Linearization Methods in the Control of PDMP Associated to Gene Networks

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Outline

- PDMP and Gene Networks
- Asymptotic Stability
- Uniform Abel-Tauber Results

[1] G, Serea (*Appl. Math. Opt. '12)*, G (*ESAIM: COCV '12*), G, Serea (*preprint '13), Buckdahn, G, Quincampoix* (*Appl. Math. Opt. '14)*

Previous Results

- **Stochastic gene networks** :
  (Delbruck '40), Cook et al. '98, Hasty et al. '00, Crudu, Debussche, Radulescu '09, '12, etc.
- **PDMP** :
  Davis '84, '86, '93, Soner '86, Costa '89, Dempster, Ye '96, Costa, Dufour, '08-'13, Wainrib, Thieullen '10, Genadot, Thieullen '13, Benaïm, Le Borgne, Malrieu, Zitt '13, Cloez '13, etc.

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- $\boxed{\mathbf{G}} \underset{k_d}{\overset{k_a}{\rightleftarrows}} \boxed{\mathbf{G^*}} \overset{J_p}{\rightarrow} \boxed{\mathbf{P}} \overset{k_p}{\rightarrow}$
- species $(g, x) \in \{0, 1\} \times \mathbb{R}$
- functions $k_a(1-g)$, $k_d g$, $J_p g$, $k_p x$
- jumps $\begin{pmatrix} 1 \\ 0 \end{pmatrix}, \begin{pmatrix} -1 \\ 0 \end{pmatrix}, \begin{pmatrix} 0 \\ 1 \end{pmatrix}, \begin{pmatrix} 0 \\ -1 \end{pmatrix}.$
- $f\begin{pmatrix} g \\ x \end{pmatrix} = \begin{pmatrix} 0 & 0 \\ 1 & -1 \end{pmatrix}\begin{pmatrix} J_p g \\ k_p x \end{pmatrix} = \begin{pmatrix} 0 \\ J_p g - k_p x \end{pmatrix},$

$$\lambda\begin{pmatrix} g \\ x \end{pmatrix} = k_a(1-g) + k_d g$$

$$Q\begin{pmatrix} g \\ x \end{pmatrix} = \frac{k_a(1-g)}{k_a(1-g)+k_d g}\delta_{\begin{pmatrix} g \\ x \end{pmatrix}+\begin{pmatrix} 1 \\ 0 \end{pmatrix}} + \frac{k_d g}{k_a(1-g)+k_d g}\delta_{\begin{pmatrix} g \\ x \end{pmatrix}+\begin{pmatrix} -1 \\ 0 \end{pmatrix}}$$

Hasty's Model for Lambda-phage (a)

$$\begin{cases} 2X & \overset{K_1}{\rightleftarrows} X_2, \\ D + X_2 & \overset{K_2}{\rightleftarrows} DX_2, \\ D + X_2 & \overset{K_3}{\rightleftarrows} DX_2^*, \\ DX_2 + X_2 & \overset{K_4}{\rightleftarrows} DX_2X. \\ DX_2 + P & \overset{K_t}{\rightarrow} DX_2 + P + nX \\ X & \overset{K_d}{\rightarrow} . \end{cases}$$

Hasty's Model for Lambda-phage (b)

- $f_\nu(x_1,x_2) = f(x_1,x_2) = \left(-2k_1{x_1}^2 - k_d x_1 + 2k_{-1}x_2,\ \ k_1x_1^2 - k_{-1}x_2\right),$
- $f(\nu,x) = (0,0,0,0,f_\nu(x)),$
- $\lambda(\nu,x) = k_2x_2\chi(x_2)\nu_1 + k_3x_2\chi(x_2)\nu_1 + k_4x_2\chi(x_2)\nu_2 + k_t\nu_2 + k_{-2}\nu_2 + k_{-3}\nu_3 + k_{-4}\nu_4,$
- $\lambda(\nu,x)\,Q((\lambda,x);dz) =$
  $k_2x_2\chi(x_2)\nu_1\delta_{(x_1,x_2-1,\nu_1-1,\nu_2+1,\nu_3,\nu_4)}(dz)$
  $+k_3x_2\chi(x_2)\nu_1\delta_{(x_1,x_2-1,\nu_1-1,\nu_2,\nu_3+1,\nu_4)}(dz)$
  $+k_4x_2\chi(x_2)\nu_2\delta_{(x_1,x_2-1,\nu_1,\nu_2-1,\nu_3,\nu_4+1)}(dz)$
  $+k_t\nu_2\delta_{(x_1+n,x_2,\nu_1,\nu_2,\nu_3,\nu_4)}(dz)$
  $+k_{-2}\nu_2\delta_{(x_1,x_2+1,\nu_1+1,\nu_2-1,\nu_3,\nu_4)}(dz)$
  $+k_{-3}\nu_3\delta_{(x_1,x_2+1,\nu_1+1,\nu_2,\nu_3-1,\nu_4)}(dz)$
  $+k_{-4}\nu_4\delta_{(x_1,x_2+1,\nu_1,\nu_2+1,\nu_3,\nu_4-1)}(dz),$

Asymptotic Stability (a)

- target set K, compact set of controls U
- find the set $\mathcal{D}$ of all x s.t. $X_t^{x,u}$ goes to K as $t \to \infty$.
- Zubov's method $K = \{x^*\}$: find $W : \mathbb{R}^N \to [0,1]$, $W(x^*) = 0$, s.t. $\mathcal{D} = \{x \in \mathbb{R}^N \mid W(x) < 1\}$
- $K_r = \left\{x \in \mathbb{R}^N : d_K(x) < r\right\}$, for $r > 0$
  $\forall x \in \overline{K}_r$ can be steered into K (using some piecewise open loop control u^x).
  (Usually, locally exponential (almost sure) stability)

Asymptotic Stability (b)

- admissible controls $\mathcal{A}_{ad}$: between consecutive jumps, $u\left(Y_i, \cdot\right)$
- define $\tau_{x,u} = \inf\left\{t \geq 0 : X_t^{x,u} \in K_r\right\}$
  if $\mathbb{P}\left(\tau_{x,u} < \infty\right) > 0$, extend u by setting
  $v\left(s\right) = 1_{s \leq \tau_{x,u}} u\left(s\right) + 1_{s > \tau_{x,u}, \tau_{x,u} < \infty} u^{X_{\tau_{x,u}}^{x,u}}\left(s - \tau_{x,u}\right)$
- problem : not an admissible control process
- however, one can mimic using occupation measures.

Previous Results

- **Deterministic framework** :
  (Young measures), Gaitsgory, Leizarowitz, '99, Artstein '00, Artstein, Gaitsgory '02, Gaitsgory, Nguyen '02, Gaitsgory, Rossomakhine '06, Finlay, Gaitsgory, Lebedev, '07, Gaitsgory, Quincampoix '09, etc.
- **Stochastic framework** :
  Fleming, Vermes '89, Stockbridge '90, Bhatt, Borkar '96, Basak, Borkar, Ghosh '97, Kurtz, Stockbridge '98, Borkar, Gaitsgory '05, '07, Lasserre et al. '08, Dufour, Prieto - Rumeau '12, Dufour, Stockbridge '13, etc.

Overview of the Method (a)

- $x \in \mathbb{R}^N$, $u \in \mathcal{A}_{ad}$,
  $\gamma_{x,u}(A) := \mathbb{E}\left[\int_0^\infty e^{-t} 1_A\left(X^{x,u}(t), u(t)\right) dt\right]$, $A \subset \mathbb{R}^N \times U$
- $\Gamma(x) := \{\gamma_{x,u};\ u \in \mathcal{A}_{ad}\}$
- $\Theta(x) :=$
  $$\left\{\begin{array}{c} \gamma \in \mathcal{P}\left(\mathbb{R}^N \times U\right):\ \forall \phi \in C_b^1\left(\mathbb{R}^N\right): \\ \int_{\mathbb{R}^N \times U} \left(\mathcal{U}^u \phi(y) + \phi(x) - \phi(y)\right) \gamma(dy, du) = 0 \end{array}\right\}$$
- $\mathcal{U}^u \phi(y) :=$
  $\langle \nabla \phi(y), f(y,u) \rangle + \lambda(y,u) \int_{\mathbb{R}^N} (\phi(z) - \phi(y)) Q(y,u,dz)$,
  $\forall u \in U$, $\phi \in C_b^1\left(\mathbb{R}^N\right)$, $y \in \mathbb{R}^N$

Theorem

$\Theta(x) = \overline{co}\Gamma(x)$

Overview of the Method (b)

- $g : \mathbb{R}^N \longrightarrow \mathbb{R}$ is bounded, Lipschitz continuous
  $v_g(x) = \inf_u \mathbb{E}\left[\int_0^\infty e^{-t} g\left(X_t^{x,u^1,0}\right) dt\right]$,
- $v_g(x) - g(x) + H(x, \nabla v_g(x), v_g) = 0$ (Soner '86),
  $H(x, p, \psi)$
  $$= \sup_{u \in U} \left\{ \begin{array}{c} -\langle f(x,u), p\rangle \\ -\lambda(x,u) \int_{\mathbb{R}^N} (\psi(z) - \psi(x)) Q(x,u,dz) \end{array} \right\}.$$

Overview of the Method (c)

- $\Lambda_g(x) := \inf_{\gamma \in \Theta(x)} \int_{\mathbb{R}^N \times U} g(y)\,\gamma(dy, du)$
- $\Lambda_g^*(x) =$
  $$\sup \left\{ \begin{array}{c} \mu \in \mathbb{R} : \ \exists \varphi \in C_b^1\left(\mathbb{R}^N\right) \text{ s.t. } \forall (y,u) \in \mathbb{R}^N \times U, \\ \mu \leq \mathcal{U}^u \varphi(y) + g(y) + (\varphi(x) - \varphi(y)) \end{array} \right\},$$
- $v_g \geq \Lambda_g \geq \Lambda_g^*$
- "shaking the coefficients" (Krylov, '00): " $=$ "
- separation argument : $\Theta(x) = \overline{co}\Gamma(x)$
- extension of $\Lambda_g = \Lambda_g^*$ for l.s.c. costs
- $v_g = \Lambda_g$ for u.s.c. costs.

Measure Formulation

- $\tau_{x,u,n} = \tau_{x,u} \wedge n$, for all $n \geq 1$.
- $\pi_{x,u,n} \in \mathcal{M}\left(\mathbb{R}_+ \times \mathbb{R}^N \times U\right)$, $\overline{\pi}_{x,u,n} \in \mathcal{P}\left(\mathbb{R}_+ \times \mathbb{R}^N\right)$
$$\begin{cases} \pi_{x,u,n}(A) = \mathbb{E}\left[\int_0^{\tau_{x,u,n}} 1_A\left(t, X_t^{x,u}, u_t\right) dt\right], & \text{if } \mathbb{P}\left(\tau_{x,u,n} > 0\right) > 0, \\ \pi_{x,u,n} = \delta_{0,x,u_0}, & \text{otherwise.} \end{cases}$$
$$\overline{\pi}_{x,u,n}(B \times C) = \mathbb{E}\left[1_{\tau_{x,u,n} \in B} 1_C\left(X^{x,u}_{\tau_{x,u,n}}\right)\right],$$
- $\overline{\gamma}(dsdydu) = e^{-s}\pi_{x,u,n}(dsdydu) +$
$$\int_{\mathbb{R}_+ \times \mathbb{R}^N} e^{-s'} \begin{pmatrix} 1_{\overline{K}_r^c}(z)\,\overline{\gamma}_{s',z,u}(dsdydu) \\ +1_{\overline{K}_r}(z)\,\overline{\gamma}_{s',z,u^z}(dsdydu) \end{pmatrix} \overline{\pi}_{x,u,n}(ds', dz).$$

Asymptotic Stability Domain

- $V(x) = \inf_u \mathbb{E}\left[\int_0^\infty e^{-s} 1_{K_r^c}\left(X_s^{x,u}\right) ds\right] = \inf_{\overline{\gamma} \in \overline{\Theta}(x)} \int_{\mathbb{R}_+ \times \mathbb{R}^N \times U} 1_{K_r^c}(y)\, \overline{\gamma}(dsdydu))$.
- $V(x) - 1_{K_r^c}(x) + H(x, \nabla V(x), V) = 0,$
- $H(x, p, \psi) = \sup_{u \in U}\left\{-\langle f(x,u), p\rangle - \lambda(x,u) \int_{\mathbb{R}^N} (\psi(z) - \psi(x))\, Q(x,u,dz)\right\}$

Theorem

V is the largest u.s.c viscosity subsolution ,
$$\mathcal{D} = \left\{x \in \mathbb{R}^N : V(x) < 1\right\} = \left\{x : \sup_{u \in \mathbb{L}^0(\mathbb{R}^N \times \mathbb{R}_+; U)} \mathbb{P}\left(\tau_{x,u} < \infty\right) > 0\right\}.$$

Back to Cook

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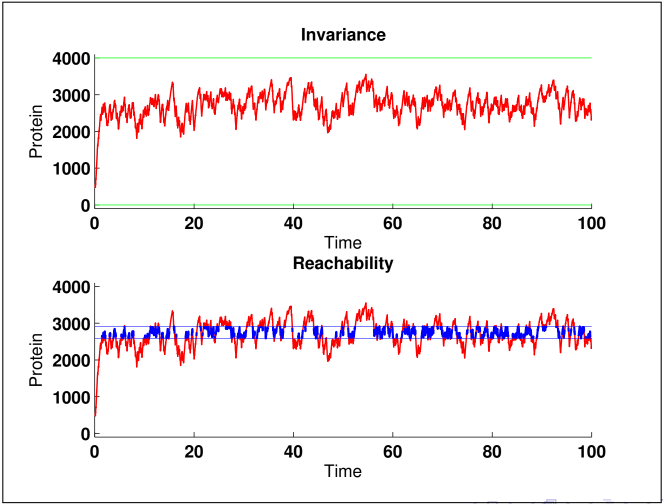
- $\alpha_{\max} = \frac{J_p}{k_p}$, $j_p(x) = \begin{cases} J_p, & \text{if } x \geq 2r; \\ 0, & \text{if } x \leq r. \end{cases}$
- $K = [0, \alpha_{\max}] \times \{0, 1\}$ is invariant,
- $0 < a < b < \alpha_{\max}$, $(a, b) \times \{0, 1\}$ is reachable with positive probability

Invariance and Reachability



Null-controllability Domain

- $K = \{0,1\} \times \{0\}$
- $(g,x) \in K_r = \{0,1\} \times [0,r)$, for every control process u,

$$\left(G^{(g,x),u}(t), X^{(g,x),u}(t)\right) \in \{0,1\} \times \left[0, e^{-k_p t} r\right),$$

for all $t \geq 0$. This is the exponential stability property.
- if positive activation/ deactivation rates, $\sup_u \mathbb{P}\left(\tau_{g,x,u} < \infty\right) \geq e^{-\frac{1}{k_p} \ln \frac{2\alpha_{\max}}{r} \inf\limits_{u \in U} (k_d(u) + k_a(u))} > 0$
- $\{0,1\} \times [0, \alpha_{\max}] \subset \mathcal{D}$.

Uniform Abel-Tauber results

- f regular
- $V_t(x) = \inf_{u \in \mathcal{U}_{ad}} t^{-1}\mathbb{E}\left[\int_0^t f\left(X_r^{x,u}, u_r\right) dr\right],$
- $V^\delta(x) = \inf_{u \in \mathcal{U}_{ad}} \delta\mathbb{E}\left[\int_0^\infty e^{-\delta r} f\left(X_r^{x,u}, u_r\right) dr\right],$
- study $\lim_{t \to \infty} V_t$ and $\lim_{\delta \to 0} V^\delta$

Previous Results

- Hardy,Littlewood, '14 : $(x_n)_{n\geq 1}$, convergence of Cesàro means $\left(\frac{1}{n}\sum_{i=1}^{n} x_i\right)_{n\geq 1} \Longleftrightarrow$ convergence of their Abel means $\left(\delta \sum_{i=1}^{\infty} (1-\delta)^i x_i\right)_{1>\delta>0}$.
- Feller '71 uncontrolled deterministic dynamics in continuous time,
- Arisawa '98 deterministic controlled dynamics
- Oliu-Barton, Vigeral, '13 deterministic controlled dynamics

Uniform Vanishing Result

- In Costa,Dufour '10
  $\inf_{T\to\infty} \inf_u \sup_{t\geq T} \frac{1}{t}\mathbb{E}\left[\int_0^t g\left(X_r^{x,u}\right) dr\right].$

Theorem

If $\left(v^{\delta}\right)_{\delta>0}$ *is a relatively compact subset of* $C\left(\mathbb{R}^N;[0,1]\right)$, $\forall v \in C\left(\mathbb{R}^N;[0,1]\right)$, $\left(\delta_m\right)_{m\geq 1}$ *s.t.* $\lim_{m\to\infty}\delta_m = 0$ *and* $v^{\delta_m} \xrightarrow{u} v$ *on* $\mathbb{R}^N$, $\liminf_{t\to\infty} \sup_{x\in\mathbb{R}^N} \left|V_t(x) - v(x)\right| = 0.$

Non-expansive yet non-dissipative (a)

- $\frac{dX}{dt} = \begin{cases} -r_0(X), \text{ if } \gamma(t) = 0, \\ r_1(X), \text{ if } \gamma(t) = 1, \end{cases}$
- $f(\gamma, x) = -r_0(x)(1-\gamma) + r_1(x)\gamma$, $\lambda(\gamma, x) = \lambda_\gamma$, $Q(\gamma, x; A) = \delta_{((1-\gamma),x)}(A)$
- dissipative needs: $\sup_u \inf_v \left\langle \begin{array}{c} (-\nu_0 r_0 + \nu_1 r_1)(x, u) \\ -(-\nu_0 r_0 + \nu_1 r_1)(y, v) \end{array}, x - y \right\rangle \leq -c\,|x-y|^2,$
- HOWEVER :

Non-expansive yet non-dissipative (b)

- $r_0(x,u) = \begin{pmatrix} ux_2 \\ -ux_1 \end{pmatrix}$, $r_1(x,u) = \frac{1}{2} r_0(x,u)$, $x \in \mathbb{R}^2$, $u \in [0,1]$.
- Then, $\sup_u \inf_v \left\langle \begin{matrix} (-\nu_0 r_0 + \nu_1 r_1)(x,u) \\ -(-\nu_0 r_0 + \nu_1 r_1)(y,v) \end{matrix}, x-y \right\rangle$ $= \sup_u \inf_v \left[(u-v)\left(\frac{1}{2}\nu_1 - \nu_0\right)(x_1 y_2 - x_2 y_1) \right] = 0$,
- Yet, $\left|X_t^{x,u}\right| = |x|$. Hence, u.c. for $f(x,u) := |x|$.
- similar to Buckdahn, G., Quincampoix (*Appl. Math. Optim. 14*).

Thank you for your patience !