

The growth of elastic cartilage

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INTRODUCTION

Cartilage is an important tissue in mammalian growth. During embryonic life cartilage forms a template for the development of most of the skeleton and, post-natally, bone growth is still regulated by cartilage. Although its cartilage is elastic, the rabbit pinna is a convenient site for studying the growth of cartilage for it is accessible, relatively rapidly growing and, for many purposes, may be regarded as a two dimensional structure.

The present paper uses the specific growth rate to examine the growth of elastic cartilage, the assumption being made that the growth of the rabbit ear reflects the growth of its underlying cartilage. The specific growth rate at different positions and its mode of change from region to region are studied, the site of maximum growth is identified, and variations that occur with time are illustrated. The site of maximum specific growth rate is compared with other sites of maximum tissue change.

MATERIALS AND METHODS

The results obtained by Cox & Peacock (1978) in their study of the velocity field of growing cartilage have been used in the present inquiry into its specific growth rate. From their Tables 3 and 4, values have been taken for the parameters f , g , m , n and s at 15, 20, 28, 36, 49, 59 and 87 days. As in that paper, the origin has been selected at approximately the tip of the rabbit ear, the Y axis being along the midline of the dorsal surface and the X axis at right angles to it. The same notation is adopted.

Co-ordinates that satisfied the solutions for the differential equations were derived using the Newton–Raphson iterative procedure and a simple Fortran program for the field lines, and a simple Fortran program alone for the level lines. Calculations were made from a remote terminal using an ICL 4–70 computer.

RESULTS

The divergence of the velocity in two dimensions is equal to the specific growth rate in area, i.e.

$$\nabla \cdot \mathbf{Q} = \frac{\partial U}{\partial X} + \frac{\partial V}{\partial Y} = \frac{1}{dA} \frac{d(dA)}{dt}$$

where

$$\mathbf{Q} = U(X, t)\mathbf{i} + V(Y, t)\mathbf{j}$$

(Cox & Peacock 1978), A being the area, U and V the components of \mathbf{Q} , the velocity, and t the time in days/10. Hence, the gradient of the specific growth rate is

$$\nabla \left(\frac{1}{dA} \frac{d(dA)}{dt} \right) = \frac{\partial^2 U}{\partial X^2} \mathbf{i} + \frac{\partial^2 V}{\partial Y^2} \mathbf{j}.$$

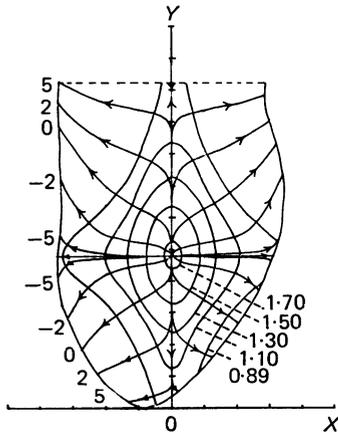


Fig. 1

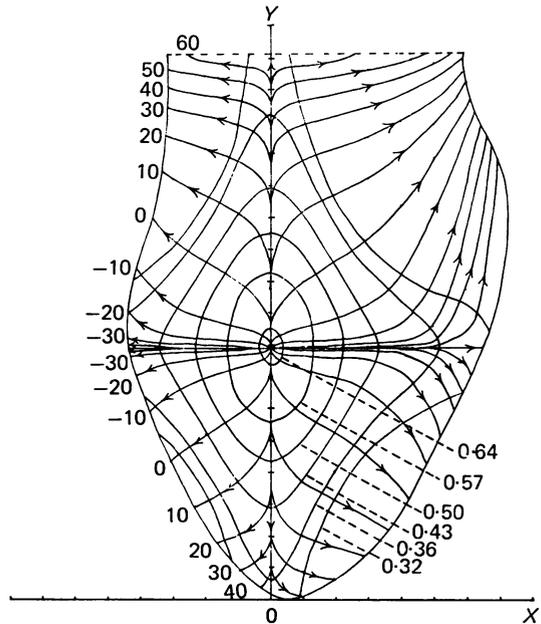


Fig. 2

Fig. 1. Field lines of the gradient of the specific growth rate and level lines of the specific growth rate for the growing right ear of a 15 days old rabbit ($t = 1.5$). The numbers on the right are values of the specific growth rate (E) and those on the left of the constants $H + (1/n^3g) - (1/m^3f)$. The X and Y units are 0.5 cm.

Fig. 2. Field lines of the gradient of the specific growth rate and level lines of the specific growth rate for the growing right ear of the same rabbit at 28 days ($t = 2.8$).

Field lines of the gradient of the specific growth rate and level lines of the specific growth rate are obtained by solving the differential equations

$$\frac{dY}{\partial^2 V / \partial Y^2} = \frac{dX}{\partial^2 U / \partial X^2} \tag{1}$$

and

$$\frac{\partial^2 V}{\partial Y^2} dY + \frac{\partial^2 U}{\partial X^2} dX = 0 \tag{2}$$

respectively, where the velocity components are given by

$$U = \frac{f}{1 + \exp(-mX)} - \frac{f}{2} \tag{3}$$

and

$$V = \frac{g}{1 + \exp(-n(Y-s))} \tag{4}$$

(Cox & Peacock, 1978). Substitutions of equations (3) and (4) in equation (1) yield

$$\begin{aligned} & \frac{(1 + \exp(-n(Y-s)))^3}{n^2 g \exp(-n(Y-s)) (\exp(-n(Y-s)) - 1)} dY \\ &= \frac{(1 + \exp(-mX))^3}{m^2 f \exp(-mX) (\exp(-mX) - 1)} dX. \end{aligned} \tag{5}$$

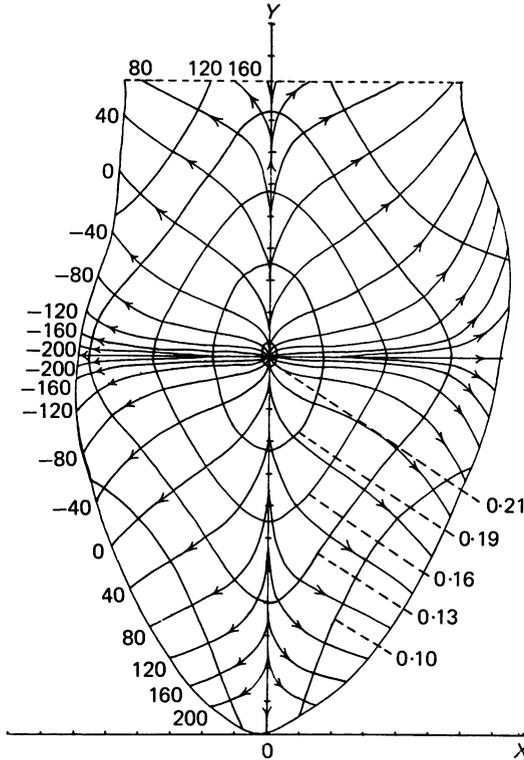


Fig. 3. Field lines of the gradient of the specific growth rate and level lines of the specific growth rate for the growing right ear of the same rabbit at 49 days ($t = 4.9$).

Integration of (5) gives

$$\frac{1}{n^3g} \left[\frac{\exp(2n(s - Y)) + 1}{\exp(n(s - Y))} + 8 \ln \{ \exp(n(Y - s)/2) - \exp(n(s - Y)/2) \} \right] = \frac{1}{m^3f} \left[\frac{\exp(-2mX) + 1}{\exp(-mX)} + 8 \ln \{ \exp(-mX/2) - \exp(-mX/2) \} \right] + H, \quad (6)$$

where H is the constant of integration. This equation represents the field lines of the gradient of the specific growth rate. For $t = 1.5, 2.8, 4.9$ and 8.7 (t in days/10) the corresponding field lines have been sketched (Figs. 1–4) after computation of the co-ordinates. $X = 0$ and $Y = s$ are also solutions of (5) and have been included in the diagrams.

In view of the natures of equations (3) and (4), equation (2) may be integrated directly to yield

$$\frac{dV}{dY} + \frac{dU}{dX} = \text{constant.}$$

Upon substitution this becomes

$$\frac{ng \exp(n(s - Y))}{(1 + \exp(n(s - Y)))^2} + \frac{mf \exp(-mX)}{(1 + \exp(-mX))^2} = E, \quad (7)$$

where E is the constant of integration and a value of the specific growth rate. This solution represents the level lines of the specific growth rate. The level lines are also shown in Figures 1–4, after computation of the co-ordinates.

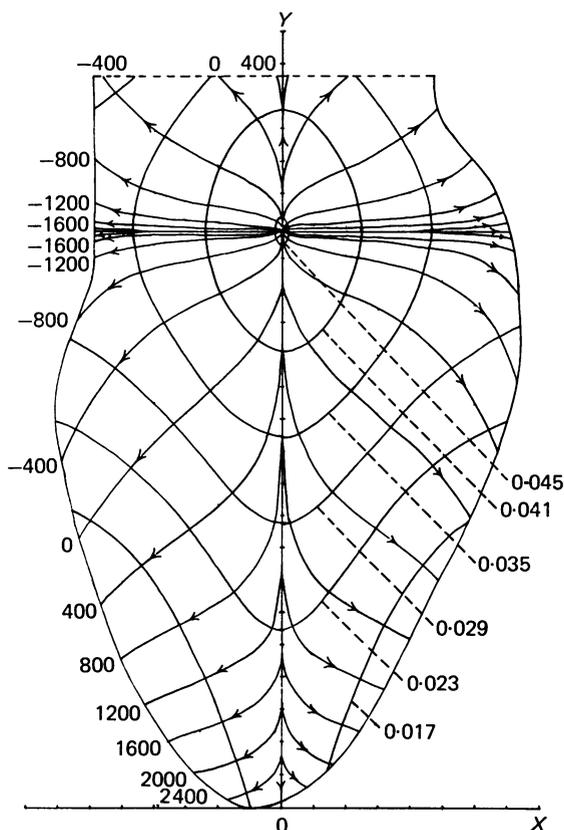


Fig. 4. Field lines of the gradient of the specific growth rate and level lines of the specific growth rate for the growing right ear of the same rabbit at 87 days ($t = 8.7$).

The distributions of the level lines depict the variations in the growth over the ear cartilage at different stages of development, the value of the specific growth rate being constant on any given level line. The maximum for the specific growth rate decreases with age, being approximately 1.70 at 15 days, 0.64 at 28 days, 0.21 at 49 days and 0.05 at 87 days. This centre for maximum growth is situated in the midline and moves from the tip of the ear towards the base with time, a finding that is consistent with the progressive increase in size of the ear cartilage and with alteration in its form. At 15 days the centre is 2.4 cm from the tip, at 20 days 3.1 cm, at 28 days 3.9 cm, at 36 days 4.7 cm, at 49 days 5.8 cm, at 59 days 6.6 cm and at 87 days 8.9 cm. The field lines of the gradient of the specific growth rate cut the level lines orthogonally, and the tangent to a field line at any point gives the exact direction of the gradient. The direction of the field lines has been drawn so as to indicate a negative gradient.

DISCUSSION

Direct estimations of the specific growth rate of an organ or of the whole body have been made by a number of authors. Huxley (1972), who has written extensively on the investigations at this level, prefers the name relative growth rate, however, and terms the ratio of two relative growth rates the differential growth ratio. Moreover, if one of these is the relative growth rate of the whole body, the ratio is called

the growth coefficient. In contrast, the specific growth rate of very small regions is obtained indirectly and requires a knowledge of the velocity vector field of the tissue concerned. The divergence of the velocity at any point of the tissue is equal to the specific growth rate in volume. Richards & Kavanagh (1943, 1945) have emphasized the continuous variation in the specific growth rate or in the ratio of two specific growth rates that this approach ensures.

Figures 1–4 illustrate not only the variations in specific growth rate in two dimensions at different sites of the ear at a given time but also the changes with time. The patterns are independent of the origin chosen for calculating the velocity vector field (Cox & Peacock, 1978), as the divergence of the velocity is invariant. The field or stream lines in the paper by Cox & Peacock (1978) indicate the direction of the tissue movement occurring during growth and are complementary to, but distinct from, the present level and field lines, which portray the growth rate and its gradient. No other comparable results appear to be available on the field of the specific growth rate of developing cartilage.

The fact that the centre of maximum specific growth rate moves with time along the midline of the ear from the tip towards the base (Figs. 1–4) immediately poses the question of the relationship of this centre to other maxima that are relevant to growth and morphological differentiation at the cellular level. The fine structure of the midline ear cartilage was studied by Cox & Peacock (1977), who noted that the intercellular material increased from the tip to the base. They thought it possible that the intercellular volume fraction also increased, but this was difficult to assess because of associated cellular hypertrophy. However, a relationship may be derived between the specific growth rate ($\nabla \cdot \mathbf{Q}$) of the whole tissue and the corresponding intercellular volume fraction (V_{Vi}). By analogy with mass density and charge density the stereologic ratios, e.g. intercellular volume fraction (V_{Vi}), cellular volume fraction (V_{Vc}) and cell surface density (S_{Vc}), may be used to denote values at a point, e.g.

$$V_{Vi} = dV_i/dV, \quad (8)$$

$$V_{Vc} = dV_c/dV, \quad (9)$$

and

$$S_{Vc} = dS_c/dV, \quad (10)$$

where V_i is the intercellular volume, V_c is the cellular volume and S_c the cell surface area. Differentiation of equation (8) with respect to time yields

$$\frac{dV_{Vi}}{dt} + V_{Vi}\nabla \cdot \mathbf{Q} = V_{Vi}\Gamma_i,$$

where $V_{Vi}\Gamma_i$ is a source term and represents the increase in intercellular material per unit time per unit volume of whole tissue. The intercellular material would be collagen, elastic tissue and ground substance. Rearrangement of this equation and consideration of the maxima gives

$$(\nabla \cdot \mathbf{Q})_{\max} = \left(\frac{1}{V_{Vi}} \left(V_{Vi}\Gamma_i - \frac{dV_{Vi}}{dt} \right) \right)_{\max}.$$

This and similar rearrangements illustrate that the maximum for the specific growth rate of a minute, elementary volume of whole tissue, the maximum for the production of intercellular material per unit time per unit volume of whole tissue, and the maximum for the material derivative (dV_{Vi}/dt) of the intercellular volume fraction, do not coincide. As stressed by Cox & Peacock (1978), the material derivative of any

pertinent quantity is an excellent measure of its morphological differentiation at the cellular level.

Since

$$V_{v_i} + V_{v_c} = 1,$$

similar considerations allow the derivation of

$$\frac{dV_{v_c}}{dt} + V_{v_c} \nabla \cdot \mathbf{Q} = V_{v_c} \Gamma_c$$

and the demonstration that the maximum for the production of cellular material per unit time per unit volume of whole tissue ($V_{v_c} \Gamma_c$), and for the material derivative (dV_{v_c}/dt) of the cellular volume fraction, do not coincide with one another or with the three maxima above. The increase in cellular material is accounted for by cell multiplication and cell enlargement, although after 20 days, when mitotic activity in the cartilage becomes rare, cellular hypertrophy would be dominant (Cox & Peacock, 1977). There could, however, be peripheral appositional contributions from perichondrial cells. Obviously, the maximum for specific growth rate would only coincide with the maximum for $V_{v_c} \Gamma_c$ or the maximum for $V_{v_i} \Gamma_i$ if one of this latter pair were zero.

Again, the maxima for the specific growth rate, for the material derivative of the cell surface density (dS_{v_c}/dt) and for the change in cell surface area per unit volume of whole tissue ($S_{v_c} \Gamma_c$) would not coincide because of the similar relationship

$$\frac{dS_{v_c}}{dt} + S_{v_c} \nabla \cdot \mathbf{Q} = S_{v_c} \Gamma_c.$$

All the above results apply in two dimensions as well as in three.

Finally, the equation of continuity in a source field when applied to growing cartilage may be written

$$\frac{d\rho}{dt} + \rho \nabla \cdot \mathbf{Q} = \rho \Gamma,$$

where ρ is the density and Γ is the source term (here the production of mass per unit time per unit mass). If the density is constant the equation reduces to

$$\nabla \cdot \mathbf{Q} = \Gamma$$

so that the specific growth rate is equal to the source term and, consequently, the distribution of the specific growth rate as shown in Figures 1–4 depicts the distribution of the source density. In the rabbit the mean density of the ear cartilage is 1.06 ± 0.04 (Cox & Peacock, unpublished). Maroudas, Muir & Wingham (1969) give a figure of 1.08 ± 0.01 for adult, human articular cartilage.

SUMMARY

Level lines of the specific growth rate and field lines of the gradient of the specific growth rate of developing ear cartilage have been computed. A single centre of maximum specific growth rate occurs in the midline and moves with time from the tip towards the base. Its movement is consistent with the progressive increase in area of the ear cartilage and with its consequent changes in form. The relationships of the centre for maximum specific growth rate to other maxima for the rates of production of cellular material, intercellular material, cell surface area and for material derivatives of intercellular volume fraction, cell volume fraction and cell surface density are discussed.

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