its sister cell; hence, the probability that it has also obtained all initiator protein (accumulated since the last initiation event) is 75%. Obviously, the cells in such a culture would greatly vary in the time intervals between divisions (the age distribution becomes very broad), DNA content and chromosome patterns, although the average properties of the culture would be accurately described by the exponential curves of Fig. 1.

We have not been able to derive an expectation for the frequency distribution of the various cell types in such cultures, but intuitively the asynchronous behavior of a population of young cells from an exponential culture should be much greater than is actually observed. Particularly for fast growing cells when $C+D \gg \tau$, e.g., $C+D = 3\tau$, corresponding to an average of eight origins per cell [equation (6)], one would expect practically continuous initiations (8 steps in one average cycle) and thus no discernable synchrony, contrary to what has been observed (Helmstetter & Cooper, 1968).

This consideration shows that, in spite of the imperfect synchrony that is found in age-fractionated cultures, the synchronous mode of initiation must be in principle correct. Therefore, the observed asynchrony, rather than being due to a sequential initiation mode, may be the result of fluctuation in a small number of initiator protein molecules required for initiation and of even smaller number of mRNA molecules for the initiator. The fact that a single mRNA molecule is translated 20–40 times (Dennis & Bremer, 1974) and thus might be expected to cause random bursts of initiations represents a conceptual difficulty for the hypothesis, which currently can only be dealt with by ad hoc hypotheses.

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The Development of Specific Visual Connections in the Monkey and the Goldfish: Outline of a Geometric Theory of Receptotopic Structure

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The anatomical structure of the primate retina-striate system and the goldfish retina-tectal system are characterized by idealized geometrical domains. The physiological retinotopic mappings are then shown to be determined by the boundary conditions of the respective anatomical surfaces. This fact is interpreted as support for the “systems-matching” hypothesis of neural development of Gaze & Keating. It is suggested that the development of specific neural mappings may be, in part, a variational problem in which two neural surfaces establish connections as “smoothly” as possible. Dirichlet’s Principle supplies a quantitative definition of the term “smooth”—the average physiological magnification factor of the neural mapping is minimized, subject to the boundary conditions of the available tissue. Three developmental rules are formulated, which deal respectively with gross specificity, polarity, and detailed map construction. The latter rule, based on Dirichlet’s Principle, supplies a link between the classical theory of fields and developmental neurobiology. Specific experimental tests are outlined in the goldfish visual system, and a general discussion of global approaches to neural structure and function is presented.

1. Introduction

A universal feature of vertebrate sensory information processing is the spatial mapping of peripheral receptor surfaces onto corresponding central neural processors. In the teleost fish and amphibians, the retinal surface projects topographically to the surface of the optic tectum. In the monkey, the retina projects (through the lateral geniculate nucleus) to an orderly map in the striate cortex, as well as to other thalamic, mid-brain, and cortical stations. The cutaneous (and deep) skin receptors of the priate project topographically to cortical area S1 (Woolsey, Marshall & Bard, 1942), the surface of the basilar membrane of the cochlea projects spatially to the central auditory processors (Lorenté de No, 1933; Merzenich, Knight & Roth, 1975) and
even the nasal mucosa project in an orderly spatial map to the olfactory bulb (Moulton, 1976).

A significant stumbling block to the interpretation of the functional significance of these diverse receptive-field mappings has been the general lack of any global mathematical description. The fact that these mappings are in general non-linear has led to the erroneous conclusion that they are "distorted" or highly inaccurate. This negative bias towards the significance of receptive-field maps has been greatly reinforced in recent years by the elegant and dramatic results of single cell sensory neurophysiology. In general, there is a large amount of "scatter" in the point-to-point representation of receptive-field maps, as measured by single-cell recording techniques. These observations have led some workers to the conclusion that the spatial organization of the sensory system is "of little if any relevance to the functional aspects of perception" (Doty, 1958). This disparaging attitude towards a serious appraisal of spatial structure in the nervous system is typified by the following statement of Somjen, in reviewing the current status of sensory neurophysiology: "The issue of the cortical movie screen, popular at first, discredited later and defended once again, is still not resolved. The presence of these topographically organized projection areas can hardly be mere accident, of course... (but) what kind of significance can we attach to them?" (Somjen, 1972).

In recent work, the retino-striate mapping of the primate has been shown to be characterized by the complex logarithm function (Schwartz, 1977a,b). In this work, both the global retinotopic mapping and the local structure of cortical hypercolumns (Hubel & Wiesel, 1974a) are characterized by the complex logarithmic conformal mapping, concisely summarizing both the anatomical retinotopic projection and the neurophysiological features of orientation tuning, sequence regularity, and binocular disparity tuning (Schwartz, 1977b). Pre-processing the visual scene via the complex logarithmic mapping has powerful advantages with respect to visual information processing. Rotation or size change of the visual stimulus reduces to a linear translation of an invariant cortical image, due to the complex logarithmic structure of the retinotopic mapping (Schwartz, 1977a,b). This fact has potential relevance to those aspects of visual perception related to size-distance relationships, depth perception, and size and rotation invariance. In a computer oriented pattern recognition context, Chaikin & Wieman (1977) provide an extensive discussion of the advantages of complex logarithmic pre-processing of the visual scene. In an optical computer context, Casasent & Psaltis (1976) point out that cross-correlation as a tool in pattern recognition suffers from extreme sensitivity to rotation and size change of the templates that are to be matched. A 1° rotation, or a 1% size change, causes a 20 dB drop in signal to noise ratio in a typical optical pattern recognition task (Casasent & Psaltis, 1976). The solution proposed by these workers is a complex logarithmic pre-processing of the templates, followed by pattern recognition in the spatial frequency plane, which eliminates sensitivity to size and rotation differences. This advantage might be of relevance to stereopsis, since the left and right eye projections of a visual stimulus may differ appreciably in their size and rotational aspects, due to differing version and vergence angles of the eyes. Thus, any role for cross-correlation in stereopsis would depend critically on the size and rotation normalization provided by the anatomical structure of the retinotopic mapping (Schwartz, 1977a,b). Finally, the fact that the complex logarithm function is a conformal mapping (Ahlfors, 1966) means that local angles are preserved in the cortical image. Despite a dramatic "distortion" of the cortical image due to the non-linear structure of the mapping, angular relations will be preserved. Since the angular relationships of a figure are a significant part of the "Gestalt" of a stimulus (Attneave, 1954), analytic mappings might be expected to occur quite generally in diverse biological visual systems.

The fact that the cortical sensory maps of the primate may be described by an analytic function, i.e. the complex logarithm, may have a simple developmental rational. Each analytic function represents a "potential flow", i.e. a solution to the Laplace equation [equation (4)] subject to specific boundary conditions. In a hydro-dynamic context, the real and imaginary parts of an analytic function may represent the streamlines and iso-potentials of the irrotational flow of a fluid (Churchill, Brown & Wrehey, 1974). Likewise, if a thin membrane is clamped and then placed under a load, the equilibrium shape of the membrane will be such that the lines of tension and compression lie along level lines of an analytic function, which is determined by the boundary conditions of the membrane (Morse & Feshbach, 1953). The statement that the Laplace equation is satisfied at each point is equivalent to the statement that the "lumpiness" of the membrane is minimized (Morse & Feshbach, 1953). In quite general terms, there is a connection between a local solution of the Laplace equation and a global variational problem. This connection is supplied by Dirichlet's Principle (Courant, 1950), and is discussed in the Appendix to this paper. The principle goal of the present work is to develop a biological application of Dirichlet's Principle. Specifically, it will be demonstrated that the boundary conditions, i.e. the anatomical "shape", of the primate retino-cortical visual system, and the goldfish retino-tectal visual system, determine the detailed structure of the respective retino-topic mappings. This analysis represents a quantitative statement of the hypothesis of "systems-matching", suggested by Gaze &
Keating (1972) in order to account for the plastic nature of neural regeneration in the lower vertebrates. Their suggestion that the retina and tectum form synaptic connections as global systems, rather than via specific cytochemical labeling, is expressed as a natural consequence of the variational statement of the Dirichlet Boundary Value problem. The advantage of this approach is that observable quantities, such as the "shape" of an anatomical structure, are linked mathematically to other observable quantities, such as the level lines of the physiological mappings. In the goldfish, it is possible to experimentally manipulate the shape of the tectum (by surgery); the regenerated map is then expected to be a function of the manipulated boundary conditions, and a direct experimental test of the ideas presented in this paper is therefore possible.

This application of analytic function theory may have significance beyond providing a simple mathematical description of the structure of receptive maps. The problems of developmental morphology may be formulated in general in terms of planar mappings: "The three dimensional morphology of embryos . . . develops by means of folding, shaping, and growth of cell layers (as in gastrulation, neurulation, and imaginal disk formation) and their three-dimensional integration is accomplished by specific inductive relationships between cell layers . . . rather than by three-dimensional pattern formation in solid tissue" (French, Bryant & Bryant, 1976). The method of choice in dealing with the structure of planar mappings is analytic function theory (Morse & Feshbach, 1953). Thus, the ability to formulate neuronal developmental problems in the language of analytic functions may provide a general method of dealing, mathematically, with the specific aspects of developmental morphology.

2. Ganglion Cell Density in the Retina of the Cat and the Monkey

Although the principle focus of discussion of logarithmic structure in the visual systems of the higher vertebrates is based on data obtained from the primate, the visual system of the cat may be included as well. The distribution of cell types in the retina, particularly with respect to the classification into $X$, $Y$, and $W$ cells (Fukuda & Stone, 1974), has been studied in greatest detail in the cat. Also, the seminal work of Fischer (1973), with respect to the mathematical relationships of cell density to receptive field size, has been based on data from the cat retina. Frustratingly, the corresponding experimental work on the retinotopic structure of the cortical maps has been done with the greatest detail for primates. Nevertheless, recent work on the cortical map of the cat (Wilson & Sherman, 1976) indicates that the magnification factor of the cat striate cortex has the same functional dependence as that of the primate (it is inversely proportional to eccentricity). Likewise, the measurements of cell spacing, density, and size in the primate retina (Rolls & Cowey, 1970) suggest that the same basic functional dependence is true both in the cat and the monkey. It is thus possible to develop a quantitative discussion of cell density in the ganglion cell layer (output layer) of the retina, to derive a potential function describing this density, and to show how a general theory, based on conformal mapping, may be advanced which shows the close relationship of cell density, geometry and retinotopy in the retina and in the striate cortex of the primate (or optic tectum of the goldfish).

**FISCHER’S LAW**

Using data from the retina of the cat, Fischer (1973) has established the following invariance law:

A point stimulus anywhere on the retina falls within the field centers of a constant number of ganglion cells. This follows because the rate at which ganglion cell density decreases is exactly compensated by the corresponding increase in receptive field diameter.

The consequence of this statement is that as one moves a point stimulus (or a collection of point stimuli making up a geometric form) across the retina, the same number of ganglion cells will be stimulated, despite the large variations in retinal ganglion cell density and receptive field size. The functional form of these two distributions exactly compensates one another. Fischer finds that the constant number of cells stimulated by a point stimulus is approximately 35, independent of eccentricity. Fischer proposed several possible geometric systems for the optic tract that would be isotropic in visual field co-ordinates, based on his observations. One of these is the complex logarithmic mapping that has been recently shown to account for the map of the striate cortex (Schwartz, 1977a). Thus, the hypothetical isotropic visual system postulated by Fischer is actually realized in the retinotopic mapping of the striate cortex (although not, apparently, in that of the optic tract prior to the LGN).

The data of Stone (1965) was used by Fischer as a source of his retinal ganglion cell density data. Fischer states that the form of the retinal ganglion cell density is (with the variable-representing eccentricity):

$$D(r) = k/r^2.$$  \hspace{1cm} (1)

Equation (1) is supported by McIlwain (1976) who shows that the inter-cell distance between (X-type) cells in the cat is well fitted by a straight line. Rolls & Cowey (1970) show a similar relationship in the retina of the primate. Thus, for the X-type cells of the retinal ganglion cell layer, which project
principally to the striate cortex, the inverse square law for density is essentially correct, both in the cat and the primate.

Since \( X \) cell receptive field size is proportional to the inverse of the eccentricity (Fukuda & Stone, 1974; McIlwain, 1976), Fischer’s numerical invariance law is valid for the case of the \( X \) cells of the cat, and presumably, the monkey retina. In order to establish more clearly the relationship of the invariance of the number of cells stimulated by a point image across the surface of the retina, to the spatial mapping of visual stimuli in the cortex, and to the size and rotation invariance properties that exist by virtue of the anatomical structure of this mapping (Schwartz, 1977a), it is useful to introduce a cellular “potential function.” This procedure will clarify the following discussion of the relation of cell densities and spatial mapping between the retina and the cortex, and will provide a specific neuronal application of classical potential theory.

Since the density of retinal ganglion cells per unit area is inversely proportional to the square of the eccentricity [equation (1)], the linear density is inversely proportional to eccentricity. Thus, the total number of cells traversed by moving a point stimulus from \( r_a \) to \( r_b \) across the surface of the retina is:

\[
\int_{r_a}^{r_b} k/r \, dr = k \ln \left( r_b/r_a \right).
\]  
(2)

If one takes the value of \( r_a \) (the reference) as unity in arbitrary units (the corresponding physiological landmark for this reference in the primate would be the central fovea, or foveola) then it is clear that one may define a “cellular” potential function \( \phi(r) \) which defines the “equidensity” bands of the retina:

\[
\phi(x, y) = \phi(r) = k \ln (r).
\]  
(3)

The analogy, in the electrostatic case, is the potential energy function surrounding a line charge, which is of the identical form of equation (3) (Panofsky & Phillips, 1962). The neuronal potential function \( \phi \) of equation (3) satisfies Laplace’s equation:

\[
\nabla^2 \phi(r) = \left[ \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial \phi}{\partial r} \right) + \frac{\partial^2 \phi}{\partial \theta^2} \right] \ln (r) = \delta(0).
\]  
(4)

Naturally, the logarithm diverges at the origin. In the physiological case, the retinal ganglion cell density falls to zero at the edge of the foveola (Rodieck, 1973); the analogy in the case of electrostatics would be of replacing the central line charge by a hollow cylinder of equal total charge.

Equation (4) establishes a neuronal application of the term potential function (Morse & Feshbach, 1953). It indicates an additional invariance property of the retina: one may define a “neuronal field” function \( E \):

\[
E = \nabla \phi(r) = k(\nabla \ln |r|).
\]  
(5)

The neuronal field \( E \) is a vector field which points towards, and increases as one moves towards, the fovea, and is numerically equal to the linear density of cells. The line integral of this field represents a conserved quantity which is independent of the path of integration, and is analogous to potential energy.

The existence of a conserved quantity under (eye) movement is interesting with regard to the question of visual world stability. Fischer’s rule is not dependent on the particular form of the ganglion cell density, but only on the reciprocity between the cell density function and the receptive field size dependence on eccentricity. However, the fact that cell density function obeys an inverse square law allows the definition of a “potential function” (Morse & Feshbach, 1953), and of a conserved line integral of the gradient of this function, which is the field of equation (5). In the electrostatic case, this conserved line-integral would simply be the work of moving a point charge in the field. In the present case, as the eye scans a stimulus (composed on “point–charges” of intensity), the line integral of equation (5) will depend only on the initial and final co-ordinates of the eye, but not on the details of the scan-path. The existence of a “scan-path invariant”, as above, might have relevance to the neuronal calculations underlying visual world stability, and this statement is directly dependent on the specific functional form (inverse square) of the retinal distribution of \( X \) cells.

Since the cellular potential function \( \phi \) is a solution of the Laplace equation, as in equation (4) above, it is a harmonic function (Ahlfors, 1966), and may be considered as the real (or imaginary) part of a complex analytic function. Morse & Feshbach (1953) prove that the unique complex function which has the logarithm as its real part is the complex logarithm:

\[
F(z) = \phi(x, y) + i\psi(x, y) = \ln (r) + i\theta.
\]  
(6)

The complex potential function for the retina, equation (6) describes the iso-potential and streamlines of the \( X \) cell density. The streamlines lie along the direction of maximal gradient of the cellular density, and the iso-potentials describe curves of equal cell density in the retina.

3. The Retinotopic Mapping of the Striate Cortex

In the previous section it was shown, based on the inverse square density function of \( X \) cells in the retina, that a complex potential function could be
defined which represents the lines of iso-density and maximal gradient of the retinal ganglion cell density. This function is the complex logarithm. In the present section, it will be demonstrated that the complex logarithm function also describes the mapping of points in the visual plane to points in the cortical plane; i.e. the retinotopic mapping. This fact will be related to the geometry of the retinal and cortical tissue surfaces; it will be shown that the “smoothest” mapping of a retina with concentric circular boundary conditions, to a cortex with (approximately) rectangular boundary conditions results in this relation between cell density, anatomy and retinotopy.

In previous work (Schwartz 1977a) it has been shown that the retinotopic mapping of the striate cortex is well represented by the complex logarithm function for the visual field from 1° to 2° out to 20° and beyond. To briefly summarize this work, the following points may be made:

(i) Since conformal mappings preserve local angles (Ahlfors, 1966) the statement that the retinotopic mapping is conformal implies that a visual stimulus consisting of intersecting locally perpendicular lines will be mapped to a cortical image of locally perpendicular lines. This is explicitly reported by Daniel & Whitteridge (1961): a radex in the visual field (concentric circles and radials lines) is mapped to an approximately rectilinear grid in the cortex. Later investigations of the cortical map find essentially the same geometry (Allman & Kaas, 1971).

(ii) The magnification factor for a conformal mapping should be locally isotropic: the magnification of a visual stimulus, which is proportional to the derivative of the retinotopic map (Schwartz, 1977a) should be the same in all directions. Again, Daniel & Whitteridge (1961) explicitly report this to be the case. (Of course, one has to be careful about the term magnification. In the mathematical sense, this is a differentially defined quantity, and it is only in the limit of making measurements with infinitesimal separation that the isotropic magnification factor of a conformal mapping should be evident. Thus, in a small structure such as the goldfish tectum, the intervals of visual field between measurement points may be as large as 10°, and consequently some anisotropy of the physiologically measured “gross” magnification factor will be evident.) Later work on the binocular structure of the striate cortex, particularly in layer IVc, where the monococular geniculate input arrives, has shown that there are two independent retinotopic maps, one for each eye, in this lamina of the cortex (Hubel & Wiesel, 1974b). These two maps are represented by parallel strips called ocular dominance columns (Hubel & Wiesel, 1974b). This double representation of the visual field will cause an apparent doubling of the magnification factor in the direction perpendicular to the ocular dominance column boundaries, compared to the direction parallel to these borders; this has been observed (Levay, Hubel & Wiesel, 1975). Nevertheless, the interleaved retinotopic mappings of the two eyes each seem to be represented by a conformal mapping of the visual field to the cortical surface (Fig. 3).

The cortical magnification factor is approximately proportional to the inverse of the eccentricity in the cat (Wilson & Sherman, 1976) and the monkey (Schwartz, 1977a). Naturally, this inverse dependence cannot continue to the very center of the fovea; the central 1–2° of visual field however, has not been carefully studied as to its retinotopic structure. In the retina, this part of the visual field corresponds to the extreme center of the fovea, or the foveola, which is free of ganglion cells (Rodieck, 1973). In the optic tract, the central macular projection is spread diffusely through the tract, unlike the remaining representation of the visual field, which is retinotopic (Hoyt & Luis, 1962). In the cortex, the central foveal field seems to project in an approximately linear manner to a (roughly) circular cap on the end of the cortical cylinder (see Plate I), and the magnification factor for the central 1–2° of field seems to be roughly constant (Rolls & Cowey, 1970). Thus, the analytic form of the retinotopic mapping may be represented by an approximately linear mapping of the central 1–2° of visual field, and a complex logarithmic mapping of the remaining foveal, parafoveal, and perifoveal visual field, as discussed in previous work (Schwartz, 1977a). This mapping may be written:

\[ w = \ln(z), \]  

where the complex variable \( z \) represents a point in the tangential plane, and the complex variable \( w \) represents a point in the cortical plane. The geometric properties of this function are illustrated in Fig. 2, along with a comparison of some anatomical and physiological data.

The approximations that are made in equation (7) are justified as follows: the use of complex variables to represent the retinal and cortical surfaces implies a planar approximation to these neural surfaces. For the central 20° of visual field, the hemispherical retinal surface is accurately approximated by a tangent plane through the fovea. The cortical representation, beyond the central 1–2°, is approximately cylindrical (Plate I) and consequently has zero Gaussian-curvature, i.e. is iso-morphic to a plane. In pragmatic terms, all measurements of cortical retinotopic structure to date have been presented in terms of planar maps. Thus, both mathematical simplicity and the lack of detailed measurements of the differential geometry of the cortical surface justify the planar approximation that is implicit in equation (7). One possible objection to equation (7) is the fact that the logarithm diverges at \( z = 0 \), i.e. the fovea. This is not a significant problem, because the central 1° of visual field is explicitly excluded from discussion; it has not been carefully mapped, although it appears that the magnification curve...
may flatten out to an approximately linear dependence (Rolls & Cowey, 1970). An analytic function that is regular at the fovea (z = 0), that is approximately linear for the central 1–2°, and which is essentially identical to the complex logarithm function, is simply ln (1 + z). In fact, this function gives a good approximation to the shape of the boundary of the primate striate cortex (the lunate sulcus, representing the vertical meridian of the visual field). This is illustrated in Fig 3.

4. Dirichlet's Principle and the Complex Logarithmic Retino-cortical System

The same function which describes retinal ganglion cell density also describes the cortical image of the visual field. This fact may be related to the solution of the following variational problem:

Given a retina with circular boundary conditions (an annulus), and specified values of cell density on the inner and outer boundary: Find the distribution of cells which has the minimal averaged density, subject to these boundary conditions.

The density of retinal ganglion cells is given by the square of the "linear density" represented by the field E of equation (5). Minimizing the average of this density is equivalent to minimizing the following integral:

$$\int \int_A E \cdot E \, dx \, dy = \int \int_A \left[ \frac{\partial}{\partial x} \phi(x, y) \right]^2 + \left[ \frac{\partial}{\partial y} \phi(x, y) \right]^2 \, dx \, dy$$  

(8)

PLATE II. (a) Shows a reconstruction of the unfolded striate cortex of the primate, (Daniel & Whitnidge, 1961). The representation of the foveal pit (0°–1°) of the visual field is a "cap" on the end of the approximately cylindrical cortical surface. This "cap" corresponds to the rod-free (and ganglion-cell free) center of the fovea. Its retinotopy has never been accurately measured. The far periphery occupies a point "cap" at the opposite end of the cortical surface. The principal part of the visual field (1°–20°) is represented on the surface of the cortical "cylinder", which is slightly tapered, as in the figure. On the right is the folded model of the cortical surface, which duplicates the cortical structure as would be seen in histological sections of the brain. (b) Shows a photomicrograph of the center of the fovea of the monkey retina from Stone (1966). This central area is free of retinal ganglion cells. (c) Is a graphic representation of the retinal and cortical surfaces of the monkey. The boundary conditions of the retina are that the central fovea has zero ganglion cell density (circle BCD). The iso-density contours are logarithmically spaced concentric circles; the streamlines are radial lines. The cortical boundary conditions are shown, for the area of cortex from 1°–20°. This is the surface of the hemi-cylinder shown in (a) from 1°–20°. The taper of the actual cortical surface would contribute a "tilt" to the borders D–E and B–A. The rectangular figure shown is, therefore, an idealization of the unfolded cortical surface, representing the central peri-foveal field (1°–20°). The complex logarithm is the unique function that maps the figure of (c) left, to right. Thus, circle BCD is mapped, under the logarithm, to line BCD on the right. Circle AFE is mapped to line AFE on the right. The radial lines on the left are mapped to the parallel straight lines on the right. The logarithmic iso-density bands on the left are mapped to the equidistant horizontal bands on the right. The rect-linear grid on the right shows the relation of a uniform "hypercolumn" covering of the cortical surface to its visual field representation, under the logarithmic mapping.
Fig. 1. (a) The cortical magnification data of Daniel & Whitteridge. Through the points is drawn the best fit to the data. (b) The measured and predicted mapping of visual landmarks in striate cortex. The upper (90°) and lower (270°) vertical meridians, the horizontal half meridian (180°), the octants (135° and 225°) and the circles of constant eccentricity are drawn as measured by Talbot & Marshall, and Daniel & Whitteridge. The data of Talbot & Marshall, on the left, does not show the correct (logarithmic) spacing between the lines of constant eccentricity; their experiment is the pioneering measurement of this data. The data of Daniel & Whitteridge is much more accurate, and is shown in the center. This is a projection, onto a horizontal plane, of a three-dimensional model; the meridians and octants are equally spaced, as they are in the theoretical prediction of these mappings under the logarithmic-conformal mapping. The theoretical prediction, on the right, actually represents a vertical meridian that is displaced by 1° from the fovea (see text) from the origin; otherwise the curved part of the contour would actually be a right angle. This displacement of the vertical meridian is equivalent to using the function \( \ln (1 + z) \) as the mapping function, as described in the text. (c) The global retinotopic mapping under the logarithm function. Concentric circles (exponentially spaced) and radial straight lines are mapped onto the equidistant cortical grid on the cortex. Note the density (derivative) of the exponentially spaced lines gives a linear dependence on the eccentricity; this is observed as a linear scaling of the receptive field size in the visual plane, with a constant (hypercolumn) size in the cortex.
where the domain of integration $A$ is the surface of the annular retina. The integral (8) is usually referred to as Dirichlet's integral (Courant, 1950) and a solution to this variational problem is equivalent to a solution to Laplaces equation [equation (4)], subject to the same boundary conditions (Courant, 1950).

The complex logarithm is the unique solution to the Laplace equation, with circular boundary conditions (Ahlfors, 1966; Morse & Feshback, 1953). Thus, the logarithmic density potential of the retina [equation (6)] has the property that it minimizes the averaged density of retinal ganglion cells for annular boundary conditions.

A similar variational problem may be formulated for the cortex. However, in the cortex, the quantity which is minimized is the averaged magnification factor, rather than the cell density. If one writes the cortical map as $f(x, y) = \phi(x, y) + i\psi(x, y)$ then the magnification factor is the derivative $f'(z)$ of this map (Schwartz, 1977a, b). Using the differential (Ahlfors, 1966):

$$\frac{d}{dz} = \frac{\partial}{\partial x} + i \frac{\partial}{\partial y}$$

and the Cauchy–Riemann equations (Ahlfors, 1966):

$$\frac{\partial \psi}{\partial x} (x, y) = \frac{\partial \phi}{\partial y} (x, y), \quad \frac{\partial \phi}{\partial y} (x, y) = -\frac{\partial \psi}{\partial x} (x, y),$$

the derivative of the complex map may be written as:

$$|f'(z)|^2 = \frac{\partial \phi^2}{\partial x} (x, y) + \frac{\partial \psi^2}{\partial y} (x, y).$$

Equation (11) defines the magnification of a complex mapping both in its mathematical context (Ahlfors, 1966) and in its physiological context (Daniel & Whitteridge, 1961).

The minimization of the magnification factor magnitude, as in equation (11), averaged over the cortical surface, is identical in form to the Dirichlet Integral of equation (8). The only difference between the retinal and cortical variational problems is the interpretation of the function $\phi(x, y)$. The complex logarithm function represents cell density in the spatially homogeneous retina, and spatial mapping in the histologically uniform cortex.

The retina and the cortex satisfy the same Dirichlet problem because they are conformally equivalent. This statement follows from the fact that the unique conformal mapping which takes an annular domain, i.e. retina, to a rectangular domain, i.e. cortex, is the complex logarithm (Churchill et al., 1974). Dirichlet's integral is invariant under conformal mappings (Courant, 1950); the solution to a Dirichlet variational problem in one domain is transformed to analogous solutions in all conformally equivalent domains. A physiological paraphrase of these ideas has been suggested by Hubel & Wiesel (1974a).

"Despite a marked difference between the retina and the cortex in histological uniformity, similar principles probably prevail in the two structures. In the cortex, magnification changes with eccentricity, while cell density remains roughly constant. In the retina, magnification is constant, but cell density varies."

The same function (the complex logarithm) describes both the retinal density distribution, and the cortical spatial mapping: the link between the two is supplied by Dirichlet's Principle, coupled with the observation that the geometry of the retina and the cortex makes them conformally equivalent domains.

This analysis supplies a framework for relating the geometry of cellular surfaces, cell densities, and receptive field structure, to the "system-matching" hypothesis of Gaze & Keating (1972), which suggests that specific synaptic connections may be related to the global nature of the systems being connected. Since access to the developing cortex is difficult, it is desirable to design an experimental test of these statements using a preparation based on the visual system of the lower vertebrates. Thus, before continuing with the discussion of neural development begun in the context of the mammalian visual system, the retina-tectal system of the goldfish will be described. It is possible to present a similar discussion of the goldfish visual system, using the language of analytic function theory. In particular, specific experimental tests may be carried out using the goldfish preparation.

5. The Retino-tectal Projection of the Goldfish

The boundary conditions of the goldfish retino-tectal projection are quite different than those of the cat and primate. The ventral hemi-retina (superior hemifield) of the goldfish projects to the medial $\frac{1}{2}$ of the contra-lateral dorsal tectum (Horder, 1974) [Fig. 2(a)]. The optic tract bifurcates into a lateral and medial branch; the medial branch, corresponding to the ventral hemi-retina, innervates slightly more than half of dorsal tectum, as above. The lateral branch innervates the ventral tectum, and part of the dorsal tectum. The ventral tectum (corresponding to the ventral hemi-retina) curves under the dorsal tectum, and is difficult to map physiologically for this reason; however, it has been mapped in a variety of teleost fish, and has been found to have the analogous retinotopy as the dorsal tectum (Schwassman & Kruger, 1965). The dorsal and ventral tectal systems are quasi-independent; Attardi & Sperry (1963) observed that in the course of regeneration following
optic tract transection, optic fibers come to occupy their original branches in the tract. In animals in which the ventral retina had been ablated, regenerated fibers filled the medial tract while the lateral tract remained largely empty. The reverse situation was observed in the tracts if the dorsal half of the retina was removed.

Thus, the dorsal hemi-retina projects to slightly more than half of the dorsal tectum; the shape of the dorsal tectum has not been quantitatively measured; however, it is close to elliptical, and may be characterized as an ellipse with the major and minor axes in the ratio of roughly 10/7. In order to simplify the mathematics, the area of projection at the tectum will be approximated as a half-ellipse, rather than as 1/4 of an ellipse. This follows because the mapping of a half-circle to a half-ellipse is a known conformal mapping, and is catalogued in standard references on conformal mapping (Nehari, 1952). The effect of this approximation on the geometrical results is slight.

The analytic function which maps the boundary and interior of the ellipse, to the boundary and interior of the unit circle is the function (Kober, 1957):

$$w = \sqrt{k} \sin \left( \frac{2K}{\pi} \sin^{-1} (z); p \right)$$

where $w$ represents a point in the visual field, and $z$ represents a point in the tectum. The function $\sin$ in equation (12) is the Jacobian elliptic function, and the parameters $p$, $k^2$ and $K$ are respectively the nome, parameter, and real quarter period of the Jacobian elliptic functions (Abramowitz & Stegun, 1964). $a$ and $b$ are the major and minor axes of the ellipse, normalized by the condition that $a^2 - b^2 = 1$. The goldfish dorsal tectum has a shape that is approximately an ellipse, with the ratio $a/b = 10/7$. This fixes all of the parameters of equations (12). The level lines of equation (12) are plotted in Fig. 2(c). Since the retinal ganglion cell density of the goldfish retina is relatively uniform (Easter, 1977), the boundary conditions of the tectal system are as shown in Fig. 2(c).

The experimental maps of the goldfish retinotectal system obtained by Horder (1974) and Sharma (1972) are shown in Figs. 2(a) and (b). The level lines of the function of equation (14) are shown in Fig. 3(c). There is a qualitative agreement between the experimental and theoretical maps, which includes the results of concave curvature of the level lines in the naso-temporal direction, and curvature towards the nasal pole (on the nasal side of the map) and towards the temporal pole on the temporal side of the map. The approximations made in the calculation of the theoretical map are forced by the lack of quantitative data; the characterization of the medial branch of the tectal map as a half ellipse (axes in the ratio 10/7) seems to be a fair approximation.

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**Fig. 2.** (a) Shows the retinal and tectal boundary conditions of the goldfish, as established by Horder (1974). The superior hemifield (stippled) corresponds to the medial half of the tectal surface (X'), which is innervated by the medial branch of the optic tract. This system (medial tract, X' tectum, hemi-retina) is taken as the basic retino-tectal "system" in the geometric context of the present analysis. Figure 2(b) Shows Sharma's (1972) mapping of the goldfish retino-tectal system. Points from Sharma's map have been deleted that correspond to the lateral optic tract, the lateral half of the tectum, and the inferior visual hemifield, in order to consider the isolated retino-tectal subsystem outlined above. (c) Shows the level lines of the conformal mapping of the hemi-retina to the hemi-ellipse, calculated in equation (12) of the text. This conformal mapping, dependent only on the (approximate) boundary conditions outlined above, gives a good approximation to the retinotopic structure measured by Sharma and Horder, and shown in (a) and (b).
approximation, based on the data of Horder, Sharma, and others, although a more precise knowledge of the tectal boundary conditions would be highly desirable. Also, there are a number of experimental difficulties in obtaining precise maps in the goldfish: the small size of the dorsal tectum (roughly 1-2 mm²) places a limit on the precision of measurement. Also, the eye of the goldfish is highly myopic in air (Charmin & Tucker, 1973). Most measurements to date have been performed in air, and this fact undoubtedly contributes error, particularly in the peripheral visual field. However, the mappings of Schwassman & Kruger (1965), performed with the fish in water, do not differ qualitatively from the maps of Sharma and Horder, performed in air. Thus, in the light of these theoretical and experimental qualifications, the function of equation (12) is suggested as a first approximation to the representation of the goldfish retinotopic map. With these reservations in mind, the agreement shown in Fig. 2 (a), (b) and (c) is good, and the focus of interest of the present discussion is on the general approach that is suggested by these results: the fact that the physiological map of the goldfish may be predicted based on the geometric boundary conditions of the retina and the tectum is interpreted as support for the systems-matching hypothesis of Gaze & Keating (1972).

6. Minimal Developmental Rules

The preceding discussion indicates that retinotopic structure in both the goldfish and the monkey may be described in terms of analytic or conformal mappings. The principle insight that follows from this description is that global boundary conditions may be sufficient to encode detailed local structure. Thus, "system matching" (Gaze & Keating, 1972) may be expressed in a quantitative manner. Naturally, genetically encoded specificity must still be postulated, although the burden of information that would have to be neuronally specified is greatly reduced, compared to models in which detailed positional information must be specified (Sperry, 1951). In order to clarify this argument, it is useful to introduce a set of "minimal developmental rules", which deal separately with the encoding of the structure of a retinotopic mapping. The first two of these rules are associated with specificity of "target" and polarity; the third rule, based on Dirichlet's Principle, asserts that the final equilibrium structure is the result of a variational process which results in a map for which the average magnification factor is minimal, subject to the boundary conditions of the available tissue. The three rules together correspond to a statement of the Reimann Mapping Theorem (see Appendix), and are minimal in the sense that they allow the final detailed structure of the retinotopic mapping to be determined by general physico-mathematical principles, rather than via biological encoding of detailed positional information.

Rule 1: Preferential pathway selection

The retinal ganglion cells, as a group, synapse preferentially with the cells of the contralateral optic tectum.

Rule 2: Specificity of retinal polarity

Two (perpendicular) axes of retinal polarity, or directional information, are encoded at the tectum. The existence of two axes of directional information at the tectum is sufficient to provide continuity of tectal position with respect to retinal position. This idea has been developed in detail in the arrow model of Hope, Hammond & Gaze (1976), who demonstrate that a continuous tectal map of the retina may be constructed by a random walk of tectal fibers, subject to the conditions that retinal polarity information is respected. This general construction of a topological map, i.e. a continuous map does not deal with the specific nature of the retinal and tectal boundary conditions explicitly. In order to do this, a third rule is necessary.

Rule 3: The Final Map is a solution of the Dirichlet Problem

The equilibrium retino-tectal map is formed such as to minimize the average magnification factor, subject to the area of tectum available. If the retino-tectal map is written as f(z), where the complex variable z represents the retinal location, then the magnification factor is f'(z) (Schwartz, 1977a). As shown earlier, Dirichlet's Principle is equivalent to the statement that the average magnification factor is minimized, subject to the condition that the retinotopic map take on constant values on the boundaries of the tectum.

Rules 1, 2, and 3 are sufficient to guide the development of a retinotopic map which would be characterized as a solution to a specific Dirichlet Boundary Value Problem. Therefore, they apply, at least in a formal sense, to both the monkey and goldfish visual systems. Of course, the original motivation to develop this analysis was the system-matching hypothesis of Gaze & Keating (1972); this, in turn, was formulated to deal with recent experimental observations concerning the visual systems of the lower vertebrates. These will be briefly reviewed, to provide experimental support for the hypothesis that systems-matching may be represented in terms of the Dirichlet Boundary Value Problem, as expressed by rules 1, 2, and 3.

Rule 1: Specificity of connection is a general feature of vertebrate development. Removal of the specific target of the retina causes the optic
fibers to synapse with secondary, less preferred targets. Thus, Schneider (1973) removed one superior colliculus in the neonatal hamster, and described a whole range of abnormal retinal projections of those fibers denied their normal site of termination. Likewise, transplanting the eye of the developing frog (*Rana pipiens*) to the position of the ear anlage results in the growth of a functional optic tract through the medulla, and down the entire length of the spinal cord. (Constantine & Capranica, 1975). This abnormal projection was consistently located in each experimental preparation, implying the existence of a gross system of gradients specifying the three co-ordinate axes throughout the entire developing nervous system. Therefore, the gross specification of neural target of the retina is clear. This statement should be contrasted with the exquisite degree of differentiation that is assumed by the chemo-affinity theory of Sperry (1951). This theory implies that each neuronal element of an array is rendered different from the other elements by processes of intrinsic differentiation, with a corresponding labeling operation occurring at the target site. It is certainly capable of explaining the construction of a specific map. However, this explanation would seem to be exorbitantly expensive in genetic terms and moreover, becomes very cumbersome when it attempts to deal with the experimentally observed plasticity of retino-tectal connections. Sharma (1972) has observed that ablation of half of the tectum causes a compression of the optic tract fibers onto the remaining tectal tissue: Yoon (1970) provided strong support for the plastic nature of retino-tectal fibers by placing absorbable, gelfoam barriers in the path of the optic tract. The initially compressed tectal maps returned to their normal configuration following absorption or removal of the mechanical barriers. Finally, the retina and tectum develop at different rates. In the tadpole, retinal growth occurs concentrically, with cells that comprised the entire retinal extent in the early developmental stages being progressively displaced towards the periphery. The tectum grows in an entirely different manner, forming by the addition of strips of cells that displace the existing tissue rostrilaterally (Straznicki & Gaze, 1972). During these early stages of growth, ordered but transitory retino-tectal connections exist. If one follows the reasoning of Sperry, then it must be assumed that the postulated cell labels are continuously changing during the larval stages. The conceptual simplicity of the chemo-affinity hypothesis, with respect to encoding specific structure, comes at a great price in regulatory and genetic complexity.

*Rule 2:* The specification of retinal polarity is related to the widespread observations of the existence of polarity in developmental preparations (Wolpert, 1969). In the case of the fish and amphibian retino–tectal system, the existence of polarities along two axes has long been known from behavioral and electrophysiological experiments. Following eye rotation experiments in *Amblystoma* (Stone, 1944, 1948, 1960) and *Triturus* (Székely, 1954), as well as electrophysiological mapping (Jacobson, 1968), it has been concluded that specificity of retinal direction is encoded independently along two axes (antero-posterior and dorso-ventral) and that the antero-posterior axis is encoded first. The existence of two axes of retinal polarity, at the tectum, would be sufficient to encode the structure of a detailed map, provided each optic tract fiber were able to “read” the appropriate pair of co-ordinates from the polarity, and to act upon this information by connecting with the appropriate tectal cells. The extreme form of this model is Sperry’s cyto-differentiation hypothesis, which supposes a “lock-and-key” relationship between specific retinal and tectal cells. An alternate hypothesis has been suggested by Jacobson (1960): retinotectal connections are assumed to be the result of a precise temporal matching of the arrival of optic fibers in synchrony with the maturation of tectal post-synaptic sites. This “timing hypothesis” seems to be incompatible with the experimental observations of the retino-tectal system: Feldman, Gaze & Keating (1971) have disrupted the normal temporal sequence of retinal input to the tectum of Xenopus, and still observed a normal retino-tectal projection. (The assumption of the present work is that the encoding of polarity, by the diffusion of some biochemical (morphogenetic) substances, serves as an approximate guide to the growing optic tract, but does not provide a detailed positional source of information for the final retino-tectal map, except by specifying the gross orientation and position of the map.)

*Rule 3.* This rule characterizes the development of connections between neuronal arrays as a “flow”. Rule 1 merely assures that synaptic contact is effected only with a specific target layer. Rule 2 guides the neuronal fibers, *en masse*, correctly polarized, to their target destination. Rule 3 is responsible for imposing a unique topographical structure expressed at the target site as a flow of afferent fibers across the available target tissue. Rule 3 asserts that the distribution of fibers across the surface of the tectum represents a solution of the Laplace equation at each point. As was demonstrated earlier, this assumption is, phenomenologically, in good agreement with the observed monkey and goldfish retinotopic maps. The specific form of this dynamic is the same as that observed in the classical Dirichlet Problem: a local conservation law, coupled with a statistical redistribution of fibers (random walk) leads directly to the formulation of the Dirichlet Problem. The attractiveness of this formulation follows from the fact that it depends only on a few simple, biologically plausible, and locally expressed developmental rules.

*The test of this experimental model is direct, at least in fish and amphibian*
visual systems. By surgical manipulation, it is possible to create various boundary conditions at either the tectal or retinal surface. Allowing a sufficient time for recovery, the retinotopic mapping will be re-established, connecting the available retinal and tectal tissues. The retinotopic structure that is expected to occur is directly predicted by the available surface of neural tissue, following the surgical manipulation: it will be the level lines of the conformal mapping that makes the boundary and interior of remaining retinal tissue to the boundary and interior points of the remaining tectum. This experiment depends only on the feasibility of obtaining accurate magnification measurements in the goldfish or amphibian retinotectal systems.

7. The Mathematical and Biological Basis of “Systems Matching”

The suggestion that the visual systems of such diverse species as the monkey and the goldfish may both be described from a single point of view merely adds one more application of analytic function theory (via the Laplace equation) to a repertoire that is already extensive. The common element shared by the widespread physical (and biological) applications is a “smoothness” quality that is best understood in terms of Dirichlet’s Principle (see Appendix). The necessity for “specificity” in describing the lines of flow of a fluid is clearly non-existent: the detailed paths of the flow arise from general physical principles (Dirichlet’s Principle) coupled with a specific local conservation law (the fluid is incompressible). In the biological case, the same “minimal” specification of structure may also be sufficient. Specificity is required to guide the optic tract, en masse, to its preferred target (Rule 1) and to encode polarity (Rule 2), but may be entirely unnecessary to encode the details of positional information, which has been attributed in the present work to Dirichlet’s Principle (Rule 3). This analysis provides a mathematical overview of “systems matching”. It does not supply the necessary biological dynamic expressed earlier as the drive to minimize the average magnification factor of the retinotopic map. The minimization of this putative biological “energy” could be related to fiber–fiber interactions, to competition of presynaptic fibers for post-synaptic targets, or could be coupled to physiological (visual) stimulation. In analogy to the case of fluid flow, a local incompressibility of synaptic density would provide a good candidate: this could be attributed to a homeostatic regulation of the density of synaptic contact between optic tract fibers and tectal neurons. Then the fluid flow metaphor would be particularly appropriate. Experimentally, this suggestion could be tested by measuring the density of synaptic contact in the normal and compressed tectum. Invariance of this quantity could be interpreted as a “neural incom-

pressibility” that might provide a local conservation law for Dirichlet’s Principle.

The specific variational nature of these arguments is similar to the remarks of Levay et al. (1975), in describing the structure of ocular dominance columns in the primate cortex. They remark that the pattern of left-eye, right-eye columns is irregular, often abruptly ending in blind ends, and suggest that the possible reason is the packing together, in the IVth layer of the cortex, of the two maps. The competition for space tends to equalize the width of the ocular dominance columns of each eye. It would seem that this statement represents a mammalian application of the “systems-matching” hypothesis of Gaze & Keating (1972): the global competition of the nasal and temporal (left and right) retinal maps results in the final equilibrium distribution of ocular dominance columns in layer IV of the primate striate cortex. It is interesting in this context to consider the global map of the ocular dominance columns reconstructed by Levay et al. (1975) in Fig. 3, and the complex logarithmic mapping. Next to the anatomical reconstruction in Fig. 3 are presented the images of a succession of (exponentially spaced) horizontal straight lines, across the retina, under the function \( \ln (1+z) \). These horizontal lines are imaged, by the logarithm, to a pattern that is quite similar to that of the actual anatomical preparation. The spacing of this pattern decreases as one moves further out in the peripheral field: as Levay et al. (suggest, it would seem that a competition of two such maps (left and right eye), with a corresponding random consolidation of ocular dominance columns, would explain the observed anatomical trajectories, based on the complex logarithmic structure of the individual retinal maps.

There is an interesting parallel of this nasal–temporal (left-right) eye competition in the retina-tectal system of the goldfish. Sharma & Tung (1975) ablated half the retina of each eye of a goldfish, and ablated the entire left tectum as well. The two semi-retinae were forced to compete for the one intact tectum. When the nasal–nasal preparation was mapped, it was observed that there was complete overlap or superposition of the tectal map of both (half) eyes. Apparently, there was no repulsion between the “nasal–nasal” retinal projections. However, when the “nasal–temporal” retinal preparation was mapped, it was observed that the nasal retina projected to the rostral half-tectum and the temporal half retina projected to the caudal half-tectum. There was complete segregation of the nasal and temporal retinal projections of the left and right eye, just as in the primate the nasal and temporal projections of the left and right eye project to segregated bands of ocular dominance columns in the striate cortex. If one were to assign a “positive charge” to the nasal halves of both retinae, and a “negative charge” to the temporal halves of both retinae, then the rule “like attracts, opposite repels” would
account for the behavior of the retinal ganglion cell fibers at the tectum (or the cortex). Coupling this polarity law with the "fine-tuning" supplied by Dirichlet's Principle may provide the outlines of a general set of minimally specified developmental rules, as suggested earlier. The gross structural relationships related to questions of polarity and the fine details of topography are described by separate developmental rules in this paper. Nevertheless, the brief mention of Sharma and Tung's data presented here is suggestive of the possibility of integrating polarity and topography into a single variational statement reflecting the overall competitive state of the retino-tectal system.

8. Discussion

In the present work, a simple planar approximation has been made in order to describe neural surfaces that are actually curved in three dimensions. This planar approximation is fairly accurate, at least for the central perifoveal visual field and its corresponding representation in the striate cortex, or the relatively flat dorsal tectum of the goldfish. A planar approximation facilitates the use of analytic function theory, the Laplace equation, and the entire apparatus of classical potential theory. Moreover, this approximation is well matched to the anatomical and physiological approximations that were made in lieu of more precise experimental data. However, the Laplace equation may be readily generalized to the Beltrami equation (Springer, 1957) which describes potential flow on arbitrary curved surfaces in terms of generalized co-ordinates. Surfaces of higher topological structure may also be handled with relative simplicity. This latter fact is not trivial, in view of Werner's (1970) elegant demonstration of the fact that the somatotopic mapping of the primate cortex has the topological structure of a "Klein bottle", i.e. a non-orientable surface of genus 1. In previous work (Schwartz, 1977a) it has been suggested that the somatotopic mapping may be represented, approximately, by a complex logarithmic mapping of the surface of the limb to the surface of the cortex, in direct analogy to the visuotopic mapping. In order to pursue this idea, it is necessary to deal with the mathematical problems of a complex curved surface (the surface of the limb), as well as the problem of "potential flow" on surfaces of higher topological structure. Both of these mathematical topics are dealt with extensively by Courant (1950) and Springer (1957).

Global approaches to neuronal structure and function are not popular among contemporary biologists and psychologists. In order to find a precedent, one must return to the work of the Victorian morphologists, of whom D'Arcy Thompson is a pre-eminent representative. The concept that global
factors might be important determinants of biological structure was fundamental to Thompson, who recounts the following anecdote:

“A great engineer, Professor Culmann of Zurich . . . happened (in the year 1866) to come into his colleague Meyer’s dissecting room, where the anatomist was contemplating the dissection of a human femur. The engineer, who had been busy designing a new crane, saw in a moment that the arrangement of the bony trabeculae was nothing more nor less than a diagram of the lines of stress, or directions of tension and compression, in the loaded structure . . . and was said to have cried out: ‘That’s my crane’.” (Thompson, 1975).

The crane head and femur are reproduced in Fig. 4.

It may be pointed out that the distribution of stresses and strains in a beam is governed by a generalization of Dirichlet’s Principle (Morse & Feshbach, 1953). Thompson comments on his observations:

“In the biological aspect of the case, we must always remember that our bone is . . . a highly plastic structure; the little trabeculae are constantly being formed and demolished, demolished and formed anew. Here, for once, it’s safe to say that “heredity” need not and cannot be invoked to account for the configuration and arrangement of the trabeculae . . .”

In this passage, Thompson suggests what his answer might have been to the question of whether receptotopic structure is (hereditarily) determined by cyto-chemical labeling, or by “system matching” operating through general physico-mathematical laws such as Dirichlet's Principle.

In summary, the principle result of the present work is the presentation of a quantitative framework for the discussion of the role of neuronal specificity in the construction of detailed receptotopic mappings. Using the variational approach suggested by Dirichlet’s Principle (and the related formalism of analytic function theory) it is seen that gross specificity is necessary to guide the optic tract to its preferred target, e.g. the optic tectum, and that polarity also must be specifically encoded, but that the detailed construction of a receptotopic mapping may rely on general variational (competitive) neuronal dynamics. There is no necessity for the hereditary encoding of detailed positional information.

Morse & Feshbach (1953) remark: “Variational principles are generally useful in unifying a subject, and consolidating a theory, rather than in breaking ground for a new advance. It usually happens that the differential equations for a given phenomenon are worked out first . . .”. In the present biological context, the reverse situation is the case: not only are the differential equations of developmental neurobiology totally unknown, but the variables upon which they might be based can only be guessed at present. Fiber-fiber interactions, chemo-taxis, morphogenetic gradients, pre- or post-synaptic competition for space, nutrients, or physiological stimulation are all potential candidates. Nevertheless, once these variables are known, and the equations constructed, it may well turn out that the most parsimonious description of the self-organizing nature of biological systems will be through variational principles.

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APPENDIX

The Dirichlet Problem, Dirichlet’s Principle and the Riemann Mapping Theorem

Among the existence proofs which dominated the mathematical thinking of the early 19th century, the most celebrated and consequential were those based on extreme problems of the calculus of variations, and which were suggested by actual or imagined physical experiments. Bernhard Riemann’s
geometric function theory, published in his doctoral thesis (1851) is the outstanding example of this approach.

To describe the physical reasoning underlying Riemann's conception, consider a surface $S$ in space with or without boundaries, of any topological structure. This surface $S$ is assumed to be covered with a thin uniform sheet conducting electricity. Imagine a stationary electric current over $S$, generated by the connection of arbitrary points on the surface with the poles of electric batteries. The potential of such a current will be the solution of a boundary value problem of a differential equation—just that type of a boundary value problem obtained from a variational problem. In general, this variational problem consists of seeking, among all possible flows, that which produces the least quantity of heat.

Mathematically, this problem can be formulated as that of minimizing an integral of the form:

$$ D(\phi) = \int_S \left( \frac{\partial^2 \phi}{\partial x^2} + \frac{\partial^2 \phi}{\partial y^2} \right) x \, y, \quad (A1) $$

in which the domain $S$ of integration and the range of functions $\phi$ admitted to competition are specified according to the particular nature of the physical problem.

The minimization of the integral of a functional, as above, may be solved by the use of the Euler–Lagrange equations (Morse & Feshbach, 1953), where the Lagrangian in the present case is the magnification factor per unit area, and may be thought of as a generalized "energy" of interaction representing a competition for space at the tectum, by the fibers of the optic tract:

$$ L(\phi_x, \phi_y) = \phi_x^2 + \phi_y^2. $$

Substituting this "Lagrangian" into the Euler–Lagrange equation:

$$ \frac{\partial}{\partial x} \frac{\partial L}{\partial \phi_x} + \frac{\partial}{\partial y} \frac{\partial L}{\partial \phi_y} - \frac{\partial L}{\partial \phi} = 0 $$

leads directly to the Laplace equation (noting that the Lagrangian contains no terms in the field):

$$ \left[ \frac{\partial^2 \phi}{\partial x^2} + \frac{\partial^2 \phi}{\partial y^2} \right] = 0. $$

The equivalence of the variational integral above, and the Laplace equation, is known as Dirichlet's Principle (Courant, 1950). It is of interest to point out that the general formalism of using the Euler–Lagrange equations to obtain a partial differential field equation, is typical of field theory in general, and consequently, the present approach represents a biological application of field theory.

The relationship of the variational approach to the differential equation approach may be best understood as follows: the Laplacian represents the divergence of a quantity; if the Laplacian is negative, then there is a "pile-up" of some quantity at that point, i.e. a "sink"; a positive divergence indicates a "source". The condition that the divergence be everywhere zero, means that there are no "sinks" or "sources", i.e. that the distribution is as free of "lumpiness" as possible, subject to the applied boundary conditions. The variational approach, symbolized by Dirichlet's integral above, explicitly represents the minimization of the average gradient, subject to the applied boundary conditions. If one clamps a membrane (and therefore imposes boundary conditions) then the loaded membrane will assume a shape that minimizes the "lumpiness" of the surface, according to these equations. Likewise, if one dips a wire frame in soap solution (the wire frame determines the boundary conditions) then the soap bubble formed will assume a shape determined by Dirichlet’s Integral, i.e. will be a surface of minimum area. Finally, if one interprets the function $\phi$ to represent cell density (or spatial mapping) then the "smoothest" possible equilibrium solution will be that which minimizes the gradients of cell density, or magnification factor, subject to the applied boundary conditions of tissue geometry. Extensive discussions of the applications of Dirichlet's Principle may be found in Morse & Feshbach (1953) and Courant (1950).

The best way to understand the equivalence between the variational statement and the differential equation statement is to consider the one dimensional case. Then, the Laplacian becomes $\partial^2/\partial x^2$, the boundary conditions consist in specifying two points, and the "surface" is the line connecting the two points. Then, the statement that the Laplacian is zero is equivalent to demanding that the curve connecting the end points is a straight line. The variational statement is equivalent to demanding that the integral of the slope of the curve is minimal, i.e. that the curve is a geodesic connecting the given end points. In this sense, surfaces that are described by conformal mappings are "geodesic" surfaces, or minimal surfaces.

The Riemann Mapping Theorem establishes that for simply connected domains, there is a unique conformal mapping which takes the boundary and interior of one surface to the boundary and interior of the other, subject to the specification of a target point, and a slope through that point. In the context of the present discussion, the specification of a target point corresponds to Rule 1, i.e. gross specificity, and the specification of a slope through that point corresponds to Rule 2 (specification of polarity). Rule 3, based on Dirichlet's Principle, is then essentially equivalent to the statement of the Riemann Mapping Theorem (Ahlfors, 1966).

Finally, for a comprehensive discussion of the mathematical subtleties of
Dirichlet’s Principle, including the question of whether the Dirichlet Variation may assume a minimal value, and the finiteness of the Dirichlet Integral, the reader should consult Courant’s (1950) monograph.

REFERENCES


