

Mathematical Oncology with Lab4IQM

Chapters 2–11: from growth laws to invasion and metastasis

Lab4IQM Mathematical Oncology module 0.3 · lab4iqm.com

This companion follows Chapters 2, 3 and 4 of M. A. J. Chaplain and L. Preziosi, *Mathematical Oncology* (Interdisciplinary Applied Mathematics 62, Springer, 2025). For each section it gives the Lab4IQM commands that draw the book's models, with the equation numbers of the book, and for each exercise a way to explore it. Read the book for the derivations; use Lab4IQM to see the models move. Type the commands in the Lab4IQM console after

```
import oncology
```

Every number in a command is a slider: drag it and the curve follows. `help(growth)` lists all options; the Examples panel has one example per section. In a Python script (Cmd+Return), `import oncology` gives the same commands as functions, e.g. `oncology.growth(model="gompertz", gamma=0.5, K=1)`. The example data files are simulated (see `data/README.txt` in the module); none are measurements from the book.

Chapter 2: Simple Models of a Growing Tumour Mass

2.2 Tumour size

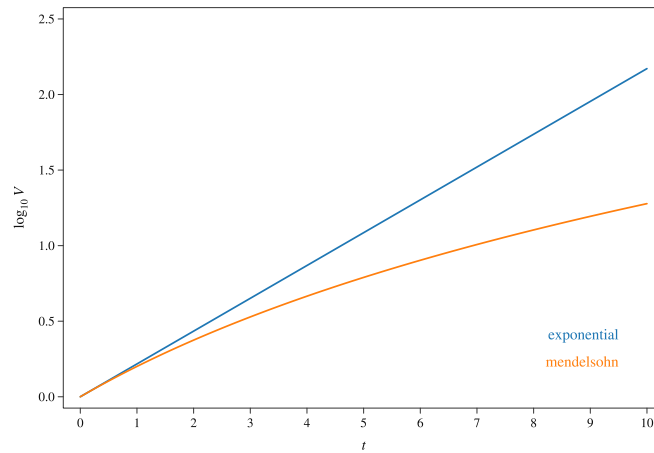
Volumes from diameters: three principal diameters give $\pi abc/6$; the longest and shortest give $\pi ab(a+b)/12$ when the middle axis is taken as their mean, and the calliper formula $\pi ab^2/6$ takes it equal to the shortest. One section of area A gives $0.752 A^{3/2}$ for a sphere. A cell of $2000 \mu\text{m}^3$ means about half a million cells per mm^3 .

```
tumourvolume(a=12, b=8)                two diameters (mm): both formulas, and cells
tumourvolume(a=12, b=8, c=10)           an ellipsoid
tumourvolume(area=50)                   one section
tumourvolume("oncology:mouse_tumour.csv", a=length_mm, b=width_mm, save="volumes.csv")
```

2.3–2.4 General features; unlimited growth

Exponential growth (2.6)–(2.9) is a straight line in a semilog plot; the power law of Mendelsohn (2.10)–(2.12) bends below it (and is straight in a log-log plot). This is the test of Fig. 2.3:

```
growth(model=(exponential, mendelsohn), gamma=0.5, V0=1, t=0..10, scale=semilog)
growth(model=mendelsohn, gamma=0.5, alpha=2/3, V0=1, t=0..100, scale=loglog)
```

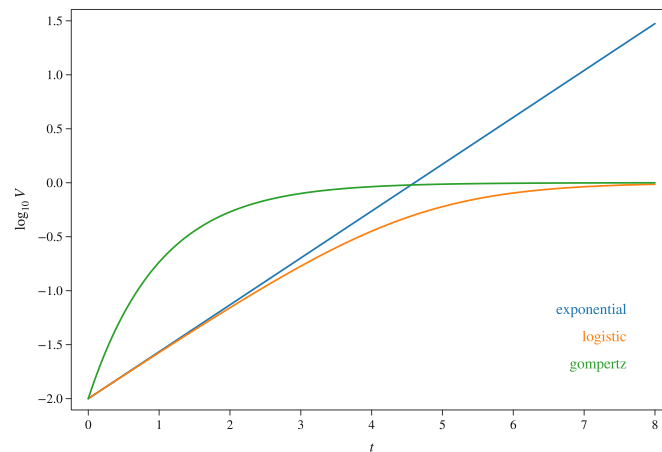


The console gives the doubling time $\ln 2/\gamma$ (2.8) of exponential growth, and the initial doubling time of every other law.

2.5 Growth-limited models

Logistic (2.18) and Gompertz (2.17) growth leave the exponential line early and level off at the carrying capacity K ; their closed-form solutions (2.19), (2.20) are used for the curves.

```
growth(model=(exponential, logistic, gompertz), gamma=1, K=1, V0=0.01, t=0..8, scale=
  semilog)
rates(model=(logistic, gompertz), gamma=1, K=1)          G(V), as in Fig. 2.4
rates(model=(logistic, gompertz), gamma=1, K=1, percapita=true) g(V) = G(V)/V, (2.3)
```



rates lists the steady states (zeros of G , (2.2)) with their stability (the sign of G'), and the volume of fastest growth, where $V(t)$ has its inflection point.

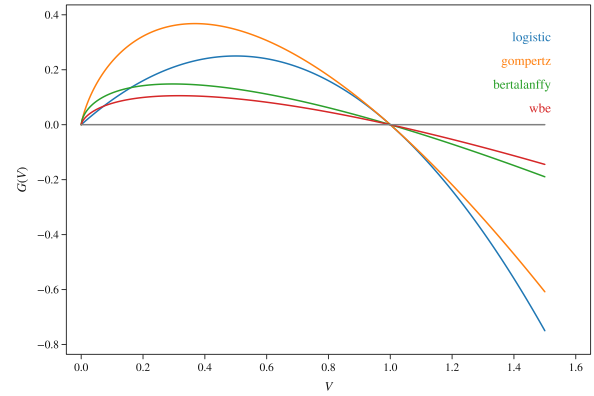
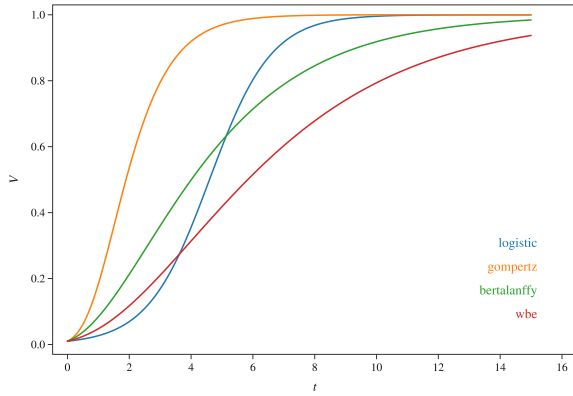
2.6 Generalized growth-limited models

All the laws of the section are available, with the book's parameter names:

model=	law	parameters
richards	generalized logistic (2.21)	gamma, K, nu
powerlogistic	power logistic (2.24)	delta, K, alpha
bertalanffy, wbe	(2.25), (2.26)	delta, K
turner	(2.31)	gamma, K, nu, p
gengompertz, hypergompertz	(2.32), (2.33)	gamma, K, alpha
twoexp	two-exponent class (2.34)	gamma, delta, alpha, beta
generic	generic class (2.35)	beta, K, n, p

`gamma=` sets the rate of every law in one command (`delta` for the power-logistic family), so laws are compared at equal rate, as in Fig. 2.5:

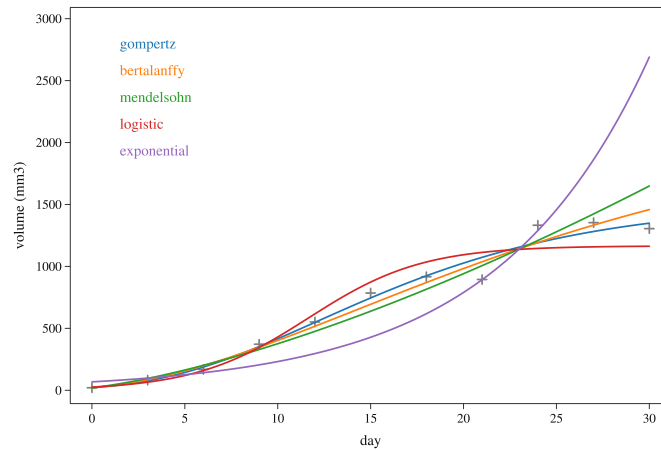
```
growth(model=(logistic, gompertz, bertalanffy, wbe), gamma=1, K=1, V0=0.01, t=0..15)
rates(model=(logistic, gompertz, bertalanffy, wbe), gamma=1, K=1)
```



The fastest growth is at $V/K = 1/2$ (logistic), $1/e$ (Gompertz), $(1 + \nu)^{-1/\nu}$ (generalized logistic) and $\alpha^{1/(1-\alpha)}$ (power logistic): 0.296 for Bertalanffy, 0.316 for WBE.

Which law fits? Studies quoted in the section fit several laws to the same data and compare them. `growthfit` does this: least squares on $\log V$ (errors proportional to the volume), the initial volume fitted too, laws ranked by AICc:

```
growthfit("oncology:mouse_tumour.csv", t=day, V=volume_mm3)
growthfit("oncology:spheroid.csv", t=day, V=volume_mm3, models=(logistic, gompertz,
    bertalanffy, wbe))
```



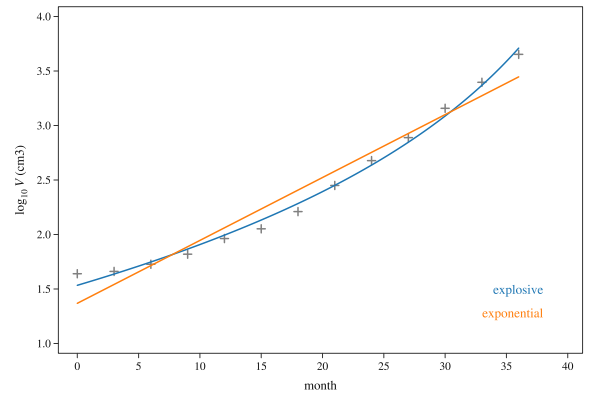
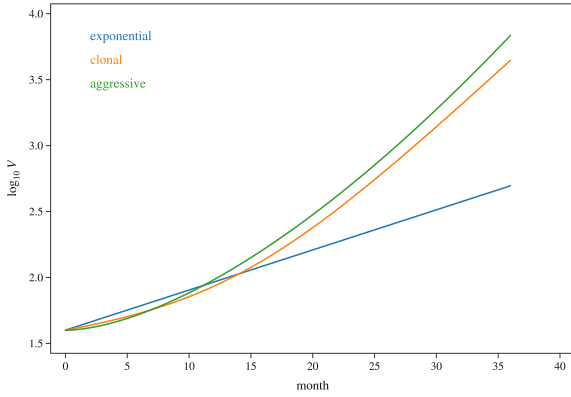
Laws within 2 AICc units are not told apart by the data. The simulated mouse tumour was made with Gompertz growth ($\gamma = 0.12/\text{day}$, $K = 1500 \text{ mm}^3$): the fit returns $\gamma = 0.120 \pm 0.007$,

$K = 1518 \pm 110$. Fitting the generalized logistic law to the same data drives $\nu \rightarrow 0$: the Gompertz limit of Exercise 2.3, which the console points out.

2.7 Super-exponential growth

Growth faster than exponential (2.36)–(2.37), the two-clone model (2.38)–(2.39) and evolving aggressiveness (2.40)–(2.41), as in Fig. 2.8a (the parameters of the clone models are those of the figure caption):

```
growth(model=(exponential, clonal, aggressive), gamma=0.07, V0=39.88, t=0..36, scale=
  semilog)
growth(model=clonal, gv=0.04, gw=0.2, eps=0.014, f0=0.001, V0=39.88, t=0..36, parts=true)
growthfit("oncology:glioma.csv", t=month, V=volume_cm3, models=(exponential, explosive),
  scale=semilog)
```

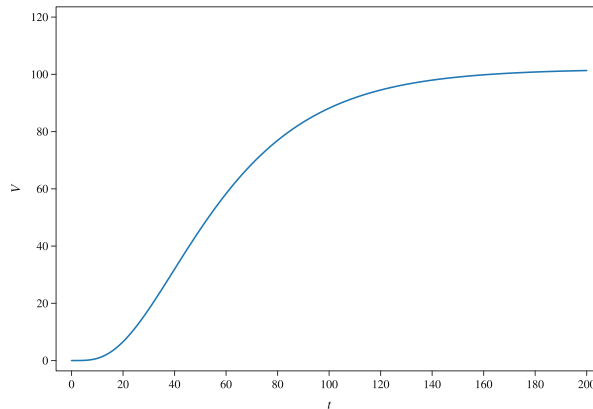


The console gives the blow-up time of (2.37). `parts=true` draws the two clones of (2.38): the aggressive one takes over.

2.8 Proliferating and quiescent cells

The constant-thickness rim model (2.42)–(2.47), with its steady volume (2.48):

```
growth(model=pq, gp=1, dp=0.1, dq=0.1, Delta=0.1, V0=0.001, t=0..200)
```

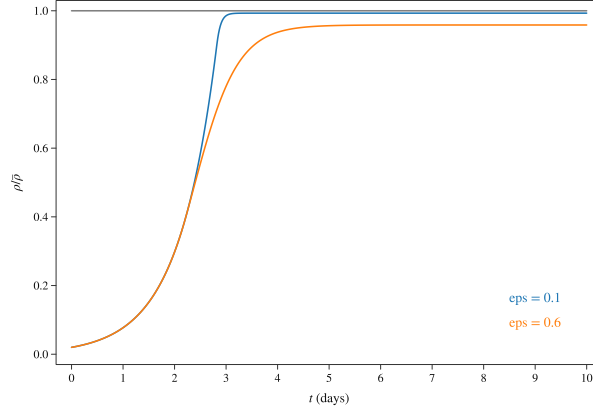


`Delta` is the thickness Δ of the proliferating rim; the model uses $\tilde{\Delta} = (4\pi/3)^{1/3}\Delta$ as in (2.43).

2.9 Contact inhibition of growth

Growth to confluence (2.49)–(2.56): the sharp switch ($\text{eps}=0$) and the gradual one (2.52), with the parameters of Fig. 2.13:

```
contact(gamma=1.45, delta=0.1, eps=(0.1, 0.6), rhobar=1, rho0=0.02, t=0..10)
growthfit("oncology:confluence.csv", t=day, V=cells_per_cm2, models=(logistic, gompertz))
```

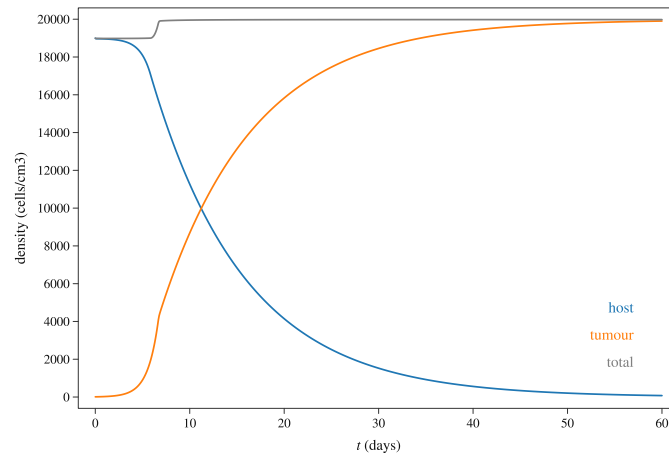


The console gives the steady density (2.54), the time t_ϵ when inhibition starts (2.56) and the confluence time (2.51) of the sharp switch. The doubling times of Table 2.1 convert to rates with $\text{gamma} = \ln(2)/T$.

2.10 Density misperception as a clonal advantage

Host and tumour cells that stop growing at different densities (2.57), as in Fig. 2.15:

```
misperception(rhoh=19000, rhot=20000, gamma=1, delta=0.1, eps=0.01, rho0=10, t=0..60)
```

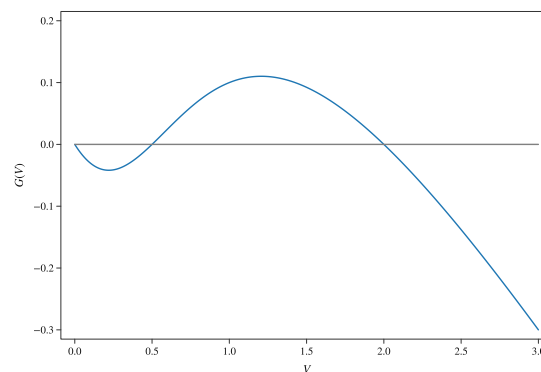


The console gives the end t_1 of the relaxed replacement phase (2.64) and the host density at that time (2.65); the three phases of Fig. 2.16 follow.

Exercises of Chapter 2

Lab4IQM does not solve the exercises for you; it lets you check your answers and see the behaviour. `growth(G=...)` and `rates(G=...)` take any growth function in V (use V for the unknown, whatever the book calls it); `ode` (a core command) draws systems of two or three equations.

-
- 2.1 `growth(model=gompertz, ..., exact=false)` against the closed form; `rates(model=(gompertz, bertalanffy, logistic), ...)` for stability.
 - 2.2 Laird's curve with $A = 2$, $\alpha = 0.3$, $V_0 = 0.1$ is Gompertz with $\gamma = \alpha$, $K = V_0 e^{A/\alpha}$: `growth(model=gompertz, gamma=0.3, K=0.1*exp(2/0.3), V0=0.1, t=0..30)`.
 - 2.3 `growth(model=(gompertz, richards), gamma=100, nu=0.01, K=1, V0=0.01)`: the generalized logistic with $\gamma = \beta n$, $\nu = 1/n$; increase n .
 - 2.4 `growth(G=mu*V^(1/2)*(1-V)^(3/2), mu=1, V0=0.1, t=0..10)`; `rates(..., V=0..1)`.
 - 2.5 `rates(G=alpha*V/(1+beta*V) - omega*V, alpha=2, beta=1, omega=0.5)`: the ultimate size $V = 3$; compare with your $(\alpha - \omega)/(\beta\omega)$.
 - 2.6 `rates(G=V^2/(1+V^2) - d*V, d=0.4, V=0..3)`: three steady states for $d < 1/2$; move d .
 - 2.7 `ode(F=(r*x*(1-x/y), -a*y+b*x-c*y*x^(2/3)), start=(0.5, 1), t=0..60, r=1, a=0.5, b=1, c=0.2)`, with $x = V$, $y = B$.
 - 2.8 `ode(F=(-alpha*x, x*y), start=(1, 0.1), t=0..20, alpha=0.3)` with $x = r$, $y = V$; compare with `growth(model=gompertz, ...)`.
 - 2.9 `growth(G=V*(phi*W+psi*V)/(k*W+lam*V), ...)` after the quasi-steady-state step, with $V = N$.
 - 2.10 `ode` with $x = P$, $y = Q$ and your choice of $r_0(N)$, $r_i(N)$.
 - 2.11 `rates(G=alpha*V/(V+n) - beta*V - kappa*V*(V+n), alpha=1, beta=0.2, kappa=0.1, n=0.5)`: move n to find n_c .
 - 2.12 `growth(G=alpha*k - alpha*k^2/V + alpha*k^3/(3*V^2), alpha=1, k=0.2, V0=0.5)`, with $V = R$.
 - 2.13 `rates(G=r*V*(1-V/K) - E*V, r=1, K=1, E=0.3)`: move E past r .
 - 2.14 `growth(model=(twoexp, gengompertz), alpha=0.5, beta=0.55, ...)`, letting $\beta \rightarrow \alpha$.
 - 2.15 `growth(model=clonal, f0=0, parts=true, ...)`: the solution (2.39).
 - 2.16 `growth(model=aggressive, c=0, ...)` with `scale=semilog`: the parabola (2.41).
 - 2.17 `misperception(gt=1.2, ...)`, `misperception(dt=0.05, ...)`, `misperception(epst=0.05, ...)`.
-



Chapter 3: Diffusion-Based Models

Chapter 3 is about steady concentrations: oxygen, nutrients and inhibitors diffuse much faster than cells divide, so on the time scale of growth each concentration is the solution of a boundary value problem. Each command draws that solution and prints the numbers the book derives from it (penetration depths, zone radii, critical sizes).

3.2 Hill's oxygen diffusion model

<code>oxygen(a=1, D=1, sigma0=1, b=1.2)</code>	oxygen everywhere (3.4)
<code>oxygen(a=1, D=1, sigma0=1, b=2)</code>	anoxic core: Hill's rim (3.8)
<code>oxygen(a=1, D=1, sigma0=1, b=2, alpha=0.5)</code>	lactic acid core (Exercise 3.1)

The slab has width $2b$ and oxygen σ_0 on both faces. The console gives the penetration depth $\hat{b} = \sqrt{2D\sigma_0/a}$ and the slope at the face (3.7). With `alpha=` lactic acid is added: produced everywhere (3.11) in a thin slab, or only in the anoxic core of a thick one, where it fills the place left by the oxygen (Exercise 3.1: the oxygen ends at $x^* = b - \sqrt{b^2 - \hat{b}^2}$, with balanced fluxes). Drag b across $\hat{b}$ to see the change.

3.3 Nutrient limited growth and spheroid structure

With linear uptake $\delta\sigma$ the nutrient decays over the diffusion length $d = \sqrt{D/\delta}$ (3.14); give `d=`, or `D=` and `delta=`.

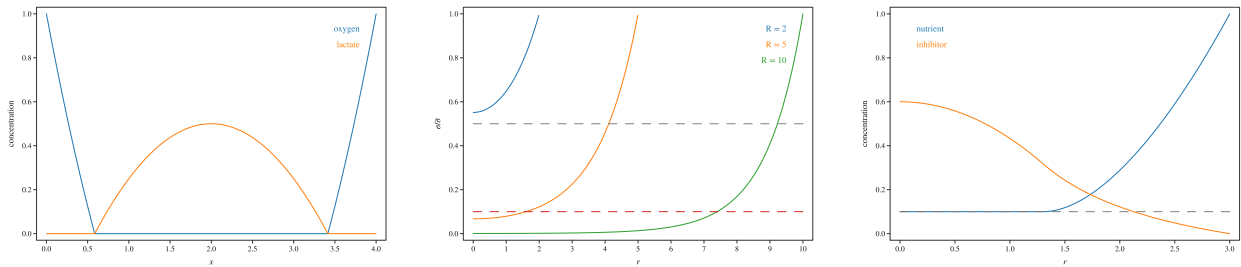
<code>nutrient(geometry=line, d=(0.5, 1, 2), sigma0=1, x=0..6)</code>	(3.14)
<code>nutrient(geometry=sphere, d=1, R=(2, 5, 10), sigmap=0.5, sigman=0.1)</code>	(3.19)–(3.21)

For a spheroid the profile is (3.19). With the thresholds `sigmap=` (proliferation) and `sigman=` (necrosis) the console tabulates $\sigma(0)$, the width of the proliferating rim and the estimate $d \ln(\bar{\sigma}/\sigma_p)$ of (3.21): the rim width stops depending on R .

With constant uptake instead, a spheroid gets a necrotic core once it is larger than $R_c = \sqrt{6D(\sigma_\infty - \sigma_c)/a}$ (Exercise 3.6, the model of Burton and Greenspan):

```
oxygen(geometry=sphere, a=1, D=1, sigma0=1, sigmac=0.1, R=3, P=1)
```

`P=` adds the inhibitor made in the core (Exercise 3.11).

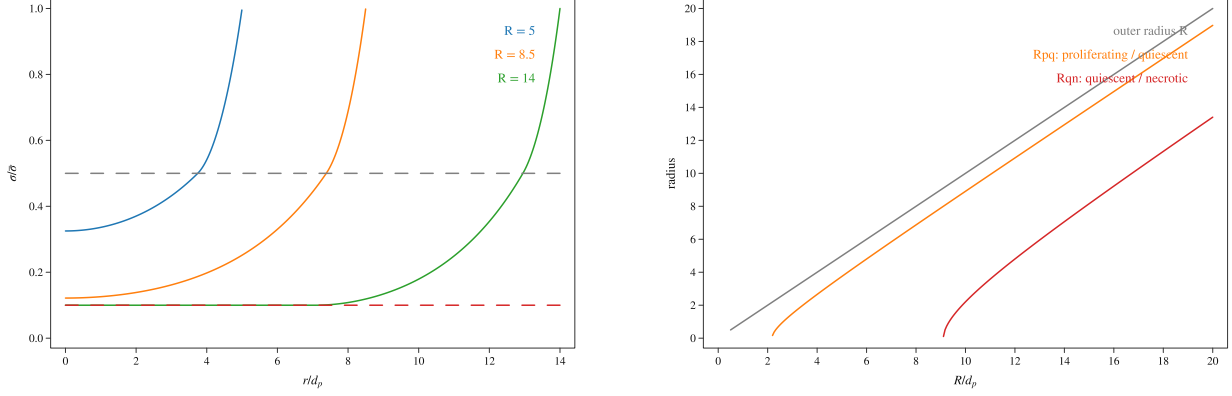


Three zones (Sect. 3.3.1). Proliferating cells take up nutrient at rate δ_p , quiescent cells at $\delta_q = q\delta_p$, necrotic cells not at all, (3.22)–(3.25):

<code>spheroid(R=(5, 8.5, 14), q=0.2, sigmap=0.5, sigman=0.1)</code>	Fig. 3.4
<code>spheroid(R=0.5..20, q=0.2, sigmap=0.5, sigman=0.1)</code>	zone radii as R grows
<code>spheroid(R=14, q=0.2, sigmap=0.5, sigman=0.1, solid=true)</code>	the spheroid cut open, in 3D

Lengths are in units of d_p . The interfaces R_{pq} and R_{qn} are found by continuity of the flux, as in the book; the console also gives the sizes at which a quiescent core and a necrotic core first appear.

For these values: a quiescent core from $R = 2.18$, a necrotic core from $R = 9.11$; at $R = 14$ the cells proliferate from $r = 12.95$ outwards and the necrotic core has radius 7.07. The caption of Fig. 3.4 quotes about 8.5, 12.9 and 7.5; the first and last differ a little from the values found by solving the interface equations exactly (the tests check that both flux conditions hold), so compare your own numbers with the console.



Induced hypoxia in 2D (Sect. 3.3.2). A round coverslip of radius R on a monolayer:

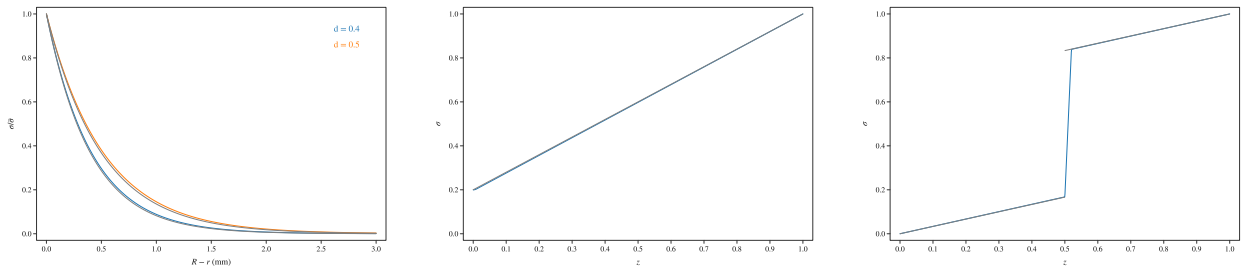
```
nutrient(geometry=disc, d=(0.4, 0.5), R=7.5, edge=true)    Fig. 3.5c (lengths in mm)
```

The profile is $I_0(r/d)/I_0(R/d)$; `edge=true` plots it against the distance $R - r$ from the edge, with the half-line profile $e^{-(R-r)/d}$ in grey: for $R \gg d$ they coincide, as the book notes. (The measured points of Fig. 3.5c are not included.)

3.4 Absorption and permeability boundary conditions

```
nutrient(geometry=monolayer, d=0.05, H=1, eps=0.01)        (3.27) and (3.28)
nutrient(geometry=membrane, H=1, h=0.5, eps=0.02, Dout=1, Dm=0.01) (3.29) and (3.30)
```

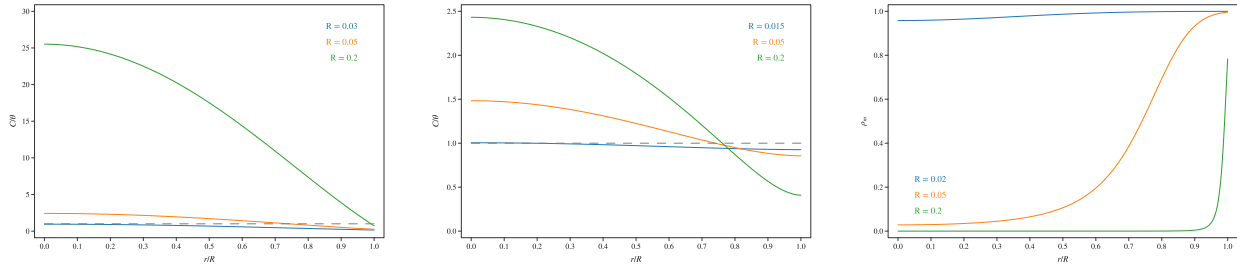
The first draws the exact solution with a cell layer of thickness ε and, in grey, the absorbing (Robin) boundary condition that replaces it, with $\alpha_{\text{eff}} = \varepsilon\delta$. The second draws a thin layer of low diffusivity and its Kedem–Katchalsky limit with $\beta_{\text{eff}} = D_\Sigma/\varepsilon$: the concentration jumps across the membrane. Make `eps` smaller (keeping D_m/eps fixed) and watch the two curves merge.



3.5 Mitotic control via growth inhibitory factors

```
gif(source=uniform, a=2, eta=0.5, L=(1, 3, 10))             3.5.1
gif(source=nonuniform, D=5e-7, P=1e-4, gamma=5e-5, R=(0.03, 0.05, 0.2),
    match=(0.74, 0.05))                                     Fig. 3.8
gif(source=nonuniform, D=5e-7, P=6e-7, gamma=1.25e-3, R=(0.015, 0.05, 0.2),
    match=(0.74, 0.05))                                     Fig. 3.9
gif(..., mitotic=true)                                     Fig. 3.10
```

The concentration is drawn in units of the threshold θ , against r/R : cells divide where it is below the dashed line. Dimensionless parameters as in (3.49) (a , L , η), or dimensional ones (D , P , γ , $\lambda = \lambda/\theta$, and R in cm). `match=(0.74, 0.05)` reproduces the book's calibration: λ/θ is chosen so that 60% of the volume divides when $R = 0.05$ cm; this gives $a = 76.764$ for Fig. 3.8. The console gives the radius where the centre stops dividing: 0.0309 cm with the parameters of Fig. 3.8, and 0.0146 cm with those of Fig. 3.9 (calibrated the same way), in the two ranges quoted in the book. For the uniform source it also gives the growth case 1, 2 or 3 of (3.43)–(3.46) and the mitotic rim width W of (3.45). `d=` takes any diffusion profile $d(r)$; that problem has no closed form and is solved by finite volumes.



3.6 A model of glioma growth and spread

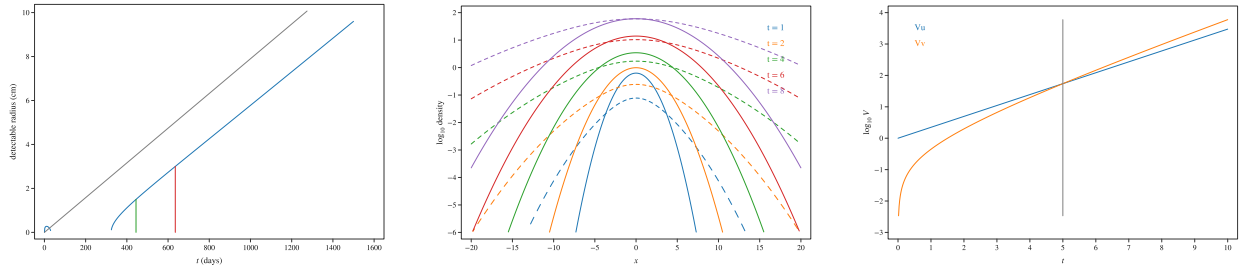
```
glioma(D=0.0013, rho=0.012, N0=1e4, cbar=4e4, t=0..1500, rdetect=1.5, rlethal=3)
glioma(D=0.0013, rho=0.012, N0=1e4, cbar=4e4, profile=(100, 300, 600), scale=semilog)
spread(Dw=0.0065, Dg=0.0013, rho=0.012, days=500, d0=1)
```

`glioma` draws the detectable radius (3.58) with its asymptote $2\sqrt{D\rho t}$ and gives the survival time from detection both exactly and by (3.59) (here 190.6 and 189.9 days; the numbers are illustrative, not the book's). `spread` solves (3.55)–(3.56) with logistic growth on a schematic brain section (not real anatomy) and draws the cell density as a 3D surface over it, with the white matter outlined: the tumour runs ahead along the white matter. The book's Fig. 3.13 uses $\rho = 0.75/\text{day}$ for 100 days; try `spread(rho=0.75, days=100)`.

Two clones (Sects. 3.6.1–3.6.2).

```
clones(alpha=0.2, beta=0.8, mu=5, t=(1, 2, 3, 4, 5, 6, 7, 8), scale=semilog)  Fig. 3.14
clones(alpha=0.2, beta=0.8, mu=5, show=volumes, t=0..10, scale=semilog)      (3.74)
-(3.77)
```

u is (3.68). v is computed exactly by superposing Gaussians (Duhamel's principle), which works for all parameters; the closed form (3.70) needs $1 - \alpha - \beta > 0$, and these values have $1 - \alpha - \beta = 0$. In the Fourier form we use, $v = \frac{\alpha e^{Et}}{4A(\mu - 1)} \left[e^{-Ax} \left(\operatorname{erf} \frac{x-2At}{2\sqrt{t}} - \operatorname{erf} \frac{x-2A\mu t}{2\sqrt{\mu t}} \right) + e^{Ax} \left(\operatorname{erf} \frac{x+2A\mu t}{2\sqrt{\mu t}} - \operatorname{erf} \frac{x+2At}{2\sqrt{t}} \right) \right]$ with $A^2 = (1 - \alpha - \beta)/(\mu - 1)$ and $E = (\mu(1 - \alpha) - \beta)/(\mu - 1)$; the tests check it against the Gaussian superposition, so compare it with (3.70) when you derive it. The volumes cross at $t_{\text{dominance}} = 1/\alpha = 5$ (the limit of (3.77) when $1 - \alpha - \beta \rightarrow 0$); the peaks cross later, just after $t = 8$ for these values, because v is spread over a wider region.



Exercises of Chapter 3

-
- 3.1 `oxygen(a=1, D=1, sigma0=1, b=2, alpha=0.5, D1=0.7)`: the console gives x^* and the maximum lactate; compare with your formulas.
 - 3.2 `nutrient(geometry=monolayer, ...)` and `nutrient(geometry=membrane, ...)`, with `eps=(0.1, 0.01, 0.001)` (keep $\varepsilon\delta$ or D_Σ/ε fixed).
 - 3.3 `nutrient(geometry=line, d=1, sigma0=1)`, `(..., flux=0.5)`, `(..., K=(0.5, 2, 10))`, `sigmab=1`.
 - 3.4 `nutrient(geometry=slab, d=0.5, L=3, sa=1, sv=0.4)`; then `Ka=(0.5, 2, 10)`, `Kv=2` for leakier arterial walls.
 - 3.5 `nutrient(geometry=capillary, d=1, Rc=0.1, sigmac=1)`, `(..., flux=1)`, `(..., K=2, sigmac=1)`: the solutions are multiples of $K_0(r/d)$.
 - 3.6 `oxygen(geometry=sphere, a=1, D=1, sigma0=1, sigmac=0.1, R=3)`: R_i , R_c and the rim thickness; drag R to watch $T \rightarrow 1/\sqrt{3}$ (in units of R_c).
 - 3.7–3.8 `gif(source=uniform, ...)` and `gif(source=nonuniform, ...)` draw (3.38) and (3.50); `gif(source=1-r^2, ...)` solves the same problem numerically, for comparison.
 - 3.9 `gif(geometry=slab, a=2, eta=0.5, L=(1, 3, 10))`: the strip, with $C(0)$, $C(L)$ and the inhibited region.
 - 3.10 `gif(source=1-b*r, b=0.5, a=2, eta=0.5, L=(1, 3, 10))`: compare with your closed form.
 - 3.11 `oxygen(geometry=sphere, ..., P=1, Db=1)`: the inhibitor made in the necrotic core.
 - 3.12 `glioma(dim=1|2|3, profile=...)`: the Gaussian solution in each dimension.
-

Chapter 4: Mass Balance and Constant Density Models

4.2–4.3 Mass balance; constant density in 1D

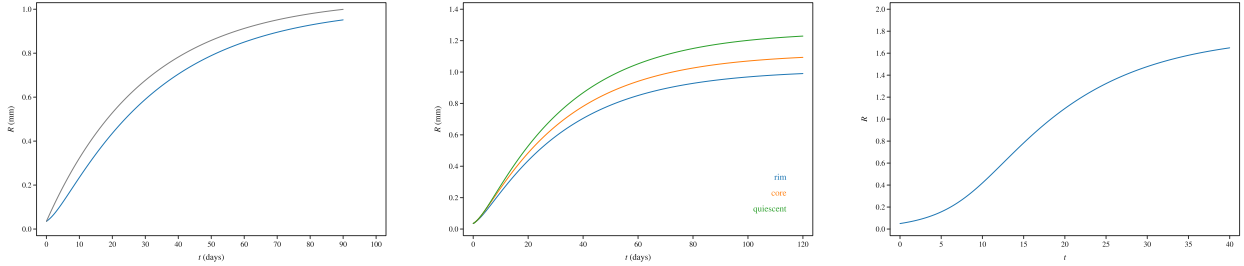
At constant density the tumour volume changes only by the growth inside it, (4.11)–(4.12):

```
radius(model=(exponential, rim), G=1, Delta=0.1, delta=0.035, R0=0.035, t=0..10)
radius(model=rim, G=1, Delta=0.1, delta=0.035, R0=0.035, t=0..90, approx=true)
```

`model=rim` is (4.14): growth $\bar{G}$ in an outer rim of thickness δ , death $\bar{\Delta}$ everywhere. Lengths in mm, time in days. The console gives the steady radius (4.15), $R_\infty = 1.014$ mm (so a 1 mm spheroid has a rim of about $35 \mu\text{m}$), and the thin-rim estimate $3\bar{G}\delta/\bar{\Delta}$ of (4.16). `approx=true` adds the thin-rim solution in grey; it gives the growth factors 7, 12, 19, 26, 29 after one week, two weeks, one, two and three months that the book quotes, while the full equation (4.14) grows more slowly at first, because R is not yet much larger than δ .

```
radius(model=(rim, core, quiescent), G=1, Delta=0.1, delta=0.035, deltaq=0.05, R0=0.035,
t=0..120)
radius(G=g*sigma - Delta, g=1, Delta=0.3, d=0.2, R0=0.05, t=0..40)
```

The models of Exercise 4.2: `core` (death only in the core), `twodeath` (`Drim`, `Dcore`), `quiescent` (a layer of thickness `deltaq` that neither grows nor dies). `G`= takes any growth term in r , R and `sigma`, the nutrient with diffusion length `d` fed at the surface (Exercise 4.3); `dim=1`, 2 gives the slab and the cylinder (Exercise 4.1).



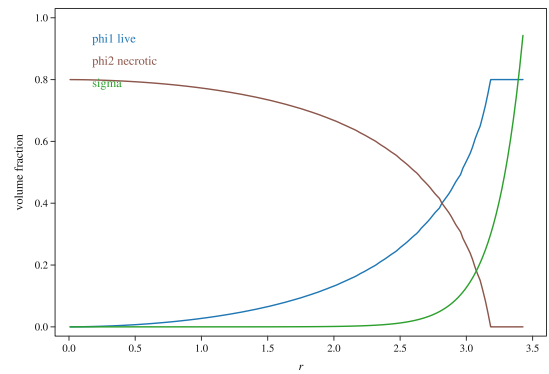
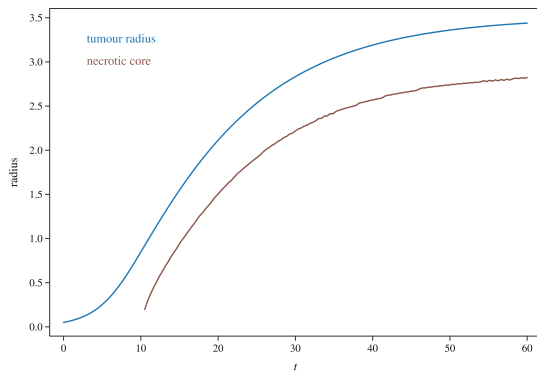
4.4 Constant density in 3D and the potential flow assumption

In 3D, (4.20) is a Poisson problem on a moving domain; the book develops it in Chapter 7, and the module will follow it there. In radial symmetry it reduces to (4.11) (Exercise 4.5), which is what `radius` solves.

4.5–4.8 Multicellular aggregates and mixtures

```
mixture(g=1, Delta=0.5, sigman=0.3, mu=0.3, d=0.2, phibar=0.8, R0=0.05, t=0..60)
mixture(t=0..60, profile=true)
```

Live cells ϕ_1 and necrotic matter ϕ_2 fill a constant fraction $\phi_1 + \phi_2 = \bar{\phi}$ (4.30) and move with one velocity: the constrained mixture (4.32), with $\nabla \cdot v = (G_1 + G_2)/\bar{\phi}$ (4.34). Live cells grow at rate $g\sigma$ and die at rate Δ where $\sigma < \sigma_n$; necrotic matter turns into liquid that leaves at rate μ , so the mixture is open and unsaturated in the sense of Sect. 4.8. The model is solved on shells that move with the cells. The tumour stops growing when proliferation in the rim balances the loss of necrotic matter in the core: the balance (4.13), found here without assuming a rim thickness.



Exercises of Chapter 4

-
- 4.1 `radius(model=exponential, dim=1|2|3, ...)`: $R_0 e^{Gt/d}$; the capillary cord is a $G=$ formula with growth only for $r > R_c$.
 - 4.2 `radius(model=(rim, core, twodeath, quiescent), ...)`: compare the steady radii in the console with yours.
 - 4.3 `radius(G=g*sigma - Delta, d=..., dim=1|2|3)`: the nutrient is (3.14)-like in a slab, I_0 in a cylinder, (3.19) in a sphere.
 - 4.4 `radius(G=gam/(1+alpha*beta) ...)` once you have the inhibitor profile $\beta(r)$ as a formula in r and R .
 - 4.5 Nothing to draw: integrate (4.25) over the ball.
-

Chapter 5: Modelling the Growth of Non-Necrotic Solid Tumours

Chapters 5 and 6 couple the nutrient and the inhibitor of Chapter 3 to the radius equation of Chapter 4. Diffusion is fast, so the module uses the quasi-steady profiles (the limit $\varepsilon \rightarrow 0$ of (5.21)–(5.22)) and integrates the radius equation.

5.3–5.4 The model and its simulations

```
nonnecrotic(sigmat=0.8, R0=(0.5, 2, 6), t=0..10)      R(t) from three sizes
nonnecrotic(sigmat=0.8, show=profile, R=3)           nutrient inside the tumour
nonnecrotic(sigmat=0.6, gamma1=1, betat=0.95, R0=(0.3, 1, 4))  with an inhibitor
```

Parameters keep the book's names: **Gamma** (vascular supply), **lam** (uptake), **sigmaB**, **sigmaR**, **gamma1** (nutrient lost to the inhibitor), **gamma2**, **D2**, **betaR**, **sigmat** ($\tilde{\sigma}$) and **betat** ($\tilde{\beta}$; leave it out for no direct action). **law=** chooses the proliferation rate: **linear** (5.20), **logistic** (5.17) with **sigmahat**, **logistic-inhibited** (5.18), **logistic-saturated** (5.19). The console lists the steady radii with their stability and, without inhibitor, the parameter Λ of (5.32) and the radius from (5.31).

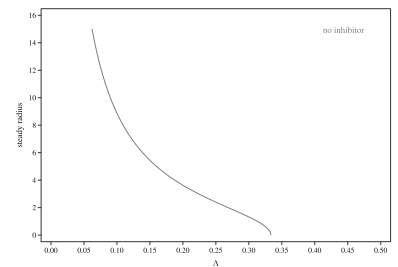
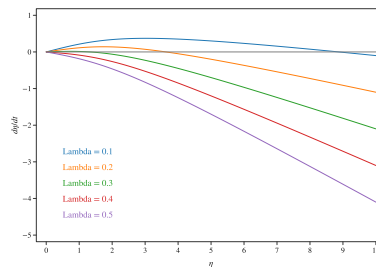
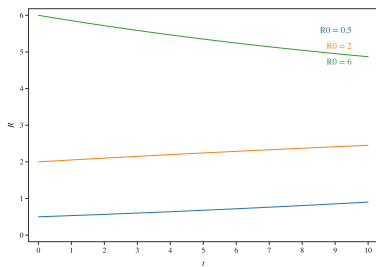
The text does not give every parameter behind Figs. 5.1–5.3 and Tables 5.1–5.2 (for example γ_2 , D_2 and β_R), and with the values in the caption of Fig. 5.1 one gets $\Lambda = 0$, for which (5.51) predicts unbounded growth; the examples use $\tilde{\sigma} = 0.8$ ($\Lambda = 1/6$) instead. Chapter 6 below reproduces the book's tables exactly.

5.5–5.6 Steady states and their stability

In the book's Λ form ($\Gamma = 0$, lengths in units of $1/\sqrt{\lambda}$, $\eta = \sqrt{\lambda}R$):

```
nonnecrotic(show=phase, Lam=(0.1, 0.2, 0.3, 0.4, 0.5))  (5.51), Fig. 5.7
nonnecrotic(show=steady)                                (5.31), Figs. 5.4 and 5.8
nonnecrotic(show=steady, L1=1, L2=(0.5, 1.1), phi=1.4)  (5.40), Fig. 5.5
nonnecrotic(show=steady, vary=L1, L0=0.1, L2=1.1, phi=1.4)  Fig. 5.6
```

The steady-state equation is linear in Λ_0 (and in Λ_1), so the module draws each branch exactly, parametrised by η , and marks it stable (solid) or unstable (dashed) from the sign of $d\eta/dt$ in (5.52), which it evaluates by quadrature. With $\Lambda_2 = 1.1$ a second, unstable branch appears: tumours smaller than it disappear, as Sect. 5.6 explains; near $\eta = 0$ the rate is $(1 - 3\Lambda_0)(1 - \Lambda_2)\eta/3$.



Exercises of Chapter 5

-
- | | |
|---------|---|
| 5.1 | Nondimensionalisation: the command's parameters are the dimensionless ones of (5.21)–(5.23). |
| 5.2 | <code>nonnecrotic(show=phase, Lam=(0.3, 1/3, 0.34))</code> : the non-trivial root disappears at $\Lambda = 1/3$. |
| 5.3–5.4 | <code>nonnecrotic(show=profile, ...)</code> draws (5.30) and (5.35)–(5.36); compare with your formulas, and <code>nonnecrotic(show=steady, L1=..., L2=..., phi=...)</code> with (5.40). |
| 5.5 | The vascular dual-action model: <code>nonnecrotic(Gamma=1, gamma1=..., betat=..., ...)</code> gives its steady radii and their stability in the console. |
-

Chapter 6: Modelling the Growth of Necrotic Solid Tumours

6.2–6.3 Necrotic tumour growth

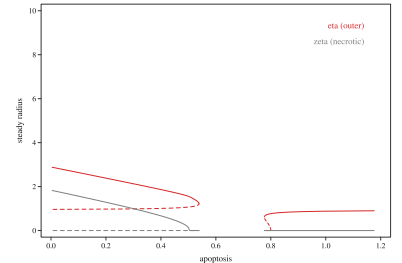
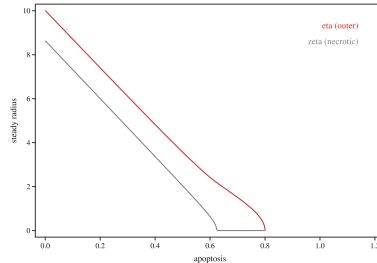
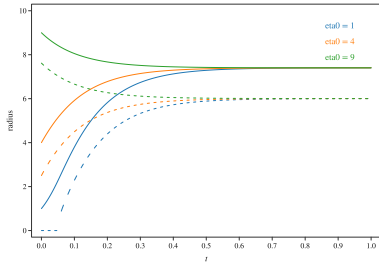
<code>necrotic(sigmat=0.2, eta0=(1, 4, 9), t=0..1, s=100)</code>	Fig. 6.1
<code>necrotic(sigmat=0.2, gamma1=0.8, betat=0.9, eta0=(0.8, 1.2, 4), t=0..1, s=100)</code>	Fig. 6.3
<code>necrotic(show=profile, sigmat=0.2, eta=7.4, gamma1=0.8, betat=5)</code>	

Lengths are scaled as in (6.13): η is the outer radius, ζ the necrotic radius, found where $\sigma = \sigma_{\text{nec}}$ (6.4). The module follows (6.1)–(6.3) with $N = 3s\lambda$ as in Exercise 6.1, which gives the steady equations (6.24)–(6.25). With these it reproduces every entry of Tables 6.1–6.3 (for example $\eta_{\infty} = 7.40$, $\zeta_{\infty} = 6.00$ without inhibitor and $\tilde{\sigma} = 0.2$; 2.38, 1.29 and 0 with $\gamma_1 = 0.8$, $\tilde{\beta} = 0.9$) and the threshold sizes of Fig. 6.3 ($\eta(0) \approx 0.98$) and of Table 6.2 (1.20). The values quoted with Fig. 6.1a (2.42, 0.63) correspond to a larger rate of necrotic loss ($\lambda \approx 2$ in this scaling).

6.4 Steady states

<code>necrotic(show=steady)</code>	Fig. 6.4
<code>necrotic(show=steady, gamma1=0.8, betat=5)</code>	Fig. 6.5
<code>necrotic(show=steady, gamma1=0.8, betat=0.9)</code>	Fig. 6.6
<code>necrotic(show=steady, gamma1=0.8, betat=0.5)</code>	Fig. 6.7

η (red) and ζ (grey) against $\tilde{\sigma}$; solid stable, dashed unstable. As in the book, without inhibitor no tumour survives for $\tilde{\sigma} > \sigma_{\infty}$; a strong direct inhibitor creates tumours there and removes them for $\tilde{\sigma} < 0.6$. For a thin proliferating rim the console gives Greenspan's estimate (6.31).



Exercises of Chapter 6

-
- | | |
|-----|---|
| 6.1 | Constant uptake: <code>oxygen(geometry=sphere, ...)</code> (Chapter 3) draws the nutrient profile of part (ii); compare your radius equation with <code>radius(G=...)</code> . |
| 6.2 | Linear uptake: this is the model of <code>necrotic</code> ; the console's steady states solve (6.24)–(6.25), the steady form of part (iv). <code>law=logistic, sigmahat=0.64</code> gives the logistic rate (6.15) of Fig. 6.2. |
-

Chapter 7: Chemo-Mechanical Models of Avascular Solid Tumours

7.2 Greenspan's chemo-mechanical model

```
greenspan(Si=0.5, lam=1, mu=1, sigmainf=1, T=0.05, R0=(0.5, 4), t=0..15) (7.23)-(7.24)
greenspan(Si=0.5, lam=1, mu=1, sigmainf=1, T=0.05, show=modes) (7.41)
greenspan(Si=0.5, T=0.02, show=solid, mode=(4, 2), R0=1, t=0..9) Fig. 7.3, in 3
D
greenspan(Si=0.5, T=0.02, show=solid, mode=((4, 2), (6, 3)), R0=1, t=0..9) Fig. 7.4
```

The radius follows (7.23) to the steady size (7.24). The console lists, for each Legendre mode $n = 2, \dots, 6$, the critical radius above which that shape perturbation grows ($f_n(R) = 0$ in (7.41)) and whether it grows at R_∞ ; larger surface tension T raises the critical radii. **show=solid** integrates (7.23) and (7.40) together from a small perturbation (**eps0**) and draws the tumour $r = R(1 + C_n Y_n^m)$ in 3D, coloured by the deformation; turn it with the mouse. As a check, $-f_0(R)$ equals dR/dR from (7.23), which the tests verify.

7.3 A generalised chemo-mechanical model

```
chemomech(sigmainf=1, sigmat=0.6, lam0=0.5, alpha=0.2, R0=(1.2, 4), t=0..40) (7.61)
chemomech(show=steady, vary=sigmainf, alpha=0.2) Fig. 7.5a
chemomech(show=steady, vary=alpha, sigmainf=1) Fig. 7.5b
chemomech(show=profile, R=4, sigmaN=0.05)
```

The nutrient satisfies the Gibbs–Thomson condition $\sigma = \sigma_\infty - 2\alpha/R$ on the surface; cells are quiescent where $\sigma < \sigma_Q$ and necrotic where $\sigma < \sigma_N$ (give **sigmaN** to allow necrosis), with the inhibitors of (7.57) (**lam1, lam2, betainf, lam3, lam4**). The module solves the radial problem exactly at each radius (piecewise polynomials) and integrates (7.56). With the values of Fig. 7.5 it finds no steady state for $\sigma_\infty < 0.93$ and two above, the upper one stable, and $\alpha_{\max} = \sqrt{5}(\sigma_\infty - \tilde{\sigma})^3/(9\lambda_0)$. The point Q, where the upper branch acquires a quiescent core, comes out at $\sigma_\infty = 1.06$ (Fig. 7.5a, $\alpha = 0.2$) and $\alpha = 0.10$ (Fig. 7.5b); the caption places it at 1.00 and 0.20, so compare with your own calculation from (7.60).

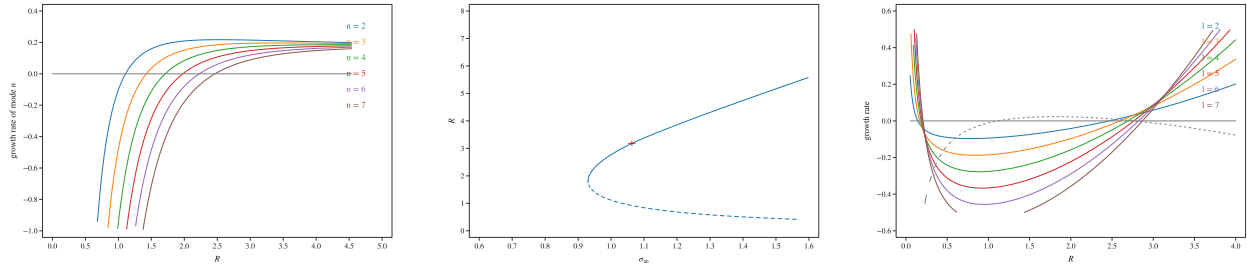
7.4 Asymmetric growth

```
chemomech(show=modes, alpha=0.2) Fig. 7.6: (7.88) for  $l = 2..7$ 
chemomech(show=unstable) Fig. 7.7
chemomech(show=solid, alpha=0.05, R=3.3) a tumour perturbed by its fastest mode,
in 3D
```

The growth rate of the mode Y_{lm} used here, derived again for this companion, is

$$\frac{1}{s\rho_{lm}} \frac{d\rho_{lm}}{dt} = -\frac{l-1}{3} \left[(\sigma_\infty - \tilde{\sigma}) - \frac{l}{2l+3} \frac{\alpha}{R} - \frac{2l+9}{15(2l+3)} \lambda_0 R^2 \right],$$

which vanishes for $l = 1$ and reduces to (7.89) at a steady state. For the parameters of Fig. 7.6 the console finds the stable steady state unstable to $l = 2, \dots, 5$, as in the book. **show=unstable** follows the upper branch as α grows: the largest unstable mode and the fastest mode (7.90) fall, and every mode decays from $\alpha \approx 0.245$ (the book quotes 0.27, close to $\alpha_{\max} = 0.267$).



Exercises of Chapter 7

-
- | | |
|-----|--|
| 7.1 | The 2D Petri dish: <code>nutrient(geometry=disc, ...)</code> (Chapter 3) for the nutrient; compare your R_∞ with <code>greenspan</code> as a 3D check. |
| 7.2 | Greenspan with a necrotic core: <code>chemomech(sigmaN=..., lam3=..., ...)</code> has the same structure; compare R_N . |
| 7.3 | <code>radius(G=B*sigma - A, B=1, A=0.3, d=1, R0=0.5, t=0..20)</code> (Chapter 4) solves the radius equation of part (ii); the potential does not enter, as the exercise asks you to explain. |
| 7.4 | <code>greenspan(show=modes)</code> : check your f_n against the curves. |
| 7.5 | This is <code>chemomech</code> with $2\alpha = 2\gamma c_\infty$ and $\tilde{\sigma} = \tilde{c}$. |
-

Chapter 8: Models for the Immune Response to Cancer

8.3 A basic model: critical size

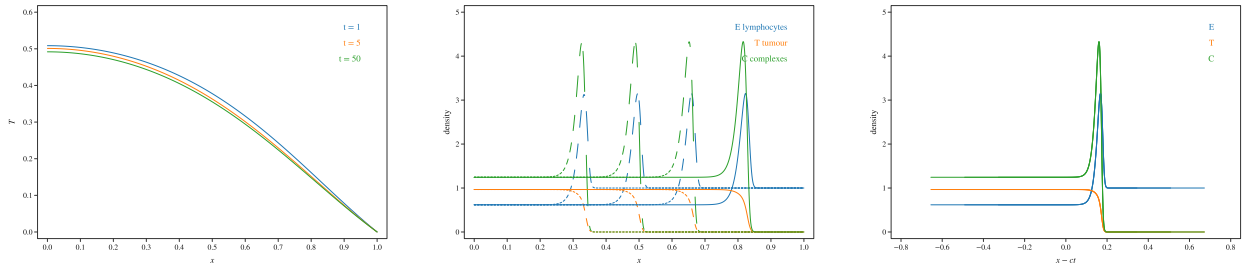
```
immunebasic(a=0.5, b=1.5, d=0.04, t=(1, 5, 50))      tumour persists:  $L > L_c$ 
immunebasic(a=0.5, b=1.5, d=1, t=(0.1, 0.5, 2))      immune response wins:  $L < L_c$ 
immunebasic(a=0.25, b=0.5, d=0.02, t=(1, 10, 100))     $b < 1$ : two tumour states
```

This is (8.18) with the Michaelis–Menten kill term (8.16). The console lists the homogeneous states (8.23)–(8.25) and their stability, and compares d with $d_c = f'(0)/\pi^2$ (8.32): the tumour-free state is stable exactly when the tumour region is smaller than L_c (8.34)–(8.35), and $L/L_c = \sqrt{d_c/d}$. The tests confirm with the PDE that the tumour persists just above L_c and disappears just below. `geometry=slab, kill=linear` is the melanoma model of Exercise 8.3, with critical thickness $\frac{\pi}{2}\sqrt{D/(r-E)}$.

8.4 Lymphocytes against tumour cells

```
immune(t=(2e-4, 4e-4, 6e-4, 8e-4))                  Figs. 8.12–8.14
immune(show=collapse, t=(4e-4, 6e-4, 8e-4))          the same profiles against  $z = x - ct$ 
immune(show=kinetics, t=0..0.01)                     (8.57)–(8.59) in 3D
```

The defaults are the values of Table 8.1 ($p = 0.99$). The complexes relax in $1/\psi \approx 3 \times 10^{-8}$, so the spatial model takes them in quasi-steady state. The console lists the four steady states of the kinetics with their eigenvalues: the healthy state $(1, 0, 0)$ is a saddle, the invaded state $(0.62, 0.97, 1.24)$ (the x_0 of (8.69)) is stable, and a dormant state near $(18, 0.02, 0.77)$ is an unstable focus (the dormancy values quoted in Sect. 8.4.1 are for $p = 0.9997$, whose full parameter set is in Matzavinos et al. (2004b)). The tumour invades as a travelling wave; the measured front speed is about 815, close to the minimal speed $2\sqrt{\omega(\beta_1 - \kappa)} = 825$ with $\kappa = \phi - \lambda\mu/\psi$ (the book estimates $c \approx 850$ from its simulations). The kinetics are stiff, and the module integrates them with a Rosenbrock method: from near the dormant state the trajectory spirals out to the invaded state.



Exercises of Chapter 8

-
- 8.1 `immunebasic(a=..., b=...)`: the console's steady states and $f'(T)$.
 - 8.2 The six cases: `immunebasic(a=0.5, b=1.5, d=0.04)`, `(..., d=1)`, `(a=0.25, b=0.5, d=0.02)`, `(..., d=1)`, `(a=0.53, b=0.5, d=0.02)`, `(..., d=0.0001)`; L/L_c is in the console.
 - 8.3 `immunebasic(geometry=slab, kill=linear, a=E/r, d=D/(r H^2))`.
 - 8.4–ODE systems: the core command `ode(F=(...), start=(...), t=...)` draws their trajectories; compare with your steady states.
 - 8.7, 8.9
 - 8.8 The QSSA (8.15) is what `immunebasic` uses.
 - 8.10 A chemotaxis-driven instability; `turing(show=modes, f=..., g=...)` (Chapter 9) draws the analogous dispersion relation for reaction-diffusion kinetics.
-

Chapter 9: Reaction-Diffusion Pre-pattern Theory

9.3 Turing pre-patterns on a sphere

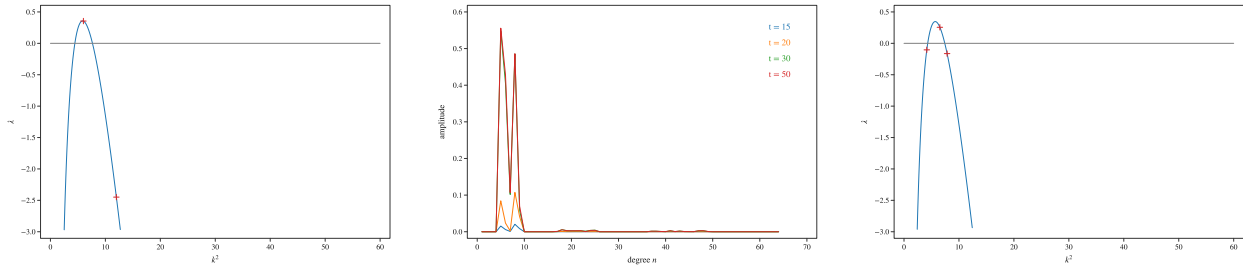
<code>turing(d=18, k2=6)</code>	analysis, (9.6)–(9.17)
<code>turing(d=18, k2=6, show=sphere, N=8, t=50)</code>	Fig. 9.2, in 3D
<code>turing(d=18, k2=20, show=sphere, N=8, t=30)</code>	Fig. 9.3
<code>turing(d=18, k2=6, show=spectrum, N=8, t=(15, 20, 30, 50))</code>	Fig. 9.1

The default kinetics are Schnakenberg's (9.10) with $a = 0.2$, $b = 1$; any $\mathbf{f} =$ and $\mathbf{g} =$ in u, v may be given instead. The console checks (9.6), gives $d_c = 17.0056$ (9.16) and the unstable band (9.7), and $k2 =$ chooses $\gamma = \gamma_c$ (9.17) so that a single degree n grows. `show=sphere` solves (9.10) by a spectral method of lines in real spherical harmonics of degree $< N$ (Galerkin coefficients from Gauss–Legendre quadrature, diffusion implicit), from a random perturbation of size 10^{-4} , and draws u on the sphere in 3D. As in Numerical Experiment 1, the $n = 2$ coefficients start to grow near $t = 15$, are large at $t = 20$ and settle by $t = 50$.

9.4–9.5 Tumour surfaces, growing tumours

<code>turing(d=25, gamma=100, show=sphere, N=12, t=40, eps=0.5)</code>	Figs. 9.6 and 9.8
<code>turing(d=100, gamma=5, grow=0.1, show=sphere, N=12, t=21)</code>	(9.28), Fig. 9.10
<code>turing(d=18, gamma=20, show=modes, domain=disc, radius=1.5)</code>	Exercises 9.1–9.3

`eps =` pushes the surface out where the activator is high, giving the columns of invading cells of Fig. 9.8. `grow =` solves on a sphere of radius $R(t) = 1 + \alpha t$: the band (9.29) moves to higher wavenumbers and higher modes appear as the tumour grows. `show=modes` draws the dispersion relation with the modes of a sphere, a line, a rectangle or a disc marked.



Exercises of Chapter 9

-
- | | | |
|---------|---|---|
| 9.1 | <code>turing(show=modes, domain=rectangle, width=..., height=...):</code> | the modes $\cos(m\pi x/a) \cos(n\pi y/b)$ with $k^2 = \pi^2(m^2/a^2 + n^2/b^2)$. |
| 9.2 | <code>domain=discsym, radius=a:</code> | $J_0(kr)$ with $J'_0(ka) = 0$. |
| 9.3 | <code>domain=disc, radius=a:</code> | $J_n(kr) \cos n\theta$ with $J'_n(ka) = 0$. |
| 9.4–9.7 | Annuli, Robin balls and spheroids are not built in; the dispersion curve of <code>show=modes</code> still tells which k^2 grow once you have the eigenvalues. | |
-

Chapter 10: Mathematical Modelling of Tumour-Induced Angiogenesis

10.3–10.5 Endothelial cells and VEGF in one dimension

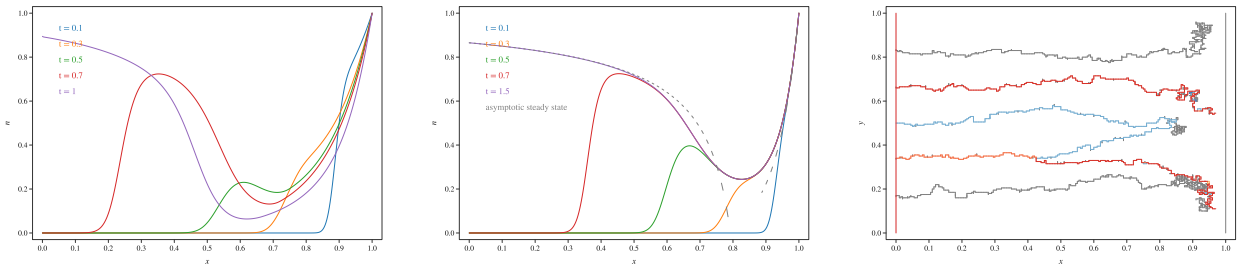
```
angiogenesis(t=(0.1, 0.3, 0.5, 0.7, 1))          Fig. 10.1b
angiogenesis(t=(0.1, 0.3, 0.5, 0.7, 1), show=c)   Fig. 10.1a
angiogenesis(t=(0.6, 0.7, 0.8, 1), remove=0.6)    Fig. 10.2
angiogenesis(model=caricature, t=(0.1, 0.3, 0.5, 0.7, 1.5), steady=true)  Figs.
10.3–10.4
```

The tumour is at $x = 0$ and the parent vessel at $x = 1$, as in (10.14)–(10.18), with the parameters of Fig. 10.1 as defaults. VEGF is solved implicitly, the cells with an upwind scheme for chemotaxis. The sprout tips first reach the tumour between $t = 0.7$ and 0.8 (the book: about 0.7 , some 11 days), with the brush border of high density behind the tips. `model=caricature` is (10.23); `steady=true` adds the matched asymptotic steady state, the outer solution (10.32) for $x < \hat{x} = 1 - \beta/\mu$ and the boundary layer (10.45) near $x = 1$ (dashed), which, as in Fig. 10.4, fits well except near $\hat{x}$. The console gives $\hat{x}$ and the minimal speed $\kappa + 2\sqrt{D(\mu - \beta)}$ of Exercise 10.3.

10.6–10.8 Haptotaxis, a hybrid model, blood flow

```
sprouts(seed=1)          Fig. 10.7: a capillary network
sprouts(seed=3, flow=true) blood flow through it, (10.50)–(10.51)
sprouts(seed=2, branching=false) sprouts that never branch
```

Each endothelial tip cell moves on a 200×200 grid with the probabilities $P_0, \dots, P_4$ of the finite-difference scheme (10.49) for (10.48): it climbs the VEGF gradient (chemotaxis $\chi/(1 + \alpha c)$) and the fibronectin gradient (haptotaxis ρ). Tips leave vessels behind, take up VEGF and make fibronectin; old tips branch more often where VEGF is high; a tip that meets another vessel fuses with it. The parameter values are illustrative (`help(sprouts)` lists them); every `seed` gives a different network. `flow=true` then computes the flow: Poiseuille's law (10.50) in each vessel, conservation of mass at every junction (10.51), pressure 1 on the parent vessel and 0 at the tumour, and colours the vessels from blue (little flow) to red (most), grey where no blood moves (dead ends).



Exercises of Chapter 10

10.1	Plot your steady state $n_0(1 - m\alpha\chi x/D_0)^{1/m}$ with the core <code>plot</code> command for several m .
10.2–	Lower and upper bounds: <code>angiogenesis(model=caricature, mu=0, ...)</code> removes proliferation (the lower bound of 10.2); the console's minimal speed is 10.3(iv).
10.3	
10.4	<code>angiogenesis(model=caricature, D=1e-6)</code> : almost no diffusion, the method of characteristics.
10.5–	<code>angiogenesis(model=caricature, steady=true)</code> : compare your bounds and inner solutions with the curves.
10.6	
10.7–	Other chemotaxis models: the core <code>ode</code> command, or <code>angiogenesis</code> with your parameters as a first check.
10.8	
10.9–	Random walks: <code>sprouts(branching=false)</code> is exactly such a biased walk.
10.11	

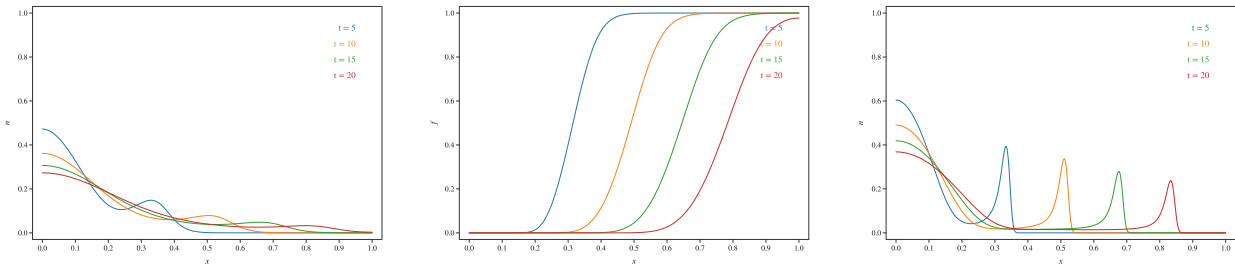
Chapter 11: Models of Cancer Invasion and Metastasis

11.2–11.3 Haptotaxis: continuum and individual cells

<code>invasion(t=(5, 10, 15, 20))</code>	Fig. 11.1, cells n
<code>invasion(t=(5, 10, 15, 20), show=f)</code>	Fig. 11.1, the matrix f
<code>invasion(t=(5, 10, 15, 20), chemokinesis=true)</code>	Fig. 11.2, (11.17)
<code>invasion(dim=2, t=10)</code>	Figs. 11.3–11.4, in 3D
<code>cells(t=(1, 2, 4))</code>	Fig. 11.5

`invasion` solves the model of Anderson et al. (11.5) with the parameters of Fig. 11.1 ($d_n = d_m = 0.001$, $\gamma = 0.005$, $\eta = 10$, $\alpha = 0.1$, $\beta = 0$) and the initial data (11.8), by finite volumes with upwind haptotaxis; the matrix is integrated exactly in each step. A small cluster of cells breaks away from the main mass and invades the matrix it has degraded; the console follows the farthest cluster (at $x \approx 0.33, 0.51, 0.66, 0.80$ for $t = 5, \dots, 20$). With chemokinesis ($D = d_n m$) the cluster is sharper and travels as a narrow pulse, as in Fig. 11.2. `mu=` adds logistic growth. In 2D the matrix is a random pattern of dense and sparse patches (`seed=` draws another; the book's Fig. 11.3 is one such pattern, not reproduced exactly) and the cells are drawn as a surface over the square.

`cells` is the discrete version (11.18): each of 500 cells moves to a neighbour with the probabilities $P_0, \dots, P_4$ of the finite-difference scheme, at most one cell per site, and divides after 500 time steps when a neighbour is free. The matrix is drawn in grey under the cells, one panel per time; the console counts the cells that have detached from the main mass. As in Fig. 11.5 single cells move deep into the tissue.

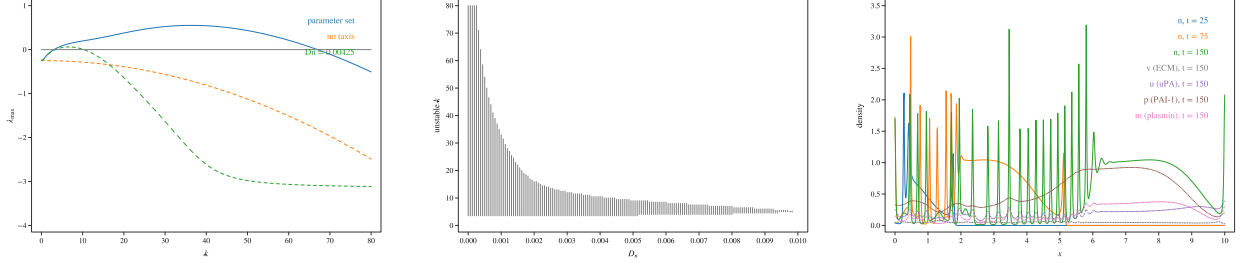


11.4 The uPA system

<code>upa(show=dispersion)</code>	Fig. 11.7
<code>upa(show=region, vary=Dn)</code>	Fig. 11.8 (also <code>vary=mu1</code> , <code>vary=phi53</code>)
<code>upa(t=(25, 75, 150))</code>	Fig. 11.9
<code>upa(show=spacetime, t=200)</code>	Fig. 11.10
<code>upa(show=spacetime, t=200, Dn=0.014)</code>	Fig. 11.12a: a travelling wave
<code>upa(t=(20, 75, 150), volume=true)</code>	(11.28), Fig. 11.13
<code>upa(show=square, t=100)</code>	Fig. 11.15, in 3D
<code>upa(t=(50, 60, 100, 150), progression=true)</code>	(11.29)–(11.30), Fig. 11.16

The defaults are parameter set $\mathcal{P}$. The console first finds the uniform steady state (11.24), $(n, v, u, p, m) = (1, 0.0472, 0.2224, 0.8892, 0.3428)$, and the eigenvalues of the kinetic Jacobian (11.25): the largest real part is -0.244 , so without movement the state is stable. With diffusion and taxis, $\lambda_{\max}(\hat{k})$, the largest real part of the eigenvalues of $J_R - \hat{k}^2 J_T$ (11.27), is positive for $3.3 \leq \hat{k} \leq 66.8$; without taxis (`taxis=false`) it is negative for every $\hat{k}$, so the instability is taxis-driven. With $D_n = 0.00425$ the band is narrow and peaks near $\hat{k} \approx 6.3$, which the book links to the regular peaks of Fig. 11.12b; with $D_n = 0.014$ every mode is stable and the solution is a travelling wave. `show=region` shades the unstable $\hat{k}$ as one parameter varies.

The simulations use the method of lines on $(0, 10)$ with 800 intervals, upwind taxis, and the initial data (11.20)–(11.23). The cells form clusters that emerge and merge; the front is near $x = 5$ at $t = 75$ and the cells have invaded the whole domain by $t = 150$, as in the book. Volume filling slows the invasion (the front is near 3.1 at $t = 75$). In the progression model the aggressive population appears after $t = 50$ where the matrix is dense and makes up 84% of the cells by $t = 150$. In 2D the clusters are only a few grid cells wide, because the band of unstable modes reaches wavelengths of about 0.1; N refines the grid.

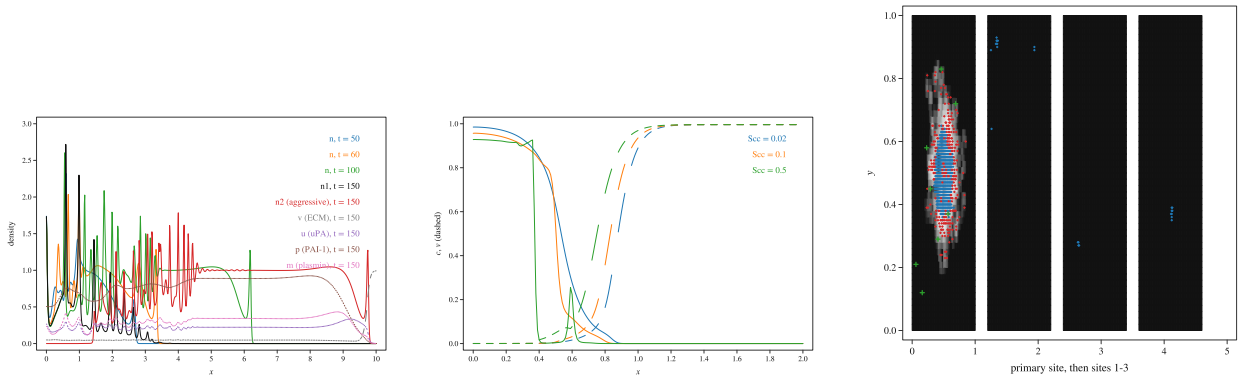


11.5–11.6 Adhesion and metastatic spread

<code>adhesion(Scc=(0.02, 0.1, 0.5), t=50)</code>	Fig. 11.19a
<code>adhesion(Scc=5, mu2=0.1, t=(10, 50, 100))</code>	Fig. 11.19b
<code>metastasis()</code>	Sect. 11.6
<code>metastasis(survive=0.6, vessels=12, seed=2)</code>	

`adhesion` solves (11.31) in 1D with the non-local adhesion velocity (11.32): the difference between $g = (S_{cc}c + S_{cv}v)(1 - c - v)_+$ (11.34) to the right and to the left of each point, weighted by the kernel Ω_1 or Ω_2 (11.35)–(11.36) over the sensing radius R . The book does not give its parameter values, so the defaults are illustrative; the result is the same as in Fig. 11.19a, stronger cell-cell adhesion holds the cells back.

`metastasis` is a compact version of the multi-grid framework of Franssen et al.: a primary grid and three secondary grids. Epithelial-like and mesenchymal-like cells move with the probabilities of (11.41)–(11.42); the mesenchymal-like cells degrade the matrix on contact and secrete MMP-2 (11.39)–(11.40); epithelial-like cells divide faster but can only move into degraded matrix. Cells on a vessel entry point intravasate, circulate, survive with probability `survive`, and extravasate on a secondary grid with the probabilities `extravasate`, where they grow. It shows the cascade of Fig. 11.22, not the calibrated model of the paper.



Exercises of Chapter 11

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- | | |
|------------------------|---|
| 11.1 | Gatenby's competition model: the core <code>ode</code> command with <code>F=(u1*(1-u1-a12*u2), rho*u2*(1-u2-a21*u1))</code> ; try $a_{12}, a_{21} < 1$ and > 1 . |
| 11.2 | Degradation on contact: <code>invasion(mu=1, alpha=100, beta=100, eta=1)</code> makes $m \approx n$, so $f_t \approx -nf$; measure the speed of the front in the console. |
| 11.3–
11.4,
11.6 | Travelling-wave ODEs: draw your (N, N') phase planes with the core <code>ode</code> command. |
| 11.5 | Porous-medium diffusion is not built in. |
| 11.7 | <code>adhesion(Scc=..., Scv=..., kernel=1)</code> : compare with your linear analysis. |
| 11.8–
11.9 | Branching and velocity-jump random walks: <code>cells</code> is a lattice version of such processes. |
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How the results are checked

Chapter 2: the module's tests compare every closed-form solution of the chapter ((2.7), (2.11), (2.19), (2.20), (2.22), (2.30), (2.37), (2.39), (2.41), (2.48), (2.50)–(2.56), (2.59)–(2.67)) with an adaptive Runge–Kutta solver, the fastest-growth volumes with the values of Section 2.6, and the fits with an independent least-squares solver. Results agree to better than 10^{-6} . Chapters 3 and 4: every steady profile is checked against its differential equation and its boundary conditions by finite differences ((3.4), (3.8), (3.14), (3.19), (3.24)–(3.25), (3.26), (3.27), (3.29), (3.38), (3.50), Exercises 3.1, 3.3–3.6, 3.9, 3.11); the thin-layer limits (3.28) and (3.30); the numerical GIF solver against (3.38) and (3.50); the Bessel functions against reference values; the glioma solution (3.57) by its total cell number; the two-clone solution against its volumes (3.74)–(3.76) and (3.77); the book's numbers for Figs. 3.4, 3.8, 3.9, (4.15) and (4.16). Chapters 5 and 6: the profiles against their equations, the closed forms (5.31), (5.42), (5.51), (6.24)–(6.26) and the thin-rim limit (6.31); Tables 6.1–6.3 and the threshold sizes of Figs. 6.2 and 6.3 are reproduced. Chapter 7: (7.23)–(7.24), (7.61), (7.65)–(7.66) and the unstable modes $l = 2, \dots, 5$; the spherical harmonics are checked to be orthonormal. Chapter 8: the steady states and critical size (8.32)–(8.35), Exercise 8.3, the stiff solver against a reference solution, and the wave speed. Chapter 9: $d_c = 17.0056$ (9.16), the single growing mode, the spectral Laplacian on the sphere, the modes of discs and rectangles. Chapter 10: (10.21), the asymptotic steady state, conservation of flow at every junction of the network. Chapter 11: the uPA steady state (11.24) and its eigenvalues, the taxis-driven band of Fig. 11.7, conservation of cells in (11.5), and the invasion distances quoted in the book.

Where the module differs from the book

- Fig. 5.1 is drawn with $\tilde{\sigma} = 0.8$ (the caption's $\Lambda = 0$ gives unbounded growth); Tables 5.1 and 5.2 are not reproduced (their parameters are incomplete).
- Fig. 6.1a's values (2.42, 0.63) correspond to $\lambda \approx 2$ in this scaling.
- Chapter 7: the point Q of Fig. 7.5 is at $\sigma_\infty = 1.06$ ($\alpha = 0.10$) instead of 1.00 (0.20); all modes are stable from $\alpha \approx 0.245$ instead of 0.27.
- Chapter 8: the front moves at about 815 (the book: about 850; minimal speed 825).
- Chapter 9: on the growing sphere the excited modes are of lower degree than the book's.
- Chapter 10: the sprout tips reach the tumour at $t \approx 0.75$ (the book: about 0.7); the parameters of the hybrid model are illustrative.
- Chapter 11: the matrix of Fig. 11.3, the adhesion parameters of Fig. 11.19 and the metastasis framework are illustrative, not the published ones.