

# Mechanisms of eye-specific visual circuit development

## Andrew D Huberman

Eye-specific visual connections are a prominent model system for exploring how precise circuits develop in the CNS and, in particular, for addressing the role of neural activity in synapse elimination and axon refinement. Recent experiments have identified the features of spontaneous retinal activity that mediate eye-specific retinogeniculate segregation, the synaptic events associated with this process, and the importance of axon guidance cues for organizing the overall layout of eye-specific maps. The classic model of ocular dominance column development, in which spontaneous retinal activity plays a crucial role, has also gained new support. Although many outstanding questions remain, the mechanisms that instruct eye-specific circuit development are becoming clear.

### Addresses

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### Introduction

What mechanisms induce development of precise CNS circuitry? A classic model circuit for investigating this question is eye-specific visual connections: axons carrying visual information for the left and right eyes are segregated into non-overlapping domains in the lateral geniculate nucleus (LGN) and into ocular dominance columns (ODCs) in the visual cortex. The cellular events involved in eye-specific retinogeniculate refinement are well characterized: after an initial overlap phase, axons from the two eyes segregate by elaborating synapses and axon terminals in the same-eye territory and by eliminating synapses and axon terminals in opposite-eye territory [1,2]. Spontaneous retinal activity is known to be required for segregation to occur [3], but several important questions have remained unanswered: which features of spontaneous retinal activity are instructive for eye-specific segregation? What are the molecular mechanisms for eliminating weaker synapses and maintaining strong ones? What factors dictate the

overall layout of eye-specific maps? Similar questions exist regarding ODC development as well. In the past decade, however, even the basic cellular events associated with ODC development have become controversial as several high profile studies [4,5] challenged the idea that ODCs are sculpted by early retinal activity. Here, I review recent advances in our understanding of retinogeniculate and ODC development, and I suggest experiments that could further elucidate how these circuits form.

### The role of patterned retinal activity in eye-specific retinogeniculate segregation

Neural activity mediates development of eye-specific retinogeniculate projections through competitive interactions involving the relative levels of retinal ganglion cell (RGC) spiking in the two eyes [3,6]. Hebbian models predict, however, that correlated firing — and not simply activity levels per se — of neighboring RGCs is crucial for eye-specific segregation [7]. In theory, retinal waves [8] induce patterns of RGC spiking optimal for Hebbian-based axonal refinement but, surprisingly, the first experiments to perturb retinal waves did not observe any accompanying disruptions to eye-specific segregation in the LGN [9]. Moreover, some mutant mice with altered retinal waves exhibit severe eye-specific retinogeniculate defects [10], and yet pharmacologically inducing waves in these mutants does not rescue segregation [11]. Thus, to elucidate which aspects of spontaneous retinal activity instruct eye-specific segregation, Feller and colleagues [12\*\*] undertook a systematic analysis of RGC spiking patterns in different strains of mutant mice, each with differently altered retinal waves but with varying degrees of eye-specific segregation in the LGN. They found that high frequency correlated bursting ( $>10$  Hz) of neighboring RGCs is a key parameter required for eye-specific segregation. They also found that the precise time-window for RGC firing is not crucial for segregation, provided that the degree of correlated firing among closely spaced RGCs remains relatively higher than the degree of correlation among distant RGCs. Their results suggest why in previous experiments where retinal waves were disrupted, the anticipated defects in retinogeniculate refinement were not observed [6,9]. They also suggest which types of synaptic plasticity can (and cannot) drive segregation. For instance, because low frequency ( $\sim 1$  Hz) RGC firing is not related to segregation [12\*\*], it is unlikely that typical forms of long-term depression (LTD) mediate synaptic elimination in this system. By contrast, the importance of high frequency RGC bursts suggests that bursts trigger plasticity mechanisms that both stabilize same-eye inputs and eliminate opposite-eye inputs onto single LGN cells (i.e. heterosynaptic depression). Through the use

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**Perception: from Sensation to Cognition** Leslie B. Cohen, Philip Salapatek, 2013-09-24 Infant Perception From Sensation to Cognition Volume I Basic Visual Processes focuses on the study and programmatic investigations of infant perception examining early sensory perceptual and cognitive systems This book is divided into five chapters Chapter 1 analyzes the major physiological and behavioral techniques used to measure infant vision Each technique is critically evaluated in terms of the method employed type of data that can be obtained and anatomy of the visual system The neuronal model to explain developmental changes and techniques used to assess infant visual preferences for patterns varying in amount of contour are discussed in Chapter 2 Chapter 3 demonstrates the value of the corneal reflection technique for the study of infant attention and visual scanning patterns while Chapter 4 examines the developmental changes and individual differences in early pattern perception The last chapter concentrates on the evidence of infant visual preferences for novelty and on the implications of such evidence for models of early recognition memory This publication is a good reference for pediatricians and clinicians concerned with infant perception **The Visual Process** Hugh Davson, 2014-05-12 The Eye Volume 2 The Visual Process is

a compendium of papers that describes the physiology of the eye particularly the visual functions the photobiology of the visual process and the visual pathway One paper describes the light stimuli used in physiological experiments concerning vision in terms of their spectral energy distribution particularly the amounts of light absorbed by the photosensitive substances contained in the retinal receptors Another paper explains the mosaic like arrangement of the receptors and the variations of this mosaic in the different regions of the retina including the Purkinje phenomenon which can cause errors in visual measurements One paper examines the directional properties of the rods at long wavelengths and the theory of the Stiles Crawford effect Other papers investigate the limits of the visible spectrum the scotopic luminous efficiency theories of

dark adaptation as well as the minimum retinal illumination the minimum flux of energy and the minimum amount necessary for vision One paper notes that whereas one rod can be stimulated by one quantum a discrete process involving one pigment molecule it is not sufficient to make a human subject see a light stimulus The compendium is invaluable for researchers and investigators involved in physiology psychology ophthalmology and in all branches of ocular physiology **Catalog of Copyright Entries. Third Series** Library of Congress. Copyright Office,1972 The Skeffington Perspective of the Behavioral Model of Optometric Data Analysis and Vision Care Earl P. Schmitt O.D Ed.D D.O.S.,2006-04-28 No systematic analysis of optometric clinical data can be undertaken unless the findings are referred to a logical model that allows comparisons to be made of interaction characteristics that exist between the accommodative and convergence mechanisms inherent to the human vision system Concomitantly many of the concepts applied during any such analytical process are based on hypothetical constructs This text re examines the elements originally proposed by Dr A M Skeffington and offers a revised insight into how performance changes may occur as individual visual behavior adapts to the impact of environmental demands In depth research and extensive references attempt to substantiate the Skeffington paradigm of professional vision analysis Long standing challenges to the optometric profession are identified As presented the contents are appropriate for use as a classroom text for reference and for identifying areas for clinical research **Models Of Oculomotor Control** George K Hung,2001-10-31 This monograph is a structured review of models of oculomotor control systems that is geared toward biomedical engineers vision scientists and optometry students It aims to provide the biomedical engineer with a thorough understanding of how various engineering control principles are applied to oculomotor systems and the non engineer with knowledge of how various physiological and clinical concepts can be represented quantitatively and efficiently by control system models Basic control system concepts and oculomotor physiology are first introduced along with a glossary to provide background for the more advanced topics Then these concepts are applied to static linear and nonlinear analysis of various oculomotor systems In addition advanced topics are presented on the application of dynamic linear and nonlinear modeling techniques to the oculomotor system with a particular emphasis on myopia development This book can thus serve as a unique reference for quantitative analysis of oculomotor control and as a foundation for future research on the oculomotor system *Ocular Accommodation, Convergence, and Fixation Disparity* David A. Goss,1995-07-12 This popular manual introduces the organization and analysis of clinical optometric data used in writing prescriptions for glasses This edition has been greatly expanded to include new information on accommodative disorders and fixation disparity among others Case reports integrated throughout the text illustrate the management process *Strabologie* Marie-Andrée Espinasse-Berrod,2018-08-28 L objectif de cet atlas de r f rrence est d orienter chaque praticien n ophyte ou sp cialiste dans la conduite de l examen clinique le bilan diagnostique et la prise en charge de l immense majorit des pathologies rencontr es en strabologie et d apporter une meilleure compr hension des troubles oculomoteurs depuis la physiopathologie jusqu au

traitement Cette 3e édition richement illustrée comprend des mises à jour sur les progrès en imagerie en génétique et les actualités thérapeutiques Les annexes largement détaillées sont dotées d'arbres de cisionnels reprenant les grands syndromes L'ouvrage se compose de quatre grands axes Les notions fondamentales anatomie physiologie et contrôle visuomoteur classification des déséquilibres oculomoteurs et mécanismes de leur développement L'examen moteur et sensoriel ainsi que des principes de l'imagerie Les pathologies o Strabismes prismes tropies exotropies et déviations verticales dissociées o Les autres anomalies oculomotrices paralysies oculomotrices syndromes oculomoteurs et autres déséquilibres plus rares o Le dépiégeage le nystagmus et les pathologies supranucléaires La prise en charge thérapeutique la prise en charge chirurgicale est précisée depuis les injections de toxine botulique jusqu'aux différentes chirurgies Ces principes chirurgicaux sont développés en général puis détaillés par type de déviation ou de muscles oculomoteurs impliqués sans oublier les complications et leur prise en charge Cet atlas de strabologie s'adresse tout ophtalmologiste et orthoptiste professionnel ou en formation ainsi qu'au pédiatre et médecin généraliste impliqués dans la prise en charge de patients atteints de strabisme

*Report*, 1970 Infant Perception Leslie B. Cohen, Philip Salapatek, 1975 *Developmental Visual Dysfunction* Rhoda P. Erhardt, MS, OTR/L, FAOTA, 1990-11-05 This book follows 3 case studies of children with cerebral palsy mild moderate and severe from infancy to adulthood Traditional frames of reference from medical educational and developmental models are presented to create a functional approach to the assessment and management of the motor components of vision The wire coil bound edition of 210 pages contains 134 photographs and illustrations which help to clarify normal and atypical development of vision and suggest ways to integrate intervention programs into home school and community activities The Psychobiology of Sensory Coding William R. Uttal, 2014-06-27 Originally published in 1973 this book deals with what were even at that time the well known neural coding processes of the sensory transmission processes The book was written to demonstrate the common features of the various senses It concentrates on the most peripheral neural aspects of the senses starting with the physical transduction process and culminating in the arrival of signals at the brain Handbook of Visual Optics, Two-Volume Set Pablo Artal, 2017-06-27 Handbook of Visual Optics offers an authoritative overview of encyclopedic knowledge in the field of physiological optics It builds from fundamental concepts to the science and technology of instruments and practical procedures of vision correction integrating expert knowledge from physics medicine biology psychology and engineering The chapters comprehensively cover all aspects of modern study and practice from optical principles and optics of the eye and retina to novel ophthalmic tools for imaging and visual testing devices and techniques for visual correction and the relationship between ocular optics and visual perception Vision and Its Disorders United States. National Advisory Neurological Diseases and Blindness Council. Subcommittee on Vision and Its Disorders, 1968 Communicative and Cognitive Abilities Fred D. Minifie, Lyle L. Lloyd, 1978 *Visual Space Perception* Maurice Hershenson, 1999 A renewed interest in the study of vision has attracted scholars from such diverse fields as neuroscience computer science mathematics

physics and philosophy At the same time the development of imaging devices and popularization of stereoscopic effects has increased student interest in vision This primer provides an overview of the principles of space perception in a handbook format that should appeal to researchers as well as students Topics covered include geometrical and distal proximal relationships spatial localization stereopsis cyclopean perception stimulus inadequacy pictorial cues perceived size and shape Gibsonian psychophysics lateral motion motion in depth perceived object motion and motion detection Eye Movements and the Higher Psychological Functions John W. Senders, Dennis F. Fisher, Richard A. Monty, 2017-03-27 Originally published in 1978 this volume reflects the proceedings of a conference held in February 1977 in California and is a natural successor to the earlier volume Eye Movements and Psychological Processes Monty information about the position of the eye in the head and the perception of visual space saccades and visual functioning and masking In further parts it goes on to look at methodology and models cognitive processes reading processes looking at static and dynamic display and finally chapters on problems and applications *Mechanisms of Clinical Signs - E-Book* Mark Dennis, William Talbot Bowen, Lucy Cho, 2011-11-15 A robust understanding of the pathophysiological mechanisms behind clinical signs is crucial for medical students and junior doctors Being able to accurately identify the clinical sequelae of disease during physical examination and connecting cause with consequence is the first step in correct diagnosis and treatment For example a patient with rheumatoid arthritis has distinctive hand changes a patient with Parkinson s disease has a particular tremor and a patient with liver disease may present with red palms Each of these signs has a mechanism or pathway which results in the characteristic presentation Currently in medical school tutorial groups time is set aside to discuss mechanisms of clinical signs and disease processes However current textbooks on clinical examination are mainly organized by disease systems and disease states This new book bridges the gap between identification of clinical signs and understanding the causes behind them first consolidated text explaining the mechanism of clinical signs commonly seen in medicine easy reference guide for clinical signs seen on the ward or during examinations a resource for those preparing for Viva or OSCE practical stations where students see patients and are asked specific questions relating to the clinical examination organised by body system it reviews the common clinical signs seen in diseases by the main system or specialty of medicine in a convenient handbook style each chapter contains all the clinical signs a description of the sign the disease s in which the sign appears and an explanation as to the mechanism evidence base and clinical value of the sign is discussed to assist interpretation Online Student Consult resources accompany the text **A Text Book of Physiology: comprising the remainder of bk. 3. The senses and some special muscular mechanisms, and bk. 4. The tissues and mechanisms of reproduction** Sir Michael Foster, 1891

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