research since June 2015
Review 8-15 Manuscripts/year total for *Journal of Neurophysiology, Journal of Comparative Physiology, Science, Journal of Neurobiology, Brain Research, Journal of Neuroscience, Toxicology in Vitro, Toxicological Sciences, Environmental Health Perspectives, Environmental Health, Neural Regeneration Research, PLos one, J. Neuroinflammation, Progress in Neurobiology*
Ad Hoc Reviewer, NIH, NSF Neurobiology Grant Applications in Synaptic Plasticity, Nerve Regeneration, or Glial Function, 1985 – present
Member NIH BNVT panel study section, panel to review/score R-01, R-21, U-01, U-03 etc grant applications. 8/2014.
Member Editorial Board. Neural Regeneration Research. 2019-present
Guest Editor, Frontiers in Cellular Neuroscience, Edition on *Restoring Function After Traumatic Peripheral Nerve Injury.* 2021-2022

G. *INVITED SEMINARS/PRESENTATIONS (2005-)*
Robert Wood Johnson Medical School, Piscataway, NJ (April, 2005)
NIEHS Campus, Research Triangle Park, NC (April, 2005; August, 2006)
Lone Star Paralysis Foundation, Austin, May 2006
Brain, Spine Center, Brackenridge Hospital, Nov 2006

Department of Biology, North Carolina State University, Raleigh NC (March 2007)
Breast Cancer Foundation/Fund San Francisco, Ca. Detection of estrogenic activity in plastics (Jan, 2008)
Lone Star Paralysis Foundation, Axonal repair using polyethylene glycol (April, 2008)
NIH/NIEHS Campus Raleigh, NC detection of estrogenic activity. (March, 2009).
A Robotic MCF-7 Cell Proliferation Assay to Detect Estrogen Receptor Agonists and Antagonists 2010. C.Z. Yang, N. Bodon and G.D. Bittner, Society of Toxicology., March 2010, Salt Lake City
Almost all plastics release chemicals having estrogenic activity: a health problem that can be solved. NIEHS research campus, NC. 1.14.11.
Rapid Repair of Severed Nerve Axons. Harvard Medical School, Dept of Orthopedic Surgery . Dec. 2011
Rapid Repair of Severed Nerve Axons. Concordia University, Dept of Biology, Feb, 2012
Rapid Repair of Severed Nerve Axons. University of Texas, Psychology Dept, Feb 2012
Rapid Repair of Severed Nerve Axons. Wayne State Medical School, Anatomy/Cell Biology, Feb 2012
Rapid Repair of Severed Nerve Axons. U. Miami Medical School, Dept. of Orthopedic Surgery, March 2012
Rapid Repair of Severed Nerve Axons. Department of Biology, North Carolina State University, April, 2013
Rapid Repair of Severed Nerve Axons. Department of Biomedical Engineering, NC State University, April, 2013
Rapid Repair of Severed Nerve Axons. Department of Neurosurgery, Duke University Medical School, April, 2013
Rapid Repair of Severed Nerve Axons. Department of Orthopedics and Plastic Surgery and Neuroscience Program, Wake Forrest Medical School, April, 2013.
Plastics and Chemicals in the Environment. Sierra Club. Austin, TX September 2013.
Bioengineered repair of severed limb nerves. UT Quest. March 2014.
Rapid restoration of behaviors lost after completely severing peripheral limb nerves: It's not just for Luke Skywalker and (Mr.) Crabs anymore U. Virginia, Biology Dept. Oct 2014.
Rapid restoration of behaviors lost after completely severing peripheral limb nerves: It's not just for Luke Skywalker. University of Indiana Medical School. March, 2015.
Biotech Advances in Hormone Free products. UT Quest. March, 2015.
A battery of in vitro assays to detect estrogenic activity. ICCVAM Conference, NIH, May, 2016

2019-10	Metis Foundation, San Antonio,Tx	Axonal Repair by PEG-fusion
2019-10	UT Lifelong learning	Rapid repair of severed axons... Its not just for Mr. Crabs and Luke Skyw
2019-12	Johns Hopkins Medical School	Rapid Repair of severed axons by PEG-fusion
2020-6	Univ of Illinois Med Sch	Rapid repair of severed axons by PEG-fusion
2021 -3	Univ. Wyoming	Rapid Repair of Nerve Axons by PEG-fusion
2022-4	Am Assoc Neuro Surgeons Invited Speaker	Rapid Repair of Nerve Axons by PEG-fusion
2023-8	Baylor Medical School, Orthopedics and Plastic Surgery	Rapid, effective and permanent repair of severed peripheral and spinal axons

H. *AWARDS AND HONORARY SOCIETIES*
First Prize, Florida State Science Fairs, 1958, 1959
Valedictorian, Robert E. Lee High School (Class size ~800)

Phi Eta Sigma, Freshman Honorary, Duke University, 1959 - 1960
Phi Beta Kappa, Phi Eta Sigma, Duke University, 1962
A.B., Magna Cum Laude, Duke University, 1962
NIH, NSF predoctoral fellowships, Stanford University, 1965 - 1966
NIH postdoctoral fellowship, UCLA, 1967 - 1969
Fellow, Neurosciences Study Program, Boulder, CO, Summer 1969
NIH Career Development Award, 1975-1980
Elected Fellow, American Association for the Advancement of Science, Spring, 1994
ICCVAM/NICEATM Advisory panel 2018-2021
Guest Editor, Frontiers in Cellular Neuroscience, Edition on *Restoring Function After Traumatic Peripheral Nerve Injury.* 2021- 2023 (publication date)
Associate Editor, Frontiers in Cellular Neuroscience, 9/22-

I. *UNIVERSITY AND DEPARTMENTAL COMMITTEES (Since 1985)*
Zoology, Long Range Planning Committee, 1984 - 1986
Zoology, Chairman Recruitment Committee, 1985 - 1986
Faculty Advisor Graduate Fellows Program, 1985 - 1986
Selection Committee, Churchill Scholar Program, 1985 - 1987
Plan II Advisory Committee, 1986 - 1990
Zoology Computer Committee, 1987 - 1990
Zoology, Admissions Committee, 1989 - 1990
Dean's Committee to Revise Plan II Curriculum, 1986 - 1992
Zoology, Cell Biology Search Committee (Chair), 1991 - 1992
Zoology, Departmental Visiting Committee, 1988 - 1993
Dean of Natural Science, Industrial Associates Committee, 1988 - 1994
Zoology Electron Microscope Committee, 1985 - 1998
Zoology, Industrial Liaison, 1988 - 1996
Zoology, Fellowship Committee, 1990 – 1998
Natural Sciences Courses and Curricula committee (2003-2005)
Biology Fellowship Committee (1999-2018)
CNS Scholarship Committee (2002-present)
University of Texas Libraries Committee (8/2014-8/2020); Chair 9/2018- 8/2019
Student Conduct Hearing Officer (9/2016-2020
Reviewer URF proposals 2018-present
Letters of recommendation for 8-15 students/yr to graduate/medical schools 2000-present
Reviewer for Faculty Research Assignment Competition. 2020- present

J. *COURSES TAUGHT*

1.Undergraduate Courses

Mammalian Physiology (Zoology 465M)
Vertebrate Physiology (Zoology 365L, Biology 365R, NEU 365R)
Vertebrate Physiology Laboratory (Zoology 165P)
Human Physiology (Zoology 316K)
Structure and Function of the Mammalian Central Nervous System (Zoology 371L)
Physiology of Organismic Adaptations (Zoology 363L, 363M)
Adaptive Physiology Laboratory (Zoology 263P)
Current Limits of Scientific Knowledge (TC 659: Plan II Honors Section)
The Neuronal Basis of Brain and Behavior (Zoology 371L, Biology 371M)
Comparative Physiology (Biology 361T)
Nerve Regeneration in Invertebrates and Vertebrates. Writing component course (NEU 337 or NEU365N)

BIO 370C Directed reading course to 2-5 undergraduates Fall, Spring, and summer semesters 2019-present

2.Graduate Courses

Advanced Cell Biology (Zoology 388M)
Principals of Neuroscience (Zoology 688QA, B;NEU 382T; NEU 383T, BIO 437; NEU 482T)
Developmental Neurobiology (Zoology 390K; Biology 390K)
Adaptive Physiology of Marine Organisms (MNS 382.12 at The University of Texas Marine Station at Port Aransas)
Cellular Neurobiology (Anatomy 449 at Case Western Reserve University)
Basic Properties of Nerve Cells: Axonal Conduction and Synaptic Transmission (Zoology 385L.13a; Biology 381K))
Basic Properties of Nerve Cells: Trophic Interactions and Regeneration (Zoology 385L.13b; Biology 381K)
Current Concepts in Cellular/Molecular Neuroscience (Zoology 385L.15; Biology 381K))
Neurophysiology of Nerve and Muscle, (UTSA Department of Physiology)
Environmental Physiology (Marine Science 354 at The University of Texas Marine Science Institute, Port Aransas, TX)
Basic Properties of Nerve Cells: Metabolic, Glial-Neuronal, and Regeneration. (BIO. 381K.10/NEU 385L.1).
Nerve Regeneration in Invertebrates and Vertebrates (NEU 381N.1, NEU 381N)

K. *INDIVIDUAL INSTRUCTION*

Supervision of Undergraduate Students

I perform a significant amount of individual research instruction with undergraduates who often register for BIO research courses, Biology Honors, or Plan II thesis courses. Whether they officially register or not, each student makes a commitment to work 10-20 hours per week for at least 18 months and to take a series of courses in cell, molecular, and/or neurobiology to give them an appropriate conceptual and factual basis for their research. By the time they graduate, most such students are a co-author in at least one peer-reviewed publication and participate in weekly lab journal club/data presentation meeting. Those undergraduate students in my lab doing such meeting such criteria in the past ten years were as follows:

Student	In Lab
Cameron Ghergherehchi	2011-2015
Christopher Driscoll	2012-2014
Robert Hastings	2012-2014
Chris McGill	2012-2018
Colton Riley	2012-2014
Ti Ha	2013-2015
Nicholas Munoz	2013-2015
Andrew Poon	2014-2018
Monika Pyarali	2013-2016
Michael Bounajem	2014-2016
Alex Mazal	2014-2016
Aakarshita Bansal	2015-2016
Patrick Dunne	2015-2017
Maui Guitterrez	2014-2017
Nicole Wong	2015-2017
Amir Ali	2015-2018
Zach Burgess	2016-2017
Adrian Gorszawski	2016-2017
Sarah Nguyen	2016-2019

Matthew Hooper	2016-2018
Karthik Jagannath	2016-2018
Edward Kang	2017-2019
Milki Negeri	2018-2019
Meghana Gogineni	2018-2019
Kenneth Pham	2018-2020
Ted Zhao	2018-2020
Bryan Nyakiti	2018-2021
Shruti Kumar	2018-2019
Sara Vargas	2018-2020
Monzer Alatrach	2018-2021
Grace Massamillo	2018-2019
Sruja Arya	2019-2023
Mario Carrera	2019- 2023
Razan Hussein	2019-2020
` Vanessa Nuval	2019-2020
Marshal Mencel	2019-5/2021
Anirudh Sudarshan	2020-2021
Rhea Sachdeva	2020-2022
Menizhe Mohsin	2021-2023
Anish Pandya	2021-2022
Yessennia Montoya	2021-2024
Alexa Olivarez	2021-2023
Karthik Venkudusamy	2021-2024
Jesus Jimenez	2022
Stone Nwamadi,	2022
Anaya Sampathkumar	2022
*Varun Gokhale	2023-present
Zeal Pathak	2023-2024
*Guhan Periyasamy	2023-present
*Rhea Sood	2023-present
*Arjun Agarwal	2023-present
Seo yun (Christina) Kim	2023-2024
*Yiming (Grace) Hao	2024-present
*Neha Nagarajan	2024-present
*Sreekriti Sista	2024-present
*Sushant Sanklipur	2024-present

* currently active

Many undergraduates in my laboratory (Aesher, Baskind, Cummings, Farnam, Garcia, Hsu, Lichstein, Loftin, Lusco, Nguyen, Storm, Thomas, Truchard, and Weiner) have been awarded NIH or Howard Hughes Fellowships for the summer, four (Bobb, Eddleman, Sterkenburg, and Todora) have been awarded fellowships at Woods Hole, and five (Bobb, Brown, Loftin, Sunio, Wade, Vargas, Montoya) have been awarded ATP or other Minority Fellowships. Almost all students who had worked in my laboratory have been admitted to excellent medical or graduate schools (Cummings - Cell and Molecular Biology, UCSF; Cobb - Biology, UC Berkeley; Storm - Cell and Molecular Biology, Stanford; Truchard - Biology, UC Berkeley; Todora - Neurobiology, Harvard; Weiner - Cell and Molecular Biology, UCSF; Hristov – Johns Hopkins Medical School; Marzullo – Neuroscience, Univ. of Michigan: Truong –University of Texas Medical School at Houston; Rossano, Driscoll, Burgess: UT Medical School San Antonio; Covington/Figard – Rice University; Boydston, Ha-Southwestern Medical School, Hastings: Neuroscience, Texas A&M, Riley: Georgetown Medical School. Mazal-Southwestern Medical School: Pyarali-Baylor Medical School; McGill, Yale; Ali, Jagannath: UT Me4dical School, Houston; Zhao-UT Medical School Houstoun; Alatrach- UT Medical School; El Paso; Arja- Southwestern Medical School). Many have won

Research Grants or other honors at UT (Cummins, Hsu, Truchard, Todora, Weiner, Rossano, Robinson, Jang, Covington, Boydston, Ha, Pyarali, Mazal, Kang, Zhou, Poon, McGill, Mencel, Vargas, Carrera, Vendukusamy, Sood)

Publications since 1996 of former undergraduates (asterisked*):

T.D. Raabe, T. Nguyen,* and G.D. Bittner. 1996. Calcium activated proteolysis of neurofilament proteins in goldfish Mauthner axons. J. Neurobiol. 6:253-261.

T.D. Raabe, T. Nguyen,* C. Archer,* G.D. Bittner. 1996. Mechanisms for the maintenance and eventual degradation of neurofilament proteins in the distal segments of sered goldfish Mauthner axons. J. Neurosci. 16:1605-1613.

O. Weiner,* A.M. Zorn, P.A. Krieg, and G.D. Bittner. 1996. Medium weight neurofilament mRNA in goldfish Mauthner axoplasm. Neurosci. Lett. 213:83-86.

Sunio* and G.D. Bittner. 1997. Cyclosporin retards the Wallerian degeneration of peripheral mammalian axons. Exp. Neurol. 146:46-56.

C.S. Eddleman,* M.L. Ballinger, M.E. Smyers, C.M. Godell,*H.M. Fishman, and G.D. Bittner. 1997. Repair of plasmalemmal lesions by vesicles. PNAS 94:4745-4750.

C.M. Godell,* M.L. Ballinger, C.S. Eddleman,* M.E. Smyers, H.M. Fishman, and G.D. Bittner. 1997. Calpain promotes the sealing of severed giant axons. PNAS 94:4751-4756.

M.L. Ballinger, A.R. Blanchette, T.L. Krause,* M.E. Smyers, H.M. Fishman, and G.D. Bittner. 1997. Delaminating myelin membranes help seal the cut ends of severed earthworm giant axons. J. Neurobiol. 33:945-960.

C.S. Eddleman,* M.L. Ballinger, M.E. Smyers, H.M. Fishman, and G.D. Bittner. 1998. Endocytotic Formations of vesicles and other membranous structures induced by Ca^{2+} and axoplasmic injury. J. Neurosci. 18:4029-4041.

C.S. Eddleman,* M.E. Smyers, A. Lore,* H.M. Fishman, and G.D. Bittner. 1998. Anomalies associated with dye exclusion as a measure of axolemmal repair. Neurosci. Lett. 256:13-126.

A.B. Lore,* J.A. Hubbell, D.S. Bobb Jr., M.L. Ballinger, K.L. Loftin,* J.W. Smith,* M.E. Smyers, H.D. Garcia,* and G.D. Bittner. 1999. Rapid induction of functional and morphological continuity between severed ends of mammalian or earthworm myelinated axons. J. Neurosci. 19:2442-2454.

J.W. Lichstein,* M.L. Ballinger, A.R. Blanchette, H.M. Fishman, and G.D. Bittner. 1999. Structural changes at the cut ends of earthworm giant axons in the interval between dye barrier formation and Neuritic outgrowth. J. Comp. Neurol. 416:143-157.

C.S. Eddleman,* G.D. Bittner and H.M. Fishman. 2000. Barrier permeability at cut axonal ends progressively decreased until an axonal seal is formed. Biophys. J., 79:1883-1890.

E. Detrait, C.S. Eddleman, S. Yoo, M. Fukuda, G.D. Bittner and H.M. Fishman. 2000. Axolemmal repair requires proteins that mediate synaptic vesicle fusion. 2000 J. Neurobiol. 44:382-391.

E. Detrait, S. Yoo, T. Nguyen,* C.S. Eddleman, M. Fukuda, G.D. Bittner, and H.M. Fishman. 2000. Repair of severed neurites of PC 12 cells requires divalent cations and a concerved region of synaptotagmin. J. Neuroscience Research. 62:566-573

T. C. Marzullo*, J.S. Britt*, R. Stavisky and G.D. Bittner. 2002. Cooling enhances in vitro survival and fusion-repair of severed axons taken from the peripheral and central nervous system of rats. Neuroscience Letters. 327:9–12.

C.S. Eddleman*, G.D. Bittner, and H.M. Fishman. 2003. SEM comparison of severed ends of giant axons isolated from squid (*Loligo pealei*) and crayfish (*Procambarus clarkii*). Biol Bull. 203: 219 – 220.

S. Yoo, M. P. Nguyen*, M. Fukuda, G. D. Bittner, and H. M. Fishman. 2003. Plasmalemmal sealing of transected mammalian neurites is a gradual process mediated by Ca-regulated proteins. J. Neurosci. Res. 74:541-551.

R. C. Stavisky, J. M. Britt,* T. Pham*, T. C. Marzullo* and G. D. Bittner. 2003. Wallerian Degeneration of mammalian PNS and CNS axons is accelerated by incubation with protein synthesis inhibitors. Neuroscience Res. 47: 445 – 449.

R.C. Stavisky, J.M. Britt*, A. Zuzek*, E. Truong* and G.D. Bittner. 2005. Melatonin enhances the in vitro and in vivo repair of severed rat sciatic axons. Neurosci. Letters, 98-101.

M. G. Nguyen*,G.D. Bittner, and H.M. Fishman, H.M. 2007. Critical interval of sodium calcium transient after neurite transaction determines B104 cell survival. J. Neurosci. Res., 805-816.

J. M. Britt*, J.R. Kane, C.S. Spaeth, A. Zuzek*, G.L.Robinson*, M.Y. Gbanaglo, C.J. Estler*, E.A. Boydston*, T. Schallert, T and G.D. Bittner. (2010). Polyethylene glycol rapidly restores axonal integrity and improves the rate of motor behavior recovery after sciatic nerve crush injury. J Neurophysiol., 104: 695-703

C. S. Spaeth, E.A. Boydston*, L.A. Figard*, A. Zuzek* and G.D. Bittner (2010). A model for sealing plasmalemmal damage in neurons and other eukaryotic cells. J. Neurosci. 30: 15790-15800.

Spaeth CS, Fan, GD*, Spaeth EB, Robison T*, Wilcott RW*, Bittner GD (2012) Neurite transection produces cytosolic oxidation which enhances plasmalemmal repair. *J Neurosci Res*.90:945-954

Spaeth CS, Robison TR, Fan, JD, Bittner GD (2012) Cellular mechanisms of plasmalemmal sealing and axonal repair by polyethylene glycol and methylene blue. *J. Neurosci. Res.* 90:955-966.

Bittner, GD C.P. Keating, J. R. Kane , J.M. Britt*, C. S. Spaeth, J. D. Fan*, A. Zuzek,* R. W. Wilcott*, W. P. Thayer, J.M. Winograd, F. Gonzalez-Lima and T. Schallert . (2012) Rapid, effective and long-lasting behavioral recovery produced by microsutures, methylene blue and polyethylene glycol after complete cut of rat sciatic nerves. *J Neurosci Res*. 90:967-980.

Spaeth CS, Boydston EA*, Wilcott RW*, Fan JD*, Robison T*, Bittner,GD (2012) Pathways for plasmalemmal repair mediated by PKA, Epac and cytosolic oxidation in rat B104 cells *in vitro* and rat sciatic axons *ex vivo*. *Devel Neurol.*, 72: 1399-1414.

Zuzek A*, Fan JD*, Spaeth CS, Bittner GD. 2013. Sealing of transected neurites of rat B104 cells requires a diacylglycerol PKC-dependent pathway and a PKA-dependent pathway. Cell Molec Neurosci. 33: 31-46.

Rodriguez-Feo CL, K.W. Sexton, R. B. Boyer, A. C. Pollins, N. L. Cardwell, L. B. Nanney,R. B. Shack, M. A. Mikesh, C. H. McGill*, C. W. Driscoll*, G. D. Bittner, W. P. Thayer. 2013. Blocking the P2X7 Receptor Improves Outcomes After Axonal Fusion. J. Surgical Research. . 184(1):705-13. doi: 10.1016/j.jss.2013.04.082.

D.C. Riley*, G.D. Bittner, M.A. Mikesh, N.L. Cardwell, A.C. Pollins, C.L. Ghergherehchi*, S.R. Bhupanapadu Sunkesula, T.N. Ha,* B.T.D. Hall*, A.D. Poon*, M. Pyarali*, R.B. Boyer, A.T. Mazal*, N. Munoz*, R.C. Trevino, T.Schallert, W.P. Thayer. (2014) PEG-fused allografts produce rapid behavioral recovery after ablating sciatic nerve segments. J. Neurosci. Res. Apr;93(4):572-83. doi: 10.1002/jnr.23514. PubMed PMID: 25425242; PubMed Central PMCID: PMCPMC4329031.

G.D. Bittner, D.R. Sengelaub, R.C. Trevino, J.D. Peduzzi, M. Mikesh, C.L. Ghergherehchi*, T.Schallert, W.P. Thayer. 2015. The curious ability of PEG-fusion technologies to restore lost behaviors after nerve severance. J Neurosci Res. J Neurosci Res. 94: 207-230. online 3 Nov.2015. doi. 1002/jnr 23685

C. L. Ghergherehchi*, G. D. Bittner, R. L. Hastings*, M. Mikesh, D. C. Riley*, R. C. Trevino, T. Schallert, W. P. Thayer , S. Raju Bhupanapadu Sunkesula, T-A. N. Ha*\, N. Muno*, M. Pyarali*, A. Bansal*, A. D. Poon*, A. T. Mazal*, T. A. Smith, N. S. Wong*, P. J. Dunne*. 2015. Effects of extracellular calcium and surgical techniques on restoration of axonal continuity by PEG-fusion following complete cut- or crush-severance of rat sciatic nerves. J Neurosci Res. 94:231-235. Doi.

10.1002/jnr23704 . Epub Jan 5, 2016
G.D. Bittner, M. Mikesh, C. L. Ghergherehchi*. 2016. PEG-fusion retards Wallerian degeneration and rapidly restores behaviors lost after nerve severance. Neural Regen. Res. 11:217-219. Doi 10.4103/1673-5374.177716
C.H. McGill*, S. R. Bhupanapadu Sunkesula, A.D. Poon*, M. Mikesh, G. D. Bittner. 2016. Sealing Frequency of B104 Cells Declines Exponentially with Decreasing Transection Distance from the Axon Hillock. Exp. Neurol. 279:149-158. doi:10.1016/j.expneurol.2016.02.001 G.D. Bittner, D.R. Sengelaub, R.C. Trevino, C.L. Ghergherehchi*, M. Mikesh. 2017. Robinson and Madison have published no data on whether polyethylene glycol fusion repair prevents reinnervation accuracy in rat peripheral nerve. J Neurosci Res. 863-866. doi: 10.1002/jnr.23849. Epub 2016 Aug 12.
George D. Bittner, Christopher S. Spaeth, Andrew D. Poon*, Zachary S. Burgess*, Christopher H. McGill*. 2016. Repair of traumatic plasmalemmal damage to neurons and other eukaryotic cells. Neu. Regen. Res. Exp. Neurol. 279:149-158. doi:10.1016/j.expneurol.2016.02.001
G.D. Bittner, M. Mikesh, C. L. Ghergherehchi. 2016. PEG-fusion retards Wallerian degeneration and rapidly restores behaviors lost after nerve severance. Neural Regen. Res. 11:217-219. Doi 10.4103/1673-5374.177716
Bittner GD, Sengelaub DR, **Trevino RC**, Ghergherehchi CL, Mikesh M (2017) Robinson and Madison have published no data on whether polyethylene glycol fusion repair prevents reinnervation accuracy in rat peripheral nerve. *J Neurosci Res* 95:863-866. doi: 10.1002/jnr.23849. PMC5241247.
GD Bittner, DL Sengelaub, CL Ghergherehchi*. 2018. Conundrums and confusions regarding how PEG-fusion produces excellent behavioral recovery after peripheral nerve injuries. Neural Regeneration Research. 13: 53-57..
Andrew D. Poon*, Sarah H. McGill*, Solomon Raju Bhupanapadu Sunkesula, Zachary S. Burgess*, Patrick J. Dunne*, Edward E. Kang* and George D Bittner. 2018. CaMKII and DMSO affect the sealing frequencies of transected hippocampal neurons. J. Neurosci. Res. 96:1208-1222.
Mikesh M, Ghergherehchi CL*, Hastings RL*, Ali A, Rahesh S*, Jagannath K*, Sengelaub DR, Trevino RC, Jackson DM, Bittner GD. 2019. Polyethylene glycol solutions rapidly restore and maintain axonal continuity, neuromuscular structures and behaviors lost after sciatic nerve transections in female rats. J. Neurosci. Res. 96: 1223-1242.
Mikesh M, Ghergherehchi CL*, Rahesh *, Jagannath K*, Ali A*, Sengelaub DR, Trevino RC, Jackson DM, Tucker HO, Bittner GD. 2019. Polyethylene glycol treated allografts not tissue matched nor immunosuppressed rapidly repair sciatic nerve gaps, maintain neuromuscular functions, and restore voluntary behaviors in female rats. J. Neurosci. Res. 96:1243- 1264.
Ghergherehchi CL*, Mikesh M, Sengelaub DR, Jackson DM, Smith T, Shores JT, Bittner GD. (2019) Polyethylene glycol (PEG) and other bioactive solutions with neurorrhaphy for rapid and dramatic repair of peripheral nerve lesions by PEG-fusion. J Neurosci Methods. 314:1-12.
Vargas SA* and Bittner GD. 2019. Natural mechanisms and artificial PEG-induced mechanism that repair traumatic damage to the plasmalemma in eukaryotes. Current Topics in Membranes: Plasma Membrane Repair. 84: 129-167.
Liwen Zhou, Monzer Alatrach*, Ted Zhao*, Paul Oliphint, George D. Bittner. 2023 Differential survival of segments of rat sciatic nerves preserved in different storage solutions assessed by novel electrophysiological and morphological criteria. 2023. Neural Regeneration Research. 18:2082-2088. https://doi.org/10.4103/1673-5374.367848
Marshal Mencel* and George D. Bittner. 2023. Repair of traumatic lesions to the plasmalemma of neurons and other cells: commonalities, conflicts, and controversies. Frontiers in Cellular Neuroscience. Neural Regeneration Research. 18:2082-2088. https://doi.org/10.4103/1673-5374.367848
L Zhou, K Venkudusamy*, E Hibbard, Y Montoya*, A Olivarez*, CZ Yang, A Leung, V Gokhale*, G Periyasamy*, Z Pathak*, D Sengelaub, GD Bittner. 2023. Polyethylene glycol

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E Hibbard, L Zhou, CZ Yang, K Venkudusamy*, Y Montoya*, GD Bittner, D. Sengelaub.2023. Polyethylene glycol fusion repair of severed rat sciatic nerves reestablishes axonal continuity and reorganizes sensory terminal fields in the spinal cord. Neur. Regen. Res. In Press

L. *GRADUATE STUDENT SUPERVISION. Last known position*

1. *M.A. Degrees:*

Completed

R.T. Kopanda. 1973. Trophic interactions in the crayfish, *Procambarus clarkii*. Deputy Director of ADAMHA.

L. Boone. 1973. Trophic dependencies in a crustacean muscle. Currently a practicing M.D.

M. Nitzberg. 1973. Ultrastructural changes in transplanted segments of crustacean peripheral nerves. Currently a science advisor to a computer firm.

Obichere Nwabuko. 1976. The roles of calcium in vertebrate muscle contraction. Current position unknown.

M.S. Bouton. 1980. Mechanisms of axonal regeneration in crayfish motor axons. Currently a practicing M.D..

Todd Miller. 1990. Role of synapsin in neurotransmitter release. Current position unknown.

Melva Avalos. 1990. The effect of pentobarbital on pre- and postsynaptic channels at crayfish neuromuscular junctions. Current Position Unknown.

Guillermo Espinoza. 1992. Morphological correlates of longterm potentiation at hippocampal synapses. (Co-directed with Dr. Abraham Amsel of Psychology).

Tonya Thompson. 1992. Neurochemistry of monoamine oxidase enzymes and neurotoxins. (Co-directed with Dr. Creed Abell, Department of Pharmacology). Practicing MD..

Qi-Quan Huang. 1993. Molecular biology of muscle development. (Co-directed with Kuan Wang of Biochemistry). Research associate in Canada.

Tia Sea. 1993. Effect of temperature on survival of severed distal stumps of mammalian axons. Currently a practicing nurse.

Cecilia Smith. 1994. Neurite outgrowth in organ culture. Address Unknown

Chris Godell. 1995. Calpain-induced sealing of severed nerve axons. Practicing MD..

Arisa Sunio. 1995. The immunosuppressant cyclosporin A retads the degeneration of distal segments of mammalian axons. Research Associate, Southwestern Medical School, Dallas, TX.

Adam Blanchette. 1998. Changes in configuration and location of membranous structures that seal the cut ends of earthworm giant axons. Currently a Research Associate at UT Medical School, San Antonio, TX

2. Ph.D. Degrees:
Completed

Milton P. Charlton. 1975. Parameters of transmitter release in squid synapses. Professor Emeritus of Physiology at Toronto University.

Lawrence W. Powers. 1975. Physiological and ecological correlates of burrowing behavior in fiddler crabs. Professor and Chairman, Department of Medical Technology, University of South Alabama, Mobile, AL.

Mark E. Meyer. 1977. Histological and biochemical studies of trophic dependencies in crayfish giant axons. Professor of Biology at University of Washington (Seattle).

Stewart C. Birse. 1979. Mechanism and specificity of giant axon regeneration in the earthworm central nervous system. Practicing M.D.

Claire E. Hulsebosch. 1979. Regeneration of axons and cell bodies in the central nervous system of annelids: a test of the neuron addition hypothesis. Professor of Anatomy at U.T. Medical School, Galveston, TX.

Douglas A. Baxter. 1981. Mechanism of pre-synaptic inhibition of transmitter release in crayfish axons. Senior Staff Scientist at Sensory Sciences Center, Baylor Medical School.

Rebecca Sheller. 1989. Molecular mechanisms for long term survival of severed crayfish nerve axons. Professor, Southwestern University, Georgetown, TX.

Shobhana Sivaramakrishnan. 1989. Biophysical mechanisms of calcium and membrane depolarization in synaptic facilitation. Research Scientist, University of Connecticut.

Alvin Lyckman. 1990. Mechanisms of neuritic outgrowth, neuritic guidance, and specific functional reconnection of severed giant axons in earthworms. Current address unknown.

Stephen Massia. 1992. Surface modifications of synthetic materials for the promotion of cell adhesion. Co-directed with Dr. Jeffrey Hubbel of Chemical Engineering. Research Scientist in a private biotechnology firm.

Jeffery Moehlenbruck. 1993. Biochemical mechanisms for long term survival of severed goldfish axons. Professor, St. Edwards Univeristy, Austin, TX.

Todd Krause. 1993. Cellular mechanisms for rapid repair of severed giant axons. Patent attorney, Boston, MA .

Sandy Tanner. 1994. Protein transport and turnover in crayfish medial gaint axons. Research Director, Nymox Corporation (retired)..

Sterling Wright. 1995. Biophysical/electrophysiological mechanisms of synaptic plasticities at crayfish neuromuscular junctions. Professor, Murray State University, Ky.

Tim Raabe. 1995. Mechanisms which determine protein turnover in intact and anucleate axons in vertebrates. Professor, St. Mary's University, San Antonio, TX.

Curtis Herbert. 1996. Effect of inhibitors of fibrinogen proteolysis on neuritic outgrowth from dorsal root ganglia. Co-directed with Dr. Jeffrey Hubble of Chemical Engineering. Associate Professor, University of Minnesota, Minneapolis, Minn.

Chris Eddleman. 1999 Biophysics and molecular biology of plasmalemmal sealing. Co-directed with Dr. Harvey Fishman, UTMB Galveston. Currently a practicing MD

Soonmoon Yoon. 2003 Molecular mechanisms of axonal sealing. Co-directed with Dr. Harvey Fishman. Current position unknown

Michael Nguyen. 2006. Role of calcium in neurite sealing and cell degeneration. Co-directed with Dr. Harvey Fishman. Currently a practicing MD.

Chris Spaeth. 2011. Molecular mechanisms of plasmalemmal sealing. Research Scientist, Houston

Aleksej Zuzek. 2012. Biochemical pathways of plasmalemmal sealing. Postdoctoral Fellow at Texas A&M Medical School (Temple, TX)

Tyler Smith. 2021. Immunosuppressive Effects of PEG-fusion in Peripheral Nerve Allografts. Post-doctoral fellow with Dr. Jennifer Wu, Northwestern University

Cameron Ghergherehchi. 2021. Polyethylene glycol fusion repair of rat peripheral nerves. Post-doctoral fellow with Dr. Jaimie Shores. Johns Hopkins Medical School.

Current.

Liwen (Kevin) Zhou. Role of allografts and Schwann Cells in PEG-fusion repair of peripheral nerve injuries. 5th year PhD student. Awarded Lone Star Foundation Fellowship

Marshal Mencel. 3rd Year PhD Student. Cellular/molecular/biochemical mechanisms that repair traumatic injuries to CNS axons.3rd year PhD student. Awarded Lone Star Foundation Fellowship

Henry Garcia. 2ndYear PhD Student. Translating to the clinic PEG-fusion technology to repair ablation-type peripheral nerve injuries in rat and pig model systems. Awarded NIH PA-423 3 year fellowship

3. *Postdoctoral Fellows. Last known position.*
Completed

Dr. Thomas Hamilton, 1973 - 1974. CIA biomedical scientist and Professor of Biology, University of Virginia, Falls Church.

Dr. Larry Sewell, 1973 - 1974. Patent attorney and biomedical consultant, University of Texas Medical School, Dallas.

Dr. Samuel Velez, 1975 - 1976. Professor of Biology, Dartmouth.

Dr. Bonnie Templeton, 1975 - 1976. Research Associate, Washington University, Department of Biology, St. Louis, MO.

Dr. Thomas Anderson, 1977 - 1979. Director of the CNS Trauma Research Center, General Motors Corp.

Dr. David Falk, 1978. Current position unknown.

Dr. Robert Grossfeld, 1976 - 1979. Professor Emeritus of Zoology, North Carolina State University, Raleigh.

Dr. Douglas Baxter, 1981. Mechanism of pre-synaptic inhibition of transmitter release in crayfish axons. Senior Staff Scientist at Sensory Sciences Center, Baylor Medical School.

Dr. Terry A. Viancour, 1982 - 1984. Professor of Zoology, University of Maryland, Baltimore.

Dr. Richard A. Friedman, 1983 - 1985. Professor of Biophysics and Physiology, Vanderbilt University.

Dr. Kalpathi Seshan, 1982 - 1986. Research Associate, MD Anderson.

Dr. Steven Halls, 1986 - 1987. Current position unknown.

Dr. Bruce Winegar, 1986 - 1988. Research Associate, Department of Pharmacology, University of California Medical School, San Francisco, CA.

Dr. Scott Poehlman, 1988 - 1989. MD. Neurology, University of Wisconsin, Madison.

Dr. Alvin Lyckman, 1991 - 1992. Research Associate. NIH.

Dr. Jay Blundon, 1987 - 1993. NIH, NIAAA postdoctoral fellowships. Professor, Department of Biology, Rhodes College, Memphis, TN.

Dr. Rebecca Sheller, 1990 - 1994. NIAAA postdoctoral fellowship. Professor at Southwestern University, Georgetown, TX.

Dr. Todd Krause, 1993 - 1994. NIAAA fellowship. Co-directed with Dr. Harvey Fishman (UTMB, Galveston) Dept of Biophysics. Patent attorney. Boston, MA..

Dr. Eric Detrait. 1998-2000. Molecular mechamims of plasmalemmal sealing. Co –directed with Dr. Fishman. Currently a Research Scientist at University of Rochester Medical School.

Dr. Ronda Stavisky. 2002-2005. Role of PEG in axonal repair. Current position unknown.

Dr. Van Herd. 2010-2013. Current position unknown.

Dr. Solomon Raju Bhupanapadu Sunkesula. 5/2013 – 12/2015. Role of PEG in axonal repair; Biochemical pathways of membrane sealing. Research Scientist, MD Anderson

Dr. Cameron Ghergherehchi. 6/2021-8/2021. Polyethylene glycol fusion repair of rat peripheral nerves. Post-doctoral fellow with Dr. Jaimie Shores. Johns Hopkins Medical School.

Dr, Tyler Smith. 6/2021-8/2021. Immunosuppressive Effects of PEG-fusion in Peripheral Nerve Allografts. Post-doctoral fellow with Dr. Jennifer Wu, Northwestern University

N. *PUBLICATIONS AND CONTRIBUTIONS*

J. Chen, K.F. Killam, and G.D. Bittner. 1964. Comparison of chlorpromazine, trifluoperazine and pentobarbital on conditioned arousal to reticular stimulation in cats. Fed. Proc. 23:264-268.

G.D. Bittner. 1967. Excitation-contraction coupling in crustacean neuromuscular systems. Ph.D. Thesis. Stanford University.

R.R. Hoy, G.D. Bittner, and D. Kennedy. 1967. Regeneration in crustacean motoneurons: evidence for axonal fusion. Science 156:251-252.
G.D. Bittner. 1968. The differentiation of crayfish muscle fibers during development. J. Exp. Zool. 167:439-456.
G.D. Bittner. 1968. Differentiation of nerve terminals in the crayfish opener muscle and its functional significance. J. Gen. Physiol. 51:731-758.
G.D. Bittner and D. Kennedy. 1970. Quantitative aspects of transmitter release. J. Cell. Biol. 47:585-590.
G.D. Bittner and J. Harrison. 1970. A reconsideration of the Poisson Hypothesis for transmitter release at the crayfish neuromuscular junction. J. Physiol. 206:1-23.
H.L. Atwood and G.D. Bittner. 1971. Matching of excitatory and inhibitory inputs to crustacean muscle fibers. J. Neurophysiol. 34:157-170.
H.L. Atwood, C.K. Govind, and G.D. Bittner. 1973. Ultrastructure of nerve terminals and muscle fibers in denervated crayfish muscle. Zeit. Zellforsch. 146:155-166.
G.D. Bittner and R. Kopanda. 1973. Factors influencing molting in the crayfish *Procambarus clarkii*. J. Exp. Zool. 186:7-17.
G.D. Bittner. 1973. Trophic dependence of fiber diameter in a crustacean muscle. Exp. Neurol. 41:38-53.
G.D. Bittner. 1973. Degeneration and regeneration in crustacean neuromuscular systems. Amer. Zool. 13:379-408.
G.D. Bittner and A. Johnson. 1974. Degeneration and regeneration in crustacean peripheral nerves. J. Comp. Physiol. 89:1-21.
L.P. Boone and G.D. Bittner. 1974. Morphological and physiological measures of trophic dependence in a crustacean muscle. J. Comp. Physiol. 89:123-144.
G.D. Bittner, M. Ballinger, and J.L. Larimer. 1974. Crayfish CNS: minimal degenerative-regenerative changes after lesioning. J. Exp. Zool. 189:13-36.
M.P. Charlton and G.D. Bittner. 1974. Facilitation of transmitter release at the squid giant synapse. Biol. Bull. 147:471-472.
D. Kennedy and G.D. Bittner. 1974. Ultrastructural correlates of motor nerve regeneration in the crayfish. Cell Tiss. Res. 148:97-110.
G.D. Bittner and M. Nitzberg. 1975. Degeneration of sensory and motor axons in transplanted segments of a crustacean peripheral nerve. J. Neurocytol. 4:7-21.
G.D. Bittner and D.W. Mann. 1976. Differential survival of isolated portions of crayfish axons. Cell and Tiss. Res. 169:301-311.
S.C. Birse and G.D. Bittner. 1976. Regeneration of giant axons in earthworms. Brain Res. 113:575-581.
G.D. Bittner and L. Sewell. 1976. Facilitation at crayfish neuromuscular junctions. J. Comp. Physiol. 109:287-308.
G.D. Bittner. 1977. Trophic interactions of crustacean neurons. In: Identified Neurons and Behavior, Ed. by G. Hoyle in honor of Professor C.A.G. Wiersma. pp. 507-532.
M.L. Ballinger and G.D. Bittner. 1978. Developmental abnormalities of identifiable neurons in the crayfish *Procambarus simulans*. J. Neurobiol. 9:301-307.
G.D. Bittner and D.L. Traut. 1978. Growth of crustacean muscles: constancy of fiber number and sarcomere number. J. Comp. Physiol. 124:277-285.
M.P. Charlton and G.D. Bittner. 1978. Effect of changes in presynaptic potentials on facilitation in squid synapses. J. Gen. Physiol. 72:487-511.
M.P. Charlton and G.D. Bittner. 1978. Facilitation of transmitter release at squid synapses. J. Gen. Physiol. 72:471-486.
M.R. Meyer and G.D. Bittner. 1978. Histological studies of trophic interactions in crayfish giant axons. Brain Res. 143:195-211.
M.R. Meyer and G.D. Bittner. 1978. Biochemical studies of trophic interactions in crayfish giant axons. Brain Res. 143:212-232.
M.L. Ballinger and G.D. Bittner. 1980. Ultrastructural studies of severed medial giant and other CNS axons in crayfish. Cell and Tiss. Res. 208:123-133.

G.D. Bittner and M.L. Ballinger. 1980. Ultrastructural changes at gap junctions between lesioned crayfish axons. Cell and Tiss. Res. 207:143-153.
D.A. Baxter and G.D. Bittner. 1980. The normal accumulation of facilitation during presynaptic inhibition. Brain Res. 189:535-539.
T.E. Anderson and G.D. Bittner. 1980. Long-term alteration of electrotonic synapses. Brain Res. 184:224-228.
C.E. Hulsebosch and G.D. Bittner. 1980. Evolution of abilities to regenerate CNS neurons. Am. Naturalist 115:276-284.
T.A. Viancour, G.D. Bittner and M.L. Ballinger, 1981. Selective transfer of Lucifer Yellow CH from axoplasm to adaxonal glia. Nature. 293:65-67.
M.S. Bouton and G.D. Bittner. 1981. Regeneration of motor axons in crayfish limbs: distal stump activation followed by synaptic reformation. Cell and Tiss. Res. 219:379-392.
G.D. Bittner and M.R. Brown. 1981. Long term survival of enucleated glial cytoplasm in the leech *Macrobdella decora*. Brain Res. 218:357-364.
C.E. Hulsebosch and G.D. Bittner. 1981. Regeneration of nerve cell bodies in annelids: a test of the neuronal addition hypothesis. J. Comp. Neurol. 198:77-88.
C.E. Hulsebosch and G.D. Bittner. 1981. Morphology and number of neurons in two species of polychaetes. J. Comp. Neurol. 198:65-76.
S. Velez, G.D. Bittner, G.K. Govind and H.L. Atwood. 1981. Trophic reactions of crayfish muscle fibers and nerve synapses following denervation, tenotomy, and immobilization. Exp. Neurol. 71:307-325.
S.C. Birse and G.D. Bittner. 1981. Regeneration of earthworm giant axons following transection or ablation. J. Neurophysiol. 45:724-742.
G.D. Bittner and R.A. Schatz. 1981. An examination of the residual calcium hypothesis for transmitter release. Brain Res. 210:431-436.
G.D. Bittner. 1981. Trophic interactions of crustacean giant axons. Comp. Biochem. Physiol. 68A:299-306.
R.M. Grossfeld, G.D. Bittner, and M.A. Raymond. 1982. Inter- and intra-axonal variations in morphology and metabolic activity of the crayfish medial giant axon. J. Neurobiol. 13:191-197.
D.A. Baxter and G.D. Bittner. 1982. Intracellular recordings from crustacean motor axons during presynaptic inhibition. Brain Res. 223:422-428.
G.D. Bittner. 1983. Muscles and their neural control. Science 222:611-613.
D.A. Baxter, G.D. Bittner, and T.H. Brown. 1985. Quantal mechanisms of long-term synaptic potentiation. PNAS 82:5978-5982.
G.D. Bittner, and J.P. Segundo. 1986. Facilitation. In Encyclopedia of Neuroscience. Ed. G. Adelman. Birkhauser. p. 428-430.
G.D. Bittner, M.L. Ballinger, and M.A. Raymond. 1986. Reconnection of severed nerve axons with polyethylene glycol. Brain Res. 367:351-365.
K.R. Seshan and G.D. Bittner. 1987. Developmental and other factors affecting regeneration of crayfish CNS axons. J. Comp. Neurol. 262:535-545.
T.A. Viancour, K.R. Seshan, G.D. Bittner, and R.A. Sheller. 1987. Organization of axoplasm in crayfish giant axons. J. Neurocytol. 16:557-566.
R.N. Friedman, G.D. Bittner, and J.A. Blundon. 1988. Electrophysiological and behavioral effects of ethanol on crayfish. J. Exp. Pharm. & Therap. 246:125-131.
G.D. Bittner. 1988. Long term survival of severed distal axonal stumps in vertebrates and invertebrates. Am. Zool. 28:1165-1179.
B.D. Winegar, G.D. Bittner, and S.W. Leslie. 1988. Effects of pentobarbital on behavioral and synaptic plasticities in crayfish. Brain Res. 475:21-27.
T.A Viancour, R.A. Sheller, G.D. Bittner, and K.R. Seshan. 1988. Protein transport between crayfish lateral giant axons. Brain Res. 439:211-221.
G.D. Bittner and J.P. Segundo. 1989. Effect of stimulus timing on transmitter release and postsynaptic membrane potential at crayfish neuromuscular junctions. J. Comp. Physiol. 165:371-382.
G.D. Bittner. 1989. Synaptic plasticity at the crayfish opener neuromuscular preparation. J. Neurobiol. 20:386-408.

J.A. Blundon, R.A. Sheller, J.W. Moehlenbruck, and G.D. Bittner. 1990. Effect of temperature on long term survival of anucleate giant axons in crayfish and goldfish. J. Comp. Neurol. 297:377-391.
T.L. Krause and G.D. Bittner. 1990. Rapid morphological fusion of severed myelinated axons by polyethylene glycol. PNAS. 87:1471-1475.
S. Sivaramakrishnan, G.D. Bittner, and M.S. Brodwick. 1991. Calcium-activated potassium conductance in presynaptic terminals at crayfish neuromuscular junction. J. Gen. Physiol. 98:1161-1180.
S. Sivaramakrishnan, M.S. Brodwick, and G.D. Bittner. 1991. Presynaptic facilitation at crayfish neuromuscular junctions: role of calcium-activated potassium conductance. J. Gen. Physiol. 98:1181-1196.
R.A. Sheller, M.L. Ballinger, and G.D. Bittner. 1991. Long term survival of severed crayfish giant axons is not associated with an incorporation of glial nuclei into axoplasm. Neurosci. Letters 133:113-116.
T.L. Krause, R.M. Marquis, A.W. Lyckman, M.L. Ballinger, and G.D. Bittner. 1991. Rapid artificial restoration of electrical continuity across a crush lesion of a giant axon. Brain Res. 561:350-353.
G.D. Bittner. 1991. Long term survival of anucleate axons and its implications for nerve regeneration. Trends in Neurosci. 14:188-193.
G.D. Bittner and D.A. Baxter. 1991. Mechanisms of synaptic plasticity at crayfish neuromuscular junctions: facilitation and augmentation. Synapse. 7:235-243.
D.A. Baxter and G.D. Bittner. 1991. Mechanisms of synaptic plasticity at crayfish neuromuscular junctions: pre-synaptic inhibition. Synapse 7:244-251.
A.W. Lyckman and G.D. Bittner. 1992. Axonal conduction and electrical coupling in regenerating earthworm giant axons. Exp Neurol. 117:299-306.
R.A. Sheller and G.D. Bittner. 1992. Maintenance and synthesis of proteins for an anucleate axon. Brain Res. 580:68-80.
A.W. Lyckman, S.M. Thomas and G.D. Bittner. 1992. Analysis of neuritic outgrowth from severed giant axons in *Lumbricus terrestris*. J. Comp. Neurol. 318:426-438.
J.A. Blundon and G.D. Bittner. 1992. Effects of ethanol and other drugs on excitatory and inhibitory neurotransmission in the crayfish. J. Neurophysiol. 67:576-587.
J.A. Blundon, S.N. Wright, M.S. Brodwick and G.D. Bittner. 1993. Residual free calcium is not responsible for facilitation of transmitter release. PNAS 90:9388-9392.
R.A. Sheller and G.D. Bittner. 1993. Whole intact tissue electrophoresis of nerve proteins. J. Neurosci. Methods 49:185-191.
J.W. Moehlenbruck, J.A. Cummings and G.D. Bittner. 1994. Long term survival followed by degradation of neurofilament proteins in severed Mauthner axons of goldfish. J. Neurobiol. 25:1637-1651.
T.L. Krause, H.M. Fishman, M.L. Ballinger, and G.D. Bittner. 1994. Extent and mechanism of sealing in transected giant axons of squid and earthworms. J. Neurosci. 14:6638-6651.
T.L. Krause, H.M. Fishman, and G.D. Bittner. 1994. Axolemmal and septal conductance in the impedance of the earthworm medial giant nerve fiber. Biophys. J. 67:692-695.
M.A. Todora, H.M. Fishman T.L. Krause, and G.D. Bittner. 1994. Shortening of a severed squid giant axon is non-uniform and occurs in two phases. Neurosci. Lett. 179:57-59.
T.L. Krause, Y. Magarshak, H.M. Fishman, and G.D. Bittner. 1995. Membrane potential and input resistance are ambiguous measures of sealing of transected cable-like structures. Biophys. J. 68:795-799.
S.L. Tanner, E.E. Storm, and G.D. Bittner. 1995. Protein transport in intact and severed (anucleate) crayfish medial giant axons. J. Neurochem. 64:1491-1501.
R.A. Sheller, M. Tytell, M. Smyers, and G.D. Bittner. 1995. Glia to axon communication: Enrichment of glial proteins transferred to the squid giant axon. J. Neurochem. Res. 41:324-334.
S.L. Tanner, E.E. Storm, and G.D. Bittner. 1995. Maintenance and degradation of proteins in intact and severed axons: Implications for the mechanism of long term survival of anucleate crayfish axons. J. Neurosci. 15:540-548.
T.D. Raabe, T. Nguyen, and G.D. Bittner. 1995. Calcium activated proteolysis of neurofilament proteins in goldfish Mauthner axons. J. Neurobiol. 26:253-261. PubMed PMID: 7707045.

J.A. Blundon, S.N. Wright, M.S. Brodwick, and G.D. Bittner. 1995. Presynaptic calcium-activated potassium channels and calcium channels at a crayfish neuromuscular synapse. J. Neurophysiol. 73:178-189.

T. Sea, M.L. Ballinger, and G.D. Bittner. 1995. Cooling of peripheral myelinated axons retards Wallerian degeneration. Exp. Neurol. 133:85-95.

C.S. Eddleman, C.M. Godell, H.M. Fishman, M. Tytell, and G.D. Bittner. 1995. Florescent labelling of the glial sheath of giant nerve fibers. Biol. Bull., 189:218-219.

H.M. Fishman, T.L. Krause, A.L. Miller, and G.D. Bittner. 1995. Retardation of the spread of extracellular Ca^{++} into transected, unsealed squid giant axons. Biol. Bull., 189:208-209.

T.D. Raabe and G.D. Bittner. 1996. Phosphorylation of neurofilament proteins in isolated goldfish Mauthner axoplasm. J. Neurochem., 66:1214-1221.

C.B. Herbert, G.D. Bittner, and J. A. Hubbell. 1996. Effects of fibrinolysis on neurite growth from dorsal root ganglia cultured in two- and three-dimensional fibrin gels. J. Comp. Neurol., 365:380-391. doi: 10.1002/(SICI)1096-9861(19960212)365:3<380::AID-CNE4>3.0.CO;2-0. PubMed PMID: 8822177.

T.D. Raabe, T. Nguyen, C. Archer, and G.D. Bittner. 1996. Mechanisms for the maintenance and eventual degradation of neurofilament proteins in the distal segments of severed goldfish Mauthner axons. J. Neurosci., 16: 1605-1613. PubMed PMID: 8774429.

S.N. Wright, M.S. Brodwick, and G.D. Bittner. 1996. Presynaptic calcium currents at voltage- clamped excitor and inhibitor terminals of crayfish. J. Physiol., 496:347-361. PubMed PMID: 8910221; PubMed Central PMCID: PMCPMC1160882.

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A. Sunio and G.D. Bittner. 1997. Cyclosporin retards the Wallerian degeneration of peripheral mammalian axons. Exp. Neurol., 146:46 - 56. doi: 10.1006/exnr.1997.6484. PubMed PMID: 9225737.

C.S. Eddleman, M.L. Ballinger, M.E. Smyers, C.M. Godell, H.M. Fishman, and G.D. Bittner. 1997. Repair of plasmalemmal lesions by vesicles. PNAS. 94:4745-4750. PubMed PMID: 9114062; PubMed Central PMCID: PMCPMC20795.

C.M. Godell, M. Ballinger, C.S. Eddleman, M.E. Smyers, H.M. Fishman, and G.D. Bittner. 1997. Calpain promotes the sealing of severed giant axons. PNAS. 94:4751-4756. PubMed PMID: 9114063.

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A Olivarez, L. Zhou, GD Bittner, Repair of Spinal cord ablation by PEG-fusion of allografts in rats.

M Mencel and GD Bittner. Repair of traumatic lesions to the plasmalemma: your intuition is almost certainly wrong

Additional Service and Research

In my off-campus research begun in 2000, I developed sensitive *in vitro* robotic assays to detect xenobiotic chemicals having mammalian hormonal activity (i.e. endocrine disruptors). I used such data to develop polymer formulations and bio-engineer protocols to produce plastic and silicone products that do not release chemicals having hormonal activity (especially estrogenic or androgenic activity). In the last decade, this basic and applied research has been funded by more than 15 NIH and NSF grants totaling over $8M (over $12M from all sources). **The University of Texas at Austin was also recognized on all papers published describing these data.** I believe that my scientific colleagues and I were the leading researchers in this field, i.e., an intersection of cellular/molecular endocrinology and polymer chemistry that has obvious implications for human health and environmental contamination. This off-campus

research still has much potential to help solve a major health problem that until recently has gone largely unrecognized—the release of xenobiotic chemicals having hormonal activity by plastics and other substances. Our conclusions are strongly supported by scientists and administrators at NIH and NSF—and strongly

This off-campus research was performed by CertiChem (aka CCi) and PlastiPure (aka PPi). The mission of CertiChem was to develop sensitive, accurate, high throughput assays to detect hormonal activity. CertiChem is primarily an R&D entity. The mission of PlastiPure was to develop polymer formulations, resins and manufacturing procedures/protocols for plastic and silicone-based products that do not release chemicals having hormonal activity. Our data showed that almost all existing plastics and silicone products release chemicals having easily detectable estrogenic activity. PlastiPure completed the transition from an R&D entity in 2008 to a viable commercial entity in 2011. We closed PPi as a commercial entity in the summer of 2020.

As consulting CEO for CertiChem and consulting Chief Scientific Officer for PlastPure, my main task was to direct scientific research and development of patentable chemicals, formulations and/or products, and direct and write SBIR grant proposals in collaboration with PIs employed by the firm. We are selling and closing CCi by January 2021. An NSF or NIH SBIR PI (or co-PI) must be employed at least 51% time by CertiChem or PlastiPure (My total time combined for both firms was less than 18%). In this capacity, I was largely responsible for writing peer-reviewed research papers, deciding the Specific Aims and directing the writing of the following grants awarded since 2001:

For CertiChem:

NIH/NIEHS R44 ES026470 01-01 (PI= CZ Yang) ~12/1/2015 - 5/30/2018
Validation of an In Vitro Assay for Androgenic Activity
Total award $1,213,515

NIH/NIEHS R43 ES025075-01 (PI = CZ Yang) 09//01/2014 – 2/28/2015
Safer Personal Care Products
Total Award $141,079

NSF 0912601-03 (PI = CZ Yang) 09/15/2010 – 8/31/2014
Food antioxidants With or Without Estrogenic Activity
Total award: $500,000
Supplement about $400,000 (final amount pending)

NSF 0912601-01 (PI = CZ Yang) 07/01/2009 – 12/31/2009
Food antioxidants With or Without Estrogenic Activity
Total award: $99,898

NIH/NIEHS 5R44ES014806-03 (PI = CZ Yang) 9/01/2008 – 8/31/2009
In Vitro Robotic Assay for Anti-Estrogenic Activity
Total award: $446,359

NIH/NIEHS 2R44ES014806-02 (PI = Yang) 9/11/2007 – 8/31/2008
In Vitro Robotic Assay for Anti-Estrogenic Activity
Total Award: $476,510

NIH/NIEHS 1 R43 ES011806-01 PI = C.Z. Yang) 06/01/2006 – 12/31/2006
In vitro Robotic Assay for Anti-Estrogenic Activity
Direct Cost: $72,788, total Cost = $121,756

NIH/NIEHS 1 R44 ES011469-02 PI = C..Z. Yang 04/01/2004 – 04/30/2007
In vitro Robotic Assay for Estrogenic Activity
Direct Cost: $901,209, Total Cost: $1,350,618

1 R43 ES011469-01 PI = C.Z. Yang (PI) 04/01/2001 – 10/01/2001
In vitro Robotic Assay for Estrogenic Activity
Direct Cost: $75,000

For PlastiPure

NIEHS 1 R43 ES018083-02 PI = D.Kline 08/20/2013 – 8/19/2015
A Hard and Clear, Estrogen-Free Replacement for Bisphenol-A Based Polycarbonates
Total Cost: $956,000

NSF IIP-1127553 PI = D Kline 09/15/2011-08/31/2014
Flexible Plastic Packaging Without Estrogenic Activity (EA)
Total cost: $488,236
Supplement$100,000

NIEHS 1R44ES019442-02,03 PI = S. Yaniger 01/01/2011 – 2/28//2013
Baby bottles that release no chemicals having estrogenic activity
Total Cost: $1,285,871

NIEHS 1R44ES019442-01 PI = S. Yaniger 09/01/2010 – 12/31/2010
Baby bottles that release no chemicals having estrogenic activity
Total Cost: $141,830

NSF IIP-1013865 PI = D. Klein 07/01/2010 - 12/31/2010
Flexible Plastic Packaging Without Estrogenic Activity (EA)
Total Cost: $150,000

NIEHS 1 R43 ES018083-01 PI = S.Yaniger 06/01/2010 – 11/30/2010
A Hard and Clear, Estrogen-Free Replacement for Bisphenol-A Based Polycarbonates
Total Cost: $222,248

NIEHS 2R44ES016964-02 PI= S. Yaniger / D. Klein 08/14/2009 – 07/31/2010
Estrogen free Polymer Formulations for Food Packaging and Baby Products
Total Cost: $1,207,230

NIEHS 1R43ES016964-01 PI = J Laiz 06/01/2008 – 11/30/2008
Estrogen Free Polymer Formulations for Food Packaging and Baby Products
Total Cost: $134,264

CCi was selected by ICCVAM/NICEATM to perform a single-lab validation study using MDA-Kb2 cells to detect androgenic activity (AnA in robotic and manual formats. Items **C1 and C2** below lists some of our basic (**C1**) and applied (**C2**) peer-reviewed publications. My role in both firms was to guide their scientific direction and take the lead in writing grant proposals and peer-reviewed papers.

At CCi, we developed, robotized, and validated with ICCVAM/NICEATM/OECD a battery of *in vitro* assays using MCF-7 cells or BG1-Luc cells to detect EA** and MDA-Kb2-cells to detect AnA** that are the most accurate and sensitive currently available, in part due to our developing Confirmation Assays. Using these assays, we have demonstrated that the great majority of plastic, silicone and personal care products (PCPs) release a variety of chemicals having EA**/AnA**. Using these assays, we have created a knowledge base of commonly-used chemicals and materials that are EA**/AnA** or EA/AnA**-free and can be used to make plastics and PCPs. Using this knowledge base and a knowledge of polymer and other chemistry, we have identified or developed formulations for products that leach ***no*** chemicals having detectable EA**/AnA** after extraction with hydrophilic or hydrophobic solvents or after common-use stresses of heating, boiling microwaving, UV radiation. This approach differs from that currently used by various commercial, academic, regulatory or government entities that address problematic ingredients having EA**/AnA** (e.g., BPA) one-at-a time without considering that many other ingredients also have significant hormonal activity -- and that more than one solvent is needed for appropriate extraction and that products need be exposed to common use stresses that can create new chemicals. Furthermore, replacing chemicals one-by-one is much more costly than reformulating to eliminate all ingredients having EA**/AnA**.

At CCi, my fellow scientists and I believe that when a large variety of EA**/AnA**-free** products become available to the public, this will reduce the potential health problems associated with EDCs of which the most frequent types of hormonal activity in the "chemical commons" are from leached chemicals having EA**/AnA**. I believe that CCi is ***the*** leading laboratory in the intersection of hazard analysis, public awareness and genuine health-related product solutions to a problem now being recognized by government agencies and consumer groups.

C1. Representative peer-reviewed papers on assays to detect EDCs with EA

C.Z. Yang, W. Casey, M. Stoner, G.J .Kollessery, A.W. Wong and G.D. Bittner. 2014. A robotic MCF-7:WS8 cell proliferation assay to detect agonist and antagonist estrogenic activity. Toxological Sci. 137:335-349.

M.A.Stoner, C.Z.Yang, and G.D.Bittner. 2014. A Robotic BG1Luc Reporter Assay to Detect Estrogen Receptor Agonists. Toxicology in Vitro. 28: 916–925.

These two papers describe our robotic assays for EA that have very high concordance with ICCVAM/ECCVAM meta-analyses for test chemicals. Specifically, our robotic BG1Luc assay has high (100%) concordance for the presence or absence of detectable EA with ICCVAM meta-analyses for 27 test chemicals. When chemicals tested in common by both assays are compared, this robotic BG1Luc assay has 100% concordance with the ICCVAM manual BG1 assay for 27 test chemicals, 100% concordance with CERI for 20 test chemicals, and 100% concordance with a robotic MCF-7 assay for 27 test chemicals. In contrast, the yeast estrogen screening (YES) assay has only 47% (7/15) concordance with any of these other assays for 15 test chemicals. When sensitivities of these different assays are compared to detect the EA of the same test chemical as defined by its EC50, our robotic BG1Luc assay is more sensitive for 15/20 and one tie out of 21 chemicals reported by ICCVAM meta-analyses , i.e., is more sensitive ($p < 0.001$, Chi Squared test) for 15 chemicals whose EC50s can be directly compared. Compared to ICCVAM BG1 manual data for 22 chemicals, our robotic BG1Luc assay is more sensitive for 14/22 ($p < 0.0.001$). Compared to CERI manual assays, the robotic BG1 is more sensitive for 18/20 test chemicals ($p <0.0001$). Compared to the YES assay, the robotic BG1 assay is more sensitive ($p < 0.0001$) for 15/15 chemicals whose EC50s can be directly compared. In contrast, with respect to the robotic MCF-7 assay as reported for ICCVAM validation results, the BG1Luc is more sensitive for only 4/27 chemicals whose EC50 can be directly compared, i.e. the MCF-7 assay is more sensitive (and has as high a concordance) with a high significance ($p < 0.0001$) compared to our EC50

from our robotic BG1Luc, ICCVAM manual BG1Luc, CERI, and YES assays and ICCVAM EC50 meta-analyses.

C2. Representative peer-reviewed papers on release of EDCs having EA from various consumer products.

C. Z. Yang, S. I. Yaniger, V. C. Jordan, D. Klein and G.D. Bittner. 2011. Most Plastic Products Release Estrogenic Chemicals: A Potential Health Problem That Can Be Solved. Environmental Health Perspectives. 119: 989-996.

S.L. Myers, C.Z.Yang, G.D. Bittner, K.L. Witt, R.R. Tice, D.D. Baird. 2014. Estrogenic and Anti-Estrogenic Activity of Off –The-Shelf Hair and Skin Products. Journal of Exposure Science and Environmental Epidemiology. 25:271-277.

G.D.Bittner, M. A. Stoner, C. Z. Yang. 2014. Estrogenic chemicals often leach from BPA-free plastic products that are replacements for BPA-containing polycarbonate products. Environmental Health 13:41-54.

G.D. Bittner, M.S. Denison, C. Z. Yang. 2014. Chemicals having estrogenic activity can be released from some BPA-free, hard and clear, thermoplastic resins. Environmental Health. 13:103-121.

These papers report that consumer products in two general categories-–—plastics and personal care products (PCPs) – release chemicals thast have easily-detectable EA as measured by our two robotic assays for EA. The data for PCPs are described in the body of this proposal. The results of our two hazard studies of BPA-replacement resins (aka polycarbonate or PC resins) and PC-replacement products. Like PC resins, these PC-replacement resins are "hard, clear, and reusable". Some (4/14) of these unstressed and stressed BPA-free resins leached chemicals having significant levels of EA, including one polystyrene, and three Tritan™ resins, the latter reportedly EA-free. Exposure to UV radiation in natural sunlight resulted in an increased release of EA from Tritan™ resins. Ten unstressed or stressed glycol-modified polyethylene terephthalate (PETG), cyclic olefin polymer (COP) or copolymer (COC) thermoplastic resins did not release chemicals with detectable EA under any test condition. Similarly, many unstressed and stressed, PC-replacement-products made from acrylic, polystyrene, polyethersulfone, and Tritan™ resins leached chemicals with EA, including products made for use by babies. Exposure to various forms of UV radiation often increased the leaching of chemicals with EA. In contrast, some BPA-free PC-replacement products made from glycol-modified polyethylene terephthalate or cyclic olefin polymer or co-polymer resins did not release chemicals with detectable EA under any conditions tested.

These two hazard assessment surveys showed that many BPA-free PC- replacement resins and products still leached chemicals having significant levels of EA, as did their BPA-containing PC counterparts they were meant to replace. That is, BPA-free did not mean EA-free. However, this study also showed that some PC-replacement resins and products did ***not l***each chemicals having significant levels of EA. That is, EA-free PC-replacement resins and products can be made in commercial quantities at prices that compete with PC-replacement products that are not BPA-free. Since plastic products often have advantages (price, weight, shatter-resistance, etc.) compared to other materials such as steel or glass, our data show that is not necessary to forgo those advantages of plastics in order to avoid release into foodstuffs or the environment of chemicals having EA that may have potential adverse effects on our health or the health of future generations.

Detailed Research Support. G. Bittner = sole P.I. unless otherwise noted; direct and indirect and total costs

<u>Previous Research Support for last 5 years</u>

1) Title: Enhanced Regeneration and Repair of Severed Spinal and PNS Axons
Time Commitment: 1% [0.12 person-months]
Agency: Lone Star Paralysis Foundation

Grants Officer: Doug English, 7900 FM 1826, Bldg. II Rm. 105, Austin, TX 78737

Performance Period and Funding: Gifts. All direct costs. No overhead costs.

1/16-12/16 $60,000 +10,000 eqpt

1/16- 7/16 $20,000 Dr. Richard Trevino (PI) at WellSpan York Hospital and G Bittner (Basic science advisor) to U Pennsylvania Pharmaceutical lab for FDA IND of sterile PEG solution for York IRB

1/17-12/17 $60,000

1/18- 8/30/18 30K (3/7)+35K(5/22) +10K(8/6) +90K 8/30) = $165,000

1/17-12/17 $60,000

1/18- 8/30/19 30K (3/7/18)+35K(5/22/18) +10K(8/6/18) +90K 8/30/18) = $165,000

9/2019-5/2020 $60,000

5/2020 – 3/2021 $50,000

3/2021 - 1/2024 $195,000 direct costs to support postdoctoral fellows on spinal research

Description/Aims: The goal is to modify our PEG-fusion technology to repair spinal cord and PNS injuries. As a gift, all funds are direct costs only with no overhead costs to support pilot studies in basic research with no specific Aims

No specific scientific or budgetary overlap

2) Title: R01NS081063 A novel bioengineered technique to rapidly and permanently repair cut PNS nerves

Time Commitment: 10% [1.20 person-months]

Agency: NIH-NINDS

Grants Officer: Lyn B. Jakeman, NIH, 9000 Rockville Pike, Bethesda, Maryland 20892

Performance Period and Funding Level:

9/15/12—6/30/18 $1,860,200 Total direct + indirect costs originally awarded... Total award after across the board cut of 17.5% for all NIH R-01 non-modular grants.

Description/Aims: Use cultured B104 cells and *ex vivo* methods to develop the best sequence of solutions for PEG-fusion mostly in acutely cut rat sciatic nerves as examined *in vivo* by several behavioral and morphemetric assay methods

Aim 1. Determine what bio-engineered solutions or conditions best increase or decrease sealing *in vitro* and PEG-fuse-repair acutely severed (cut) rat sciatic nerves *ex vivo* and then *in vivo*. We have published six papers on how various substances (including PEG and MB), biochemical pathways, and transection sites increase or decrease the ability of an axolemma to seal after transection. We have used these data to develop improved PEG-fusion protocols to repair acutely cut sciatic nerves as described in eight papers whose major findings include the role of Ca^{2+}, nerve stretch, length of damaged membrane, MB, PEG concentration and application time on SFI recovery, prevention of Wallerian degeneration and plasticity responsible for behavioral recoveries.

Aim 2. Determine what bioengineered solutions best increase survival of rat sciatic axons chronically severed for up to 10 days *in vivo*.

We obtained pilot data that Ca^{2+}-free Plasmalyte^{TM} solutions at 20° C can increase survival of severed rat sciatic axons for at least three days. For this Aim, we used allograft model systems.

Aim 3. Determine what treatment solutions and temperatures best PEG-fuse-repair acute interposition autografts of rat sciatic axons *ex vivo* and *in vivo*. Pilot studies only.

Aim 4. Determine what treatments best PEG-fuse-repair acute allografts of rat sciatic axons *ex vivo* and *in vivo*. Since discovering the unexpected PEG-fusion success of

allografts in the third year (2015) of this R-01, we have examined rapid and dramatic behavioral recovery, lack of rejection of allografts even between Sprague-Dawley and Long-Evans strains, ability to store allografts in Plasmalyte™ for at least 3 days, dramatic prevention of Wallerian degeneration, and insights into mechanisms underlying neuronal plasticity.

7/15/15 - 6/30/18. $153,000 supplement total direct + indirect costs.

Supplement to support a graduate student to begin to investigate innate and adaptive immunological responses to begin to explain why PEG-fused donor allografts of rat sciatic nerves are not rejected even though they are allogenic, in an unprotected environment, not tissue matched and not immune suppressed. If not PEG-fused, such allografts are rapidly rejected within days.

No scientific or budgetary overlap

4) Title: Neuraptive,Inc. Sponsored Research Agreements (SRAs)
Time Commitment: 1% [0.12 person-months]
Agency: Neuraptive Therapeutics
Grants Officer: David Jackson, Lafayette, CO 80026
Performance Period and Funding Level:
Neuraptive Sponsored Research Agreement (SRA). Direct plus indirect costs.
5/1/2017- 1/1/2018. $56,299
Pilot study of glucocorticoids (GCs) in rat sciatic nerve PEG-fusion model $25,000
Pilot Study of Neuraptive Device Effectiveness in Rat and Rabbit Sciatic Nerve PEG-Fusion Model $31,299

Description and Aims:

P1	**Pilot study of glucocorticoids (GCs) in rat sciatic nerve PEG-fusion model** Pilot study to examine effects of methyl prednisolone, progesterone, dexamethasone, and TrA on the inflammatory response of PEG- fused sciatic axons at 7, 14, or 21 post-operative days.	Assess effects morphologically and functionally
P2	Pilot study to examine formulations of GCs for topical nerve administration in rat sciatic nerve PEG-fusion model	Assess effects morphologically and functionally
P3	Pilot structure-activity study of formulated GCs in rat sciatic nerve PEG-fusion model	Assess effects morphologically and functionally

Pilot Study of Neuraptive Device Effectiveness in Rat and Rabbit Sciatic Nerve PEG-Fusion Model $31,300

Pilot study of Neuraptive Device Effectiveness of Sciatic Nerve PEG-Fusion in rat and rabbit sciatic nerve PEG fusion, and assess the effect morphologically and functionally. Examine the effects of the Neuraptive Device on CAP fusion and SFI-scored behavior of PEG- fused sciatic axons acutely and/or at 7, 14, 21, 28, 35 and 42 post-operative days. Examine the effects using 5 acute rat experiments, 1 acute rabbit experiment, and 10 chronic rat experiments with parameters as specified by Neuraptive.

Gifts in addition to Neuraptive SRAs: (direct costs, no overhead costs)

Neuraptive Research Gift for Equipment	5/5017	$15,000
Neuraptive Research Gift for PEG-fusion Research	10/2017	$50,000
Neuraptive Research Gift for PEG-fusion Research	5/2018	$20,000

5. Title: W81XWH-19-2-0054. Log # OR180077. Immediate repair with accelerated recovery from peripheral nerve injury using PEG-fusion technologies

Time Commitment: 10% [1.2 person-months]

Agency: DOD PRORP grant

Grants Officer: Miriam Redington, Science Officer; 301.619.3477 Miriam.E.Redington.CIV@mail.mil

Performance Period and Funding: 9/15/2019 – 9/14/2022. $ 824,911 total costs. G Bittner submitting and corresponding PI. $510,046 total costs to UTA, $188,988 to Johns Hopkins Medical School (Jaimie Shores PI), and $114,877 To DOD METIS (Erik Weitzel, PI, Joseph Alderete Key Collaborator). *Pending. Transfer of additional $25,000 from METIS to UTA.*

Description/Aims: Pilot study to determine the possible efficacy of PEG-fusion technology on single transection peripheral nerve injuries (PNIs) repaired by primary PEG-fusion and segmental loss (ablation type) PNIs repaired by PEG-fused allografts in rats and swine.

Aims (9/1/2021 revision)

Specific Aims:

Aim 1. Extend the time for successful PEG-fusion repair of single transection PNIs segmental ablation-type PNIs with allografts in a rat sciatic nerve model.

Aim 1A1. Determine effects of 0.5% and 1% MB.

Aim 1A$_2$. Train new lab manager, Dr Cathy Yang (hired 6/2/2020) in behavioral testing, TEM, IHC, and microsurgery required for PEG-fusion of singly cut and ablated segment sciatic nerves, the latter called PEG-fused PNAs.

Aim 1A$_3$. Determine the maximum time after a PNI for successful PEG-fusion repair.

Aim 1B. Short term (1-2 min) exposure to high concentrations (50%w/w) of 3.235 kD PEG by itself reduces inflammatory responses in ablation type PNIs in wildtype SD/SD rat host and donor allograft repair.

Aim 1C. Allografts can be stored at least 72h in Plasmalyte at 4^{o}C and successfully used for PEG-fusion repair of ablation-type PNIs.

Aim 2 at JHU and SA (RESTOR,METIS)

Aim 2A-C. Determine if PEG-fusion repairs of single transection and ablation-type PNIs using a large animal model (swine median nerve) having nerve diameters and immune responses more like humans are comparable to results of Aims 1A-C using a small animal model (rat sciatic). In Aim 2, all surgeries will be done at Johns Hopkins or RESTOR and tissues sent to UTA for processing.

Aim 2A. Single transection or ablation type PNIs in swine median nerves can be successfully repaired by PEG-fusion at least 24h p.i. without any intervention.

Aim 2B. Single transection or ablation type PNIs in swine median nerves can be successfully repaired by PEG-fusion at least 36h p.i. and reduce inflammation if MP is directly applied to the lesioned area immediately after PEG-fusion repair.

Aim 2C. Allografts of swine median nerves can be stored at least 72h in Plasmalyte

at 4^{o}C and successfully used for PEG-fusion repair of ablation-type PNIs at 24 or 36h p.i.

6) Title: Novel PEG-fusion therapy for acute and chronic spinal cord injury

*Major Goals: **Determine success pf PEG-fusion for 0-14d after acute spinal cord injury using bridge and spanning methods of repair**

Project Number: 19-1774-13

Name of PD/PI: George D Bittner

*Source of Support: University of Texas at Austin, POC grant

*Primary Place of Performance: University of Texas at Austin

Project/Proposal Start and End Date: (MM/YYYY) (if available): 1/1/2023-12/31/2023

* Total Award Amount (including Indirect Costs): $125,000

CURRENT SUPPORT

1) Title: Enhanced Regeneration and Repair of Severed Spinal Axons
Time Commitment: 1% [0.12 person-months]
Agency: Lone Star Paralysis Foundation
Grants Officer: Doug English, 7900 FM 1826, Bldg. II Rm. 105, Austin, TX 78737
Performance Period and Funding: (Gift: all direct costs) 3/2021 - 1/2024
$195,000 direct costs to support postdoctoral fellows on spinal research
1/1/24-1/1/26. $100,000/yr direct costs to support spinal research
Description/Aims: The goal is to modify our PEG-fusion technology to repair spinal cord and PNS injuries. As a gift, all funds are direct costs only with no overhead costs to support pilot studies in basic research with no specific Aims

2) Title: W81XWH2020029. Multimodal approach to improve functional recovery following acute and delayed nerve repair [for single transections repaired by PEG-fused neurorrhaphy and segmental loss ablations repaired by PEG-fused *auto*grafts]
Role: PI: UT-Austin site on subcontract to SA (Joe Alderete, PI)
Time Commitment: 10% [1.20 person-months]
Agency: DOD AFIRM III grant
Grants Officer: Curtis McNish, Henry Jackson Foundation, san Antonio, Tx
Performance Period and Funding: 12/1/2021 - 09/30/2023; $264,534 direct costs, $419,286 total costs for UTA Subcontract Site Project Total. Subcontract for AFIRM III grant funded for about $1,800,000 to Joseph Alderete, PI. There is a separate AFIRM III grant also funded with Jamie Shores (JHU) for about $6,000,000 for clinical trials of single transections repaired by PEG-fused neurorrhaphy and segmental loss ablations repaired by PEG-fused *auto*grafts for which I am a scientific advisor.
Description. UTA subcontract to train SA surgeons in PEG-fusion and to examine some specific aspects of PEG-fusion in singly transected PNIs repaired by neurorrhaphy and segmental loss PNAs repaired by isograft PNAs.
Specific Aims:
Aim 1: Obtain multimodal PEG- fusion baseline data and Environmental Augmentation data on female *Sprague Dawley* rat sciatic, single cut, nerve model systems for behavioral recovery (SFI, von Frey tests), axonal/NMJ/muscle morphology and function (CAPs, CMAPs). Months 0-12

Aim 1A: Train four surgeons from DOD RESTOR San Antonio to PEG-fuse singly cut rat sciatic nerves.\ assayed by weekly SFI behavioral tests for 6 weeks. 6 rats/surgeon. 24 Sprague Dawley (SD) chronic rats. Months 0-6.

Aim 1B: Baseline Data . PEG-fuse *singly cut* Sprague Dawley rat sciatic nerves enhanced by FK506 application assayed by behavioral recovery (SFI, von Frey tests), axonal/NMJ/muscle morphology and function (CAPs, CMAPs). Compare to PEG and NC historical data. 15 Sprague Dawley (SD) chronic rats. Months 4-12

Aim 2: Baseline data and Environmental Augmentation data. Obtain multimodal PEG- fusion baseline data on female *Lewis* rat sciatic, autograft, nerve model systems for behavioral recovery (SFI, von Frey tests), axonal/NMJ/muscle morphology and function (CAPs, CMAPs). Months 0-24

Aim 2A. Baseline Data. PEG-fuse and Negative Control (NC) *auto*grafts of 0.5cm length sampled 3 each at 7,21,42d PO for axonal/NMJ/muscle morphology and function (CAPs, CMAPs) and at least 6 each weekly for 42d for behavioral function (SFI, von Frey tests). 15 rats for each PEG and NC protocol. 30 chronic Lewis rats, 15 acute donor Lewis rats

Aim 2B. Baseline Data. PEG-fuse and Negative Control (NC) autografts of 1.0 cm length sampled 3 each at 7,21,42d PO for axonal/NMJ/muscle morphology and function (CAPs, CMAPs) and at least 6 each weekly for 42d for behavioral function (SFI, von Frey tests). 15 rats for each PEG and NC protocol. 30 chronic Lewis rats, 15 acute donor Lewis rats Months 8-22

Aim 2C: Environmental Augmentation data. PEG-fuse and Negative Control (NC) autografts of 1.0 cm length sampled 3 each at 21,42d PO for axonal/NMJ/muscle morphology and function (CAPs, CMAPs) and at least 6 each weekly for 42d for behavioral function (SFI, von Frey tests). 12 rats for this PEG protocol. 12 chronic Lewis rats, 6 acute donor Lewis rats Months 12-22

3) Title: R-01 Proposal. Translating Novel Peripheral Nerve Allograft Technologies Toward Clinical Use

$2,220,019. George Bittner submitting and overall PI George Bittner, Jared Bushman Subcontract PI at U. Wyoming (Larimie) and originally Jaimie Shores (PI Johns Hopkins University, JHU). Dr. Shores has left JHU andabout $400,000 JHU funds are being transferred to UTA

Role: PI

Time Commitment: 10% [1.2 person-months]

Agency: NIH

Grants Officer: Linda Bambrick

Performance Period and Funding: 5/1/2023- 4/30/2027 $2,220,019. total. Austin total direct and indirect costs. About $1,500,000

Aim 1. Develop and merge axon fusion and localized ISN. Confirm strong preliminary data that show proof of principle for axon fusion and localized ISN separately and together are complementary. Determine the fate of donor cells within the PNAs and their contribution to long-term nerve function.

Aim 2: Extend the post-injury (PI) time for successful PEG-fusion of a PNA. Confirm preliminary data that PEG-fusion can be achieved at least 36 h post injury (PI). Confirm that storage solutions and conditions can be developed to slow Wallerian degeneration. Collaborate with a licensed human donor tissue procurement organization to translate the findings in rats to human nerve segments recovered under realistic conditions.

Aim 3: Confirm that axon fusion and localized ISN separately and together can also be obtain Contact Officer Margarite Matthews.ed in a larger animal (swine). Extend preliminary findings of successful axon fusion in swine and combine with method of localized ISN in both short (3 cm) and long (8 cm) ablation defects.

PA-23-189. 3 yr GRA Supplement for Henry Garcia $263,984. Diversity Supplement NS128086 (Bittner/Garcia). 6/1/2024- 4/30/2027
AIM 1: Evaluating the importance of sensory/ motor composition and graft orientation for successful PEG-fusion and behavioral recovery.

sub-Aim 1.1: Assess the influence of PEG-fusing allografts with reversed caudal-rostral and/or ventral-dorsal orientation on 2D and 3D ultrastructural morphology, electrophysiological, functional, and behavioral assays.

Sub-Aim1.2: Evaluate the influence of PEG-fusion in improving the success of cross-sutured nerves of different modalities.
AIM 2: Determine the comparative efficacy of various localized immunosuppressants (iSN) for PEG-fused allografts**.**
Aim 3: Assess morphological and ultrastructural changes in peripheral nerves via 3D reconstruction post-PEG-fusion.

4) DOD RTRP Title: A multi-modal/multi-institutional approach to reduce VCA immunogenicity and improve function
Multiple PIs: George D Bittner, PhD submitting PI Jamie Shores MD at JHU, Joseph Alderete, MD. At UTHSC San Antonio
Dr Shores is leaving JHU and JHU funds ($409,000) are bring transferred to UTA
Time Commitment: 10% [1.20 person-months]
Agency: DOD RTRP grant
Grants Officer: Leslie Beltran
Focus Area: Reduce the risks of VCA-associated immunosuppression.
1,500,000 direct plus indirect. $ about 1,000,000 direct + Indirect for UTA after transfer of funds from JHU
Specific Aim 1 examine PEG-fusion repair of nerves in VCAs
Specific aim 2 examine localized immune suppression.
Specific aim 3 test the combined treatment of axon PEG-fusion of VCAs and localized immune suppression

PENDING

1) Title: Novel PEG-fusion therapy for acute and chronic spinal cord injury

***Major Goals: Determine success f PEG-fusion after spinal cord injury**

Project Number: 26-7724-56

Name of PD/PI: George D Bittner

*Source of Support: Neuraptive Therapeutics, Inc,

*Primary Place of Performance: University of Texas at Austin

Project/Proposal Start and End Date: 1/1/2024-12/31/2027

* Total Award Amount (including Indirect Costs): $900,000: $300,000/yr for three years direct+indirect costs

2)Title: **Peripheral nerve segmental-loss injuries repaired with polyethylene glycol (PEG)-fused allografts**

Name of PI: George D. Bittner
Time Commitment: 8% [1.0 person-months]
Agency: DOD PRORP grant
Grants Officer: TBD
Performance Period and Funding: 9/15/2025 – 9/14/2027. $749,988.
Description/Aims: Aim 1. In rat sciatic nerves as a model system (University of Texas at Austin: UTA). Confirm that a locally applied immune-suppressant (Methyl Prednisolone: MP) significantly reduces the immune response and may enhance behavioral recovery of segmental-loss PNIs repaired with PEG-fused VPNAs.

Aim 2. In swine median nerves as a model system (U Tx Health Center San Antonia (UTHCSA: DOD RESTOR; UTA). Confirm rat data on that locally applied MP significantly reduces the immune response and may enhance behavioral recovery of segmental-loss PNIs repaired with PEG-fused VPNAs.

OTHER SCIENTIFIC POSITIONS held by PI:
Adjunct Professor, Department of Physiology, UTMB Medical School (no salary or other compensation)
Adjunct Professor, Department of Orthopedic Surgery, UTSA Medical School, San Antonio, Tx

SUPPORT of Undergraduate students, Graduate Students, Postdoctoral fellows

In the last 2-3 years, 5 undergraduates received from UT received $1,000 research fellowship funds (Carrera, Arya, Zhao, Alatrach, Marcel, Sood) for supplies & animals and two received summer fellowships of $2500 (Arya), $4000 (Montoya), or 6,000 (Vargas) or about $17,500 total. Undergraduates also volunteer time to be trained in animal testing or other techniques (about $10,000/yr total).. Once trained they are then paid by grant funds (about $30,000/yr total).

In the last year, four graduate students have been paid by one semester fellowships (about $12,000 each semester in tuition, fringe and tuition direct costs) by UTA or non-DOD sources (Lone Star Paralysis funds (Smith: two semesters, Ghergherehchi: two semesters; Zhou (two semesters), Mencel (one semester). About $72,000 total

In the last year, one postdoctoral fellow (Ghergherehchi) was provided postdoctoral fellowship funds ($4,000) for one month by LSPF.

PATENTS filed by G.D. Bittner
Immediate Axon Fusion with Polyethylene Glycol. EFS ID 9537805, Application number 61446803, Confirmation # 2953, Filed 2/25/2011,

PATENTS of/for G.D. Bittner
Issued
Materials and food additives free of endocrine disruptive chemicals and method for detecting endocrine disruptive activity. Filed 5/10/02. US Patent #6,894,093 Issued May 17, 2005.

Immediate Axon Fusion with Polyethylene Glycol. *EFS ID 9537805, Application number 61446803, Confirmation # 2953, Filed 2/25/2011, Provisional Patent filed on behalf of UTAustin.*

Title	File Date	Serial No.	App Type	Patent No.	Status	Expire Date	Issue Date	Publication No.	Publication
NERVE COAPTATION APPARATUS	02/27/2012	US2012/026764	Conversion		Nationalized			PCT US2012/026764	02/27/2012
Immediate Axon Fusion with Polyethylene	02/25/2011	61/446,803	Provisional		Converted				
Glycol and Antioxidant Pre-Treatment									
NERVE TREATMENT METHODS	11/27/2018	16/201,011	Continuation	10,398,438	Issued	02/27/2032	09/03/2019	US 2019-0090872 A1	03/28/2019
Kits for nerve treatment methods	10/22/2018	16/167,476	Divisional		Filed			US-2019-0117228-A1	04/25/2019
NERVE TREATMENT METHODS	05/17/2017	15/597,891	Continuation	10,136,894	Issued	02/27/2032	11/27/2018		

Repair of Spinal Lesions by PEG-fusion Provisional patent filed 4/29/2022

In September 2017, Neuraptive executed an exclusive license agreement with the University of Texas at Austin (UT) to a patent application protecting PEG-fusion.

The license agreement between Neuraptive and UT secures exclusive rights to U.S. Patent Application No. 15/597,891, entitled "NERVE TREATMENT METHODS," by George D. Bittner et al., which is a continuation filing of U.S. Patent Application No.14/001,431 (PCT/US12/26764) and derived from Provisional applications No. 61/446,803 and No. 61/578,930. The priority date for this case is February 25, 2011.

The continuation was filed to create a claim set that more comprehensively protects the PEG-fusion technology. Neuraptive directed the drafting of the claims in this continuation with the assistance of counsel, Dave Parker of Parker Highlander (Austin).

The US Patent and Trademark Office has issued a Notice of Allowance for the '891 case for claims protecting the method of inducing axonal fusion within a severed nerve using the sequential administration of pharmaceutical agents including the membrane fusogen PEG and the antioxidant methylene blue. The specification is well detailed and reduction to practice of the method is thorough. Dependent claims are directed at more specific embodiments.

Additional patents issued

5954 BIT Nerve Coaptation Apparatus US 9,955,973 issued 5/1/2018

Nerve Treatment Methods US 10,136,894 issued 11/27/2018

Nerve Treatment Methods US 10,3,98,438 issued 9/5/2019

Kits for nerve treatment methods US patent application s/n 16/167,476 filed 10/22/2018

Kits for nerve treatment methods US patent application s/n 17/578,053 filed 1/18/2022

7744 BIT Polyethylene Glycol-Fusion in Nerve Repair provisional patent application s/n 63/335,450 filed 4/27/2022 converted to PCT/US2023/066136 on 4/24/2023

8068 BIT Storage Solutions for Maintaining of Axonal Viability provisional patent application s/n 63/384,710 filed 11/22/2022

9/30/2024

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