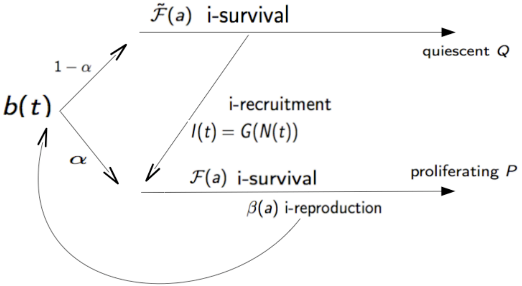
An age structured model describing transitions between quiescent and proliferating cell populations

Ph. Getto,
BCAM (Basque Center For Applied Mathematics)
www.bcamath.org
work in progress with:
S. Cuadrado-Gavilan (UAB Barcelona)
O. Diekmann (Utrecht University)

Quiescent and proliferating cell populations



age-dependent survival, "reproduction"

division $\longrightarrow$ decision about quiescence (idealization)

p-state variables (I, b)

$I(t) := G(N(t))$ i-recruitment rate,

$N(t) := P(t) + q_0 Q(t)$ weighted total population

$b(t) :=$ p-birthrate

References

cyclin $\longrightarrow$ indicator for division, e.g.

A. Goldbeter, Biochemical Oscillations And Cellular Rhythms, Cambridge University Press 1996.

$\Rightarrow$ cyclin-structured models, well-posedness, equilibria

F. Bekkal Brikci, J. Clairambault, B. Perthame, *Math. Comput. Model.* (2008)
F. Bekkal Brikci, J. Clairambault, B. Ribba , B. Perthame, *J. Math. Biol.* (2008).
R. Borges, A. Calsina, S. Cuadrado, submitted to *AIMS Journals*.

Here: stability of equilibria?
$\Rightarrow$ cyclin - structure $\longrightarrow$ age - structure: easier

AIMS: stability of p-equilibria, influences?:

$\longleftarrow$ weight of quiescent population,

$\longleftarrow$ age-structure

Population Equations

$$
\begin{aligned}
I(t) &= G\Big(\int_0^\infty b(t-a)\alpha\mathcal{F}(a)da + \int_0^\infty b(t-a)R_2(a, I_t)da \\
&\quad + q_0(1-\alpha)\int_0^\infty b(t-a)R_1(a, I_t)da\Big) \\
&\quad G(\text{not gone quiescent} + \text{recruited} + \text{weighted quiescent}) \\
&= i - \text{recruitment rate} \\
b(t) &= \int_0^\infty b(t-a)\alpha\beta(a)\mathcal{F}(a)da + (1-\alpha)\int_0^\infty b(t-a)Q(a, I_t)da \\
&\quad \text{not gone quiescent} + \text{recruited}
\end{aligned}
$$

Renewal Equations, closed, coupled, autonomous

$$(b(t), I(t)) = F(b_t, I_t),\ b_t(\theta) := b(t+\theta),\ \theta < 0$$

Tools for renewal equation:

$$\begin{aligned} x(t) &= F(x_t), \quad F : X \to \mathbb{R}^N, \quad x := (b, I) \\ x(0) &= \varphi. \end{aligned}$$

$X := L^1([-h, 0], \mathbb{R}^N)$
(Diekmann, G., Gyllenberg, *SIAM J. Math. Anal.* (2007))
$X := L^1([-\infty, 0], \mathbb{R}^N)$
(Diekmann, Gyllenberg, submitted to *J. Diff. Eq.*)

existence and uniqueness $\leftarrow$ F locally Lipschitz

linearized stability: equilibrium $\overline{x}$

$$\det(I - F'(\overline{x})e_z) = 0, \quad e_z(\theta) := e^{z\theta}, \quad \theta \in [-h, 0]$$

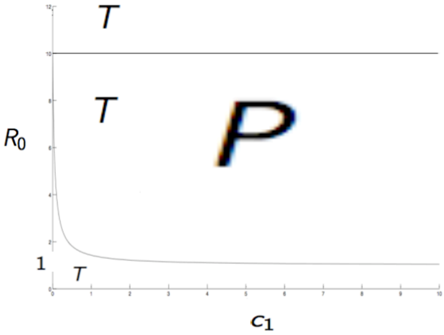
position of roots in $\mathbb{C}$ $\leftrightarrow$ stability of equilibrium

Equilibria

TWO parameters:

$c_1 := G(0)$ maximum recruitment rate,

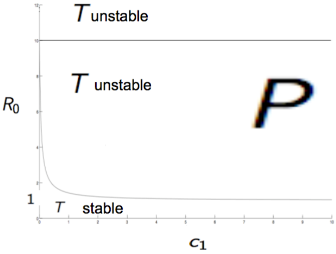
$R_0 := \int_0^\infty \beta(a)\mathcal{F}(a)da$ offspring number



trivial T, unique positive P in existence region

Stability results

linearized stability for trivial



To investigate positive, specify ingredients

$$\tilde{\mathcal{F}}(a) := e^{-\tilde{\mu}a}, \ \mathcal{F}(a) := e^{-\mu a}, \ \textit{exponential survival}$$

$$\beta(a)\mathcal{F}(a) := R_0\delta(a - a_A), \ \textit{ONE age of reproduction}$$

$$G(N) := c_1(1 - \frac{N}{c_2}), \ \textit{population decreases } i - \textit{recruitment}$$

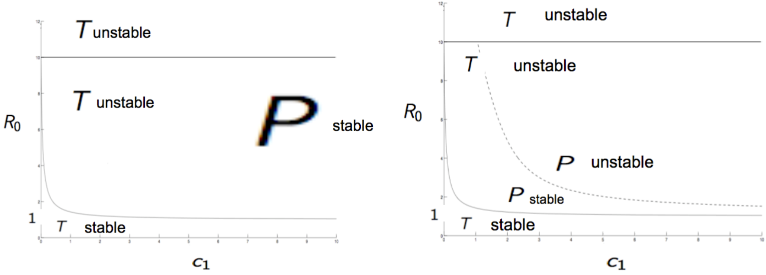


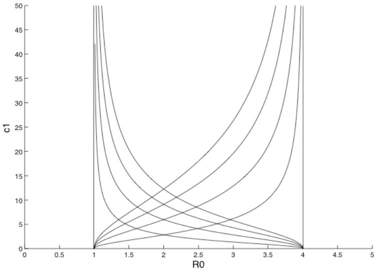
Figure: Stability for unstructured $q_0 < 1$ and $q_0 > 1$

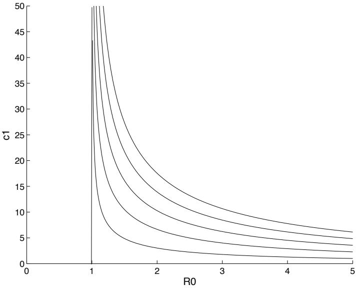
Conclusions:

- overlap of stability regions of structured and unstructured
- so far in structured model nowhere instability
- dependence on weight

differences between structured and unstructured model?

Additional specification $\tilde{\mu} = 0$, low mortality in quiescence





Trivial equilibrium:

Hopf-bifurcation curves where pairs cross

quantification of instability of trivial

$\longrightarrow$ difference with unstructured model