Some deterministic mathematical models in cancerology

D. Salort, LBCQ, Sorbonne Université

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Some deterministic model for heterogeneity in cancerology

Models without inclusion of space

- Modeling of concentration of few quantities linked the one with the other (Ordinary Differential Equation)
- Adding variables of phenotypic or genotypic heterogeneity inside a population (ODE, integro-differential equations or PDE)

Models with inclusion of space

- PDE models often of advection/diffusion type or Hele-Shaw type models
- Heterogeneity inside the tumor via dynamics of nutriments
- Models with heterogeneity spatial and phenotypic

Case of one population

Malthus model (1766-1834)

$$N'(t) = aN(t)$$

Verhulst model (1804-1849)

$$N'(t) = rN(t)\left(1 - \frac{N(t)}{K}\right), \qquad K \text{ is the capacity}$$

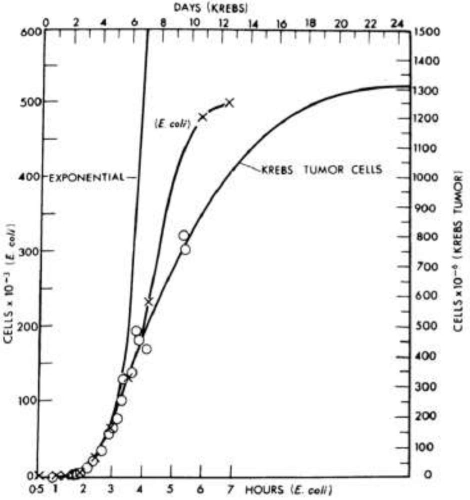
or by extension

$$N'(t) = rN(t)\left[1 - \left(\frac{N(t)}{K}\right)^{\alpha}\right]$$

Gompertz model (1779-1865).

$$N'(t) = rN(t)\ln\left(\frac{K}{N(t)}\right).$$

Gompertz model



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[1] source : Dynamic of tumor growth; Anna Kane Laird (1964).

Case of several populations

Useful to model

- Interaction between few different type of cells as quiescent and proliferative cells

$$P'(t) = F(P(t)) - bP(t) + cQ(t)$$

$$Q'(t) = bP(t) - cQ(t) - dQ(t).$$

- Introduction in the model of injections of drugs or medicine to eradicate cancer cells

$$P'(t) = F(P(t)) - (b + c_{stat})P(t) + cQ(t) - c_{tox}P(t)$$

$$Q'(t) = (b + c_{stat})P(t) - cQ(t) - dQ(t).$$

Problematic

Those models do not take into account hight heterogeneity of cells

Inclusion of heterogeneity in models

Basic model for one population

$$\partial_t n(t,y) = F(y,\rho(t))n(y,t) \quad \text{where} \quad \rho(t) := \int n(t,y)dy.$$

- The heterogeneity is modeled via a variable $y \in \mathbb{R}$, hence, we have a continuum of coupled equations.
- A typical example of F leads to

$$\partial_t n(t,y) = (a(y) - b(y)\rho(t))n(t,y).$$

Inclusion of heterogeneity in models

Adding of mutations

- In case of Brownian random mutations

$$\partial_t n(t,y) = F(y,\rho(t))n(y,t) + \epsilon \partial_{yy} n(t,y)$$

- We also can introduce kernels of mutations from one state to another

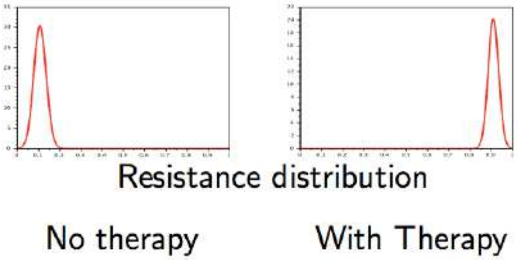
$$\partial_t n(t,y) = F(y,\rho(t))n(y,t) + \int K_1(z,y)n(t,z)dz - n(t,y)\int K_2(y,z)dz.$$

Inclusion of heterogeneity in models

Example of application in modeling

$$\partial_t n(t,y) = \left[\frac{r(y)}{1 + c_s(t)} - d(y)\rho(t) - c_T(t)\alpha(y) \right] n(t,y) + \epsilon \partial_{yy} n(t,y)$$

- y : phenotype in terms of reproduction ($y = 0$ high reproduction/low resistance, $y = 1$ low reproduction/high resistance)
- $$r' < 0, \quad \alpha' < 0, \quad d' < 0.$$

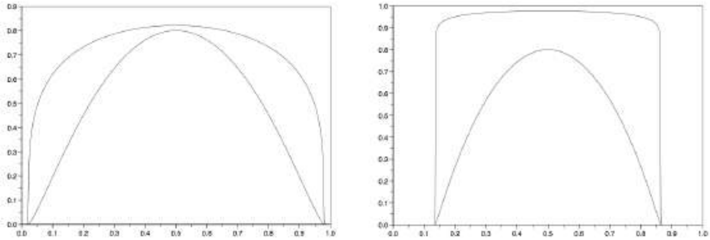


Typical model of cell density given a position

Quantities involved in the model

- $n(t,x)$: density of tumors cells at time t and position $x \in \mathbb{R}^d$
- $v(t,x)$: velocity of cells at time t and position x
- $p(t,x)$: pressure at time t and position x.

$$\partial_t n(t,x) + div(nv) = nG(p(t,x)).$$
$$v(t,x) = -\nabla p(t,x), \quad p(t,x) = n^\gamma, \quad \gamma > 1.$$



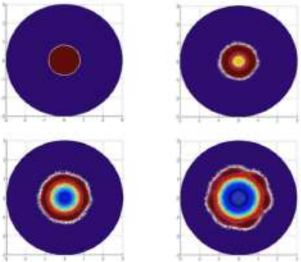
from B. Perthame

Typical model of cell density with inclusion of nutriments

Quantities involved in the model

- $n(t,x)$: density of tumors cells at time t and position $x \in \mathbb{R}^d$
- $v(t,x)$: velocity of cells at time t and position x
- $p(t,x)$: pressure at time t and position x.
- $c(t,x)$: concentration of nutriments at time t and position x

$$\partial_t n(t,x) + div(nv) = nG(p(t,x), c(t,x))$$
$$-\Delta c + \lambda c n = 0, \qquad \lim_{|x| \to +\infty} c(t,x) = c_b.$$



from B. Perthame, N. Vauchelet, M. Tang