



# Protrusion-Mediated Signaling Regulates Patterning of the Developing Nervous System

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During brain development, the tissue pattern and specification are the foundation of neuronal circuit formation. Contact-mediated lateral inhibition is well known to play an important role in determining cell fate decisions in the nervous system by either regulating tissue boundary formation or the classical salt-and-pepper pattern of differentiation that results from direct neighboring cell contacts. In many systems, however, such as the *Drosophila* notum, *Drosophila* wing, zebrafish pigmented cells, and zebrafish spinal cord, the differentiation pattern occurs at multiple-cell diameter distances. In this review, we discuss the evidence and characteristics of long-distance patterning mechanisms mediated by cellular protrusions. In the nervous system, cellular protrusions deliver the Notch ligand Delta at long range to prevent cells from differentiating in their vicinity. By temporal control of protrusive activity, this mechanism can pattern differentiation in both space and time.

**Keywords:** neuronal patterning, neuronal spacing, protrusion mediated signaling, long distance signaling, nervous system, neurogenesis

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## INTRODUCTION

During morphogenesis, the differentiation of cells must be coordinated and patterned at both short (among immediate neighbors) and long range (across several or many-cell diameters). Short-range signaling can be achieved, for example, by cell-cell contact via ligands and receptors proteins inserted into cell membranes (such as Delta-Notch or ephrin-Eph signaling) (reviewed by Cayuso et al., 2015; Henrique and Schweisguth, 2019). Long-range signaling requires mechanisms that can operate over greater distances and is traditionally thought to employ secreted ligands [for example, hedgehog (Hh), wntless (Wnt), fibroblast growth factor (FGF), or bone morphogenic protein (BMP)] that diffuse through tissues to their distant target receiving cells (Briscoe and Small, 2015). More recently, it has become apparent that morphogen and cell-to-cell contact-dependent signaling can also be achieved between distant cells via long cellular protrusions (for example, Cohen et al., 2010; Eom et al., 2015; Oswald et al., 2015; and reviewed by González-Méndez et al., 2019). Cellular protrusions that may have signalling, organizational, or mechanical roles have been described in many systems and can have a variety of morphologies, cytoskeletal structure, and names (reviewed by Kornberg, 2014). Here, we will focus on protrusions called cytonemes, nanotubes, and filopodia that include actin-based projections, which together with more substantial protrusions can contain both microtubule and actin cytoskeletons. In this discussion, we will concentrate on protrusion-mediated signals in the nervous system (Table 1). Of course, in the nervous system, the most

# Pattern Formation In The Developing Nervous System

**Derek J. Chadwick, Joan Marsh**



## **Pattern Formation In The Developing Nervous System:**

Pattern Formation in the Developing Nervous System E. M. Carpenter, 2000-01-01 This special issue features a collection of papers examining multiple aspects of central and peripheral nervous system development. They address molecular genetic and cellular aspects of central and peripheral nervous system organization and regional development. These papers highlight recent work from laboratories and investigators using vertebrate models to study processes affecting the early development of the nervous system. Several areas of the nervous system such as the developing eye and spinal cord are used as models for examining molecular and cellular events contributing to neural development. Additional studies address genetic aspects of central nervous system development and identify novel genes implicated in CNS patterning. These papers present a diversity of approaches and model systems while retaining a central focus on the early events required to shape the nervous system. Researchers and instructors in developmental biology and developmental neuroscience will profit most from this publication.

**Gene Expression and Cell-Cell Interactions in the Developing Nervous System** Jean M. Lauder, 2013-03-14 The dramatic advances in molecular genetics are becoming incorporated into neurobiologic studies at an ever increasing rate. In developmental neurobiology the importance of cell-cell interactions for neurogenesis and gene expression is becoming to be understood in terms of the molecular bases for these interactions. This book seeks to emphasize the importance of molecular technology in the study of neurogenetic mechanisms and to explore the possible relationships between specific cell-cell interactions and regulated gene expression in the developing nervous system. This volume consists of nineteen chapters which address questions of gene expression and the importance of cell-cell interactions as key factors in the developing nervous system. Rather than viewing these two processes as separate mechanisms as the organization of these chapters might suggest, we would like to emphasize the interplay of these genetic and epigenetic influences in all phases of neural ontogeny, a concept which is made clear by the subject matter of the contributions themselves. The authors of these chapters were participants in selected sessions from the Fourth Congress of the International Society of Developmental Neuroscience held in Salt Lake City, Utah, July 3-7, 1983.

**Vertebrate Pattern Formation**, 2024-05-13 Vertebrate Pattern Formation Volume 159 in the Current Topics in Developmental Biology series highlights advances in the field with this volume presenting interesting chapters on timely topics including Hox genes patterning the vertebrate body, Endodermal patterning, The use of organoids/gastruloids to understand development, Cell shape and movements controlling development, Neural crest and placodes in vertebrate development, Patterning of the neural tube, Non-canonical Wnt signaling in axial extension, The control of transitions along the main body axis, Emergence of a left-right symmetric body plan in vertebrate embryos, Formation of the vascular system, Generation of patterns in the paraxial mesoderm and more. Provides the authority and expertise of leading contributors from an international board of authors. Presents the latest release in the Current Topics in Developmental Biology series. Updated release includes the latest information on the Vertebrate Pattern Formation.

**Developmental Neuropsychobiology** William T Greenough, Janice M. Juraska, 2013-10-22 Developmental

Neuropsychobiology is a compendium of papers that deals with developmental neuroscience and developmental psychology as well as the broad range of approaches toward brain behavior development One paper reviews the embryonic mechanisms including the pattern formation that develops in a single fertilized egg particularly focusing on limb innervation as a special case of pattern formation Another paper discusses the regulation of nerve fiber elongation during embryogenesis One author analyzes the pathways and changing connections in the nervous system of the insect he shows that manipulating neural organization by grafting results in the ability of the transplanted sensory cells to find the proper central connections Another paper reviews the sex differences in developmental plasticity of behavior and the brain These differences point to the vulnerability of males during development to incidences of autism dyslexia or cerebral palsy compared to females One paper also examines alternative perceptions of parent offspring relationships This collection can prove helpful for researchers students and academicians involved in the disciplines of biological or psychological sciences

*Human Embryology and Developmental Biology* Bruce M. Carlson, MD, PhD, 2013-03-06 Master the concepts you need to know with Human Embryology and Developmental Biology Dr Bruce M Carlson's clear explanations provide an easy to follow road map through the most up to date scientific knowledge giving you a deeper understanding of the key information you need to know for your courses exams and ultimately clinical practice Visualize normal and abnormal development with hundreds of superb clinical photos and embryological drawings Access the fully searchable text online view animations answer self assessment questions and much more at [www.studentconsult.com](http://www.studentconsult.com) Grasp the molecular basis of embryology including the processes of branching and folding essential knowledge for determining the root of many abnormalities Understand the clinical manifestations of developmental abnormalities with clinical vignettes and Clinical Correlations boxes throughout Your purchase entitles you to access the web site until the next edition is published or until the current edition is no longer offered for sale by Elsevier whichever occurs first If the next edition is published less than one year after your purchase you will be entitled to online access for one year from your date of purchase Elsevier reserves the right to offer a suitable replacement product such as a downloadable or CD ROM based electronic version should access to the web site be discontinued

*Postimplantation Development in the Mouse* Derek J. Chadwick, Joan Marsh, 2008-04-30 Examines the establishment of the germ layers and other cell lineages in the early embryo including details of cell movements during the beginning stages of primitive streak formation Discusses patterns of gene expression during the development of such tissues as the limb bud skeletal muscle and the central nervous systems placing special emphasis on commitment to particular cell types Although it concentrates on the mouse as an example of mammalian development chick amphibian and Drosophila embryogenesis are employed whenever these organisms are more applicable to the study of a particular problem

Human Molecular Genetics Tom Strachan, Andrew Read, 2018-03-29 Human Molecular Genetics is an established and class proven textbook for upper level

undergraduates and graduate students which provides an authoritative and integrated approach to the molecular aspects of human genetics While maintaining the hallmark features of previous editions the Fourth Edition has been completely updated It includes new Key Concepts at the beginning of each chapter and annotated further reading at the conclusion of each chapter to help readers navigate the wealth of information in this subject The text has been restructured so genomic technologies are integrated throughout and next generation sequencing is included Genetic testing screening approaches to therapy personalized medicine and disease models have been brought together in one section Coverage of cell biology including stem cells and cell therapy studying gene function and structure comparative genomics model organisms noncoding RNAs and their functions and epigenetics have all been expanded

Self-organizing Neural Maps: The Retinotectal Map and Mechanisms of Neural Development John T. Schmidt, 2019-10-15 Self organizing Neural Maps From Retina to Tectum describes the underlying processes that determine how retinal fibers self organize into an orderly visual map The formation of neural maps is a fundamental organizing concept in neurodevelopment that can shed light on developmental mechanisms and the functions of genes elsewhere The book presents a summary of research in the retinotectal field with an ultimate goal of synthesizing how underlying mechanisms in neural development harmoniously come together to create life A broad spectrum of neuroscientists and biomedical scientists with differing backgrounds and varied expertise will find this book useful Describes the mechanisms relating to the developmental wiring of the retinotectal system Brings together the state of the art research in axon guidance and neuronal activity mechanisms in map formation Focuses on topographical maps and inclusion of multiple animal models from fish to mammals Explores the molecular guidance and activity dependent cue components involved in neurodevelopment

Development of the Nervous System Dan H. Sanes, Thomas A. Reh, William A. Harris, Matthias Landgraf, 2019-06-13 Development of the Nervous System Fourth Edition provides an informative and up to date account of our present understanding of the basic principles of neural development as exemplified by key experiments and observations from past and recent times This book reflects the advances made over the last few years demonstrating their promise for both therapy and molecular understanding of one of the most complex processes in animal development This information is critical for neuroscientists developmental biologists educators and students at various stages of their career providing a clear presentation of the frontiers of this exciting and medically important area of developmental biology The book includes a basic introduction to the relevant aspects of neural development covering all the major topics that form the basis of a comprehensive advanced undergraduate and graduate curriculum including the patterning and growth of the nervous system neuronal determination axonal navigation and targeting neuron survival and death synapse formation and plasticity Provides broad coverage of concepts and experimental strategies Includes full color schematics and photographs of critical experiments Outlines the molecular and genetic basis for most developmental events Written at a level that is appropriate for advanced undergraduates and beyond Includes designs

of critical experiments that are easy to understand

**Receptors in the Developing Nervous System** Ian S.

Zagon, Patricia J. McLaughlin, 2012-12-06 Receptors for cell hormones growth factors Fourth alterations in the development of neu and neurotransmitters are involved in the ral receptors may have profound implications control and modulation of an enormous array for the structure and function of the of biological processes The development of organism As much as possible the reper these receptors has distinct spatial and tem cussions of disrupting the orchestration of poral arrangements and alterations in this receptor development in the nervous system pattern during embryogenesis can have signi are discussed In many instances however ficant consequences for the well being of the we are just beginning to learn about some fetus infant child and adult The developing receptors and the authors may not be in a nervous system is particularly dependent on position to discuss the consequences of recep receptors because its period of structural and tor dysfunction functional organization extends through both In designing these two volumes we have prenatal and postnatal phases Moreover asked major figures in each field to review the receptors are a key element in neural com literature to apprise the audience of their munication in both the developing and adult latest findings and to provide a perspective on organism so that the ontogeny of receptors is the role of receptors in the developing nervous crucial in determining the myriad connections system These books are intended to sum forming the circuitry of the nervous system

**Synergetics and**

**Dynamic Instabilities** G. Caglioti, L. Lugiato, H. Haken, 1988-01-01 This collection of papers presented at the Enrico Fermi School considers the subject of synergetics as a firmly established field of interdisciplinary research ranging from physics chemistry and biology to subjects like economy and sociology These proceedings focus on the natural sciences

**Current**

**Topics in Developmental Biology**, 1994-11-07 Current Topics in Developmental Biology Volume 29 surveys the major issues at the forefront of developmental biology This volume like others in the serial is valuable to researchers in the fields of animal and plant development and to students and other professionals who want an introduction to current topics in cellular and molecular approaches to developmental biology Volume 29s chapters on the nervous system reproductive system and flowering introduce new models and concepts for understanding these processes Essential reading for anyone interested in Development of the nervous system Development of the reproductive system Flowering in plants Roles of homeobox related transcription factors and growth factors in axis and organ development

**Cellular Automaton Modeling of Biological**

**Pattern Formation** Andreas Deutsch, Sabine Dormann, 2007-12-26 This book focuses on a challenging application field of cellular automata pattern formation in biological systems such as the growth of microorganisms dynamics of cellular tissue and tumors and formation of pigment cell patterns These phenomena resulting from complex cellular interactions cannot be deduced solely from experimental analysis but can be more easily examined using mathematical models in particular cellular automaton models While there are various books treating cellular automaton modeling this interdisciplinary work is the first one covering biological applications The book is aimed at researchers practitioners and students in applied mathematics

mathematical biology computational physics bioengineering and computer science interested in a cellular automaton approach to biological modeling

**Somites in Developing Embryos** Ruth Bellairs, 2013-11-11 Somite development is a unique and important topic unique because somitic mesoderm is the first tissue to become segmented important because the somites once established exert a profound influence on other segmental structures which form later Somite development is of interest at a number of levels In one aspect demarcation of a specific number of somites and size regulation it is a particularly intriguing example of embryonic pattern formation especially in view of its possible relation to homeobox controlled segmentation in insects At another level somite development has long been studied by comparative anatomists but only recently has new light been thrown on such subjects as segmentation of the head proposed in the 18th century by Goethe and now a live issue for developmental biologists Somites are simple when they first appear but very complex structures arise from them These include the vertebrae and the axial and other muscles and consequently there is a wealth of morphogenetic problems to be explored Sometimes their morphogenesis is disturbed by genetic or environmental factors and there are many clinical conditions which arise as a result

*Fundamental Neuroscience* Larry Squire, Darwin Berg, Floyd E. Bloom, Sascha du Lac, Anirvan Ghosh, Nicholas C. Spitzer, Larry R. Squire, 2008-04-02 *Fundamental Neuroscience* Third Edition introduces graduate and upper level undergraduate students to the full range of contemporary neuroscience Addressing instructor and student feedback on the previous edition all of the chapters are rewritten to make this book more concise and student friendly than ever before Each chapter is once again heavily illustrated and provides clinical boxes describing experiments disorders and methodological approaches and concepts Capturing the promise and excitement of this fast moving field *Fundamental Neuroscience* 3rd Edition is the text that students will be able to reference throughout their neuroscience careers 30% new material including new chapters on Dendritic Development and Spine Morphogenesis Chemical Senses Cerebellum Eye Movements Circadian Timing Sleep and Dreaming and Consciousness Additional text boxes describing key experiments disorders methods and concepts Multiple model system coverage beyond rats mice and monkeys Extensively expanded index for easier referencing

**Developmental Neurobiology** Mahendra S. Rao, Marcus Jacobson, 2006-04-04 This consistent and well illustrated text is an up to date survey of cellular and molecular events contributing to the assembly of the vertebrate nervous system Chapters include a mixture of historical content and descriptions from literature that best illustrate specific aspects of development

**Cumulated Index Medicus**, 1999

**Brain Development in *Drosophila melanogaster*** Gerhard Martin Technau, 2009-01-08 The fruitfly *Drosophila melanogaster* is an ideal model system to study processes of the central nervous system This book provides an overview of some major facets of recent research on *Drosophila* brain development

*On Growth, Form and Computers* Sanjeev Kumar, Peter J. Bentley, 2003-10-03 Conceived for both computer scientists and biologists alike this collection of 22 essays highlights the important new role that computers play in developmental biology research Essays show how through computer

modeling researchers gain further insight into developmental processes Featured essays also cover their use in designing computer algorithms to tackle computer science problems in areas like neural network design robot control evolvable hardware and more Peter Bentley noted for his prolific research on evolutionary computation and Sanjeev Kumar head up a respected team to guide readers through these very complex and fascinating disciplines Covers both developmental biology and computational development the only book of its kind Provides introductory material and more detailed information on BOTH disciplines Includes contributions from Richard Dawkins Lewis Wolpert Ian Stewart and many other experts

**The Neurobiology of Australian Marsupials** Ken Ashwell, 2010-10-14 Australian marsupials represent a parallel adaptive radiation to that seen among placental mammals This great natural experiment has produced a striking array of mammals with structural and behavioural features echoing those seen among primates rodents carnivores edentates and ungulates elsewhere in the world Many of these adaptations involve profound evolutionary changes in the nervous system and occurred in isolation from those unfolding among placental mammals Ashwell provides the first comprehensive review of the scientific literature on the structure and function of the nervous system of Australian marsupials The book also includes the first comprehensive delineated atlases of brain structure in a representative diprotodont marsupial the tammar wallaby and a representative polyprotodont marsupial the stripe faced dunnart For those interested in brain development the book also provides the first comprehensive delineated atlas of brain development in a diprotodont marsupial the tammar wallaby during the critical first 4 weeks of pouch life



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