



# 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

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## **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

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*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

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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

**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

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**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

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