Model-free based control of a HIV/AIDS prevention model

Loïc Michel, Cristiana J. Silva, Delfim F. M. Torres, Sophie Limou

École Centrale de Nantes-LS2N, UMR 6004 CNRS, 44300 Nantes, France
Center for Research and Development in Mathematics and Applications (CIDMA)
Department of Mathematics, University of Aveiro, 3810-193 Aveiro, Portugal
École Centrale de Nantes-CRTI Inserm UMR 1064, Nantes, France
loic.michel@ec-nantes.fr

Tuesday 7th September, 2021

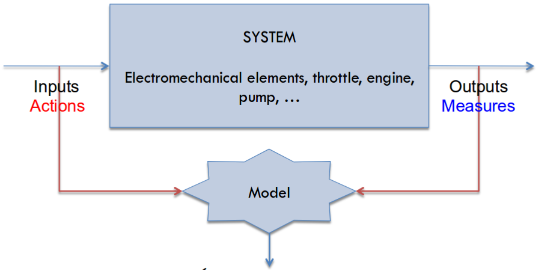
OUTLINE

- Presentation of the model-free control methodology
- Toward Para-Model control
- Para-model of the HIV-1
- Para-model control of the HIV-1 epidemiological model

Main idea of model-free control

Control today

- Most existing works: need precise mathematical (often difficult) modelling



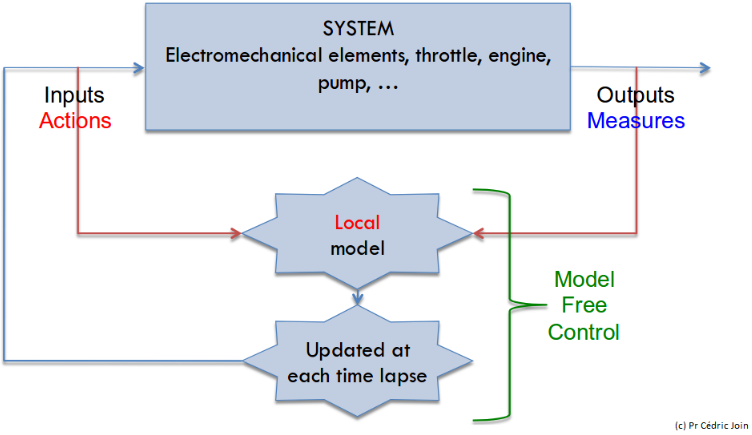
$$\begin{cases} \dot{x} = f(x, u, t) \\ y = g(x, u, t) \end{cases}$$

- PID (Proportional Integral Derivative) most common control law in practice (>95 %)

Main idea of model-free control

Model-free based control architecture

- From a complex system... to a simple local approximation



Main idea of model-free control

Model-free based control overview

Estimated and updated at each time lapse

~~Complex Model~~

$$\cancel{\begin{cases} \dot{x} = f(x, u, t) \\ y = g(x, u, t) \end{cases}}$$

Remplaced by

ultra local model

$$y^{(\nu)} = \alpha u + F$$

Ultra local model control based

$$u = \frac{1}{\alpha}\left(-F + y_*^{(\nu)}\right) + Correction(e)$$

(c) Pr Cédric Join

- Same conceptual simplicity as PID controllers
- No need of precise modelling

(Fliess, Join - 2008)

Consider an unknown system $E : u \mapsto y$,

$$E(t, y, \dot{y}, \ldots, y^{(\iota)}, u, \dot{u}, \ldots, u^{(\kappa)}) = 0$$

MFC definition

To control y relating to a reference y^*, one considers the intelligent PI (i-PI) controller that reads:

$$u_k = u_{k-1} - \frac{1}{\beta}\left(\left.\frac{\mathrm{d}y}{\mathrm{d}t}\right|_{k-1} - \left.\frac{\mathrm{d}y^*}{\mathrm{d}t}\right|_{k}\right) + \mathcal{C}(y^*|_k - y|_{k-1})$$

where $\mathcal{C}$ is a PI controller and β is a real constant; the tracking error is $\varepsilon = y^*|_k - y|_{k-1}$

- Numerical derivation of y necessary

Model-free control

In general, performances increase:

- development costs decrease
- maintenance costs decrease
- energetic costs decrease

Towards recent first applications in biology...

- Acute inflammation
- Wastewater denitrification
- Dynamic compensation for homeostasis
- Glycemia regulation

OUTLINE

- Presentation of the model-free control methodology
- Towards Para-Model control
- Para-model of the HIV-1
- Para-model control of the HIV-1 epidemiological model

Para-model control

Based on the original Model-free control...

- Modified version of the orignal model-free control

Para-model control definition

To control y relating to a reference y^*, one considers the $\mathcal{C}_\pi$ controller that reads:

$$u_k = \int_0^t K_i \varepsilon_{k-1} d\tau \Big|_{k-1} \left\{ u_{k-1} + K_p (k_\alpha e^{-k_\beta k} - y_{k-1}) \right\}$$

where $K_i, K_p, k_\alpha, k_\beta$ are real coefficients to adjust

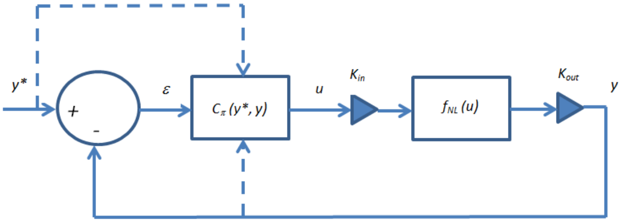
- Derivative-free algorithm

Para-model control

Structural properties

Given an output reference y^* and a nonlinear system $y = f_{nl}(u)$, it is *a priori* possible:

- to *control* dynamical or static f_{nl} systems
- to *optimize* (look for extremum) dynamical or static f_{nl} systems



Para-model control

Matlab code

```
y_int(i) = M_alpha*exp(-M_beta*tt(i));
para_exp_err = y_int(i-1) - y(i-1);
para_stand_err(i) = y_ref(i) - y(i-1);
para_u(i) = para_u(i-1) + Kp*para_exp_err;
para_G(i) = Kint*para_stand_err(i);
para_tr(i) = para_tr(i-1) + h*(para_G(i) + para_G(i-1))/2;
para_u_final = para_u(i)*para_tr(i);
```

OUTLINE

- Presentation of the model-free control methodology
- Towards Para-Model control
- A preliminary study of the para-model of the HIV-1
- Para-model control of the HIV-1 epidemiological model

Para-model control of the HIV-1 model

(Craig, Xia, Venter - 2004)

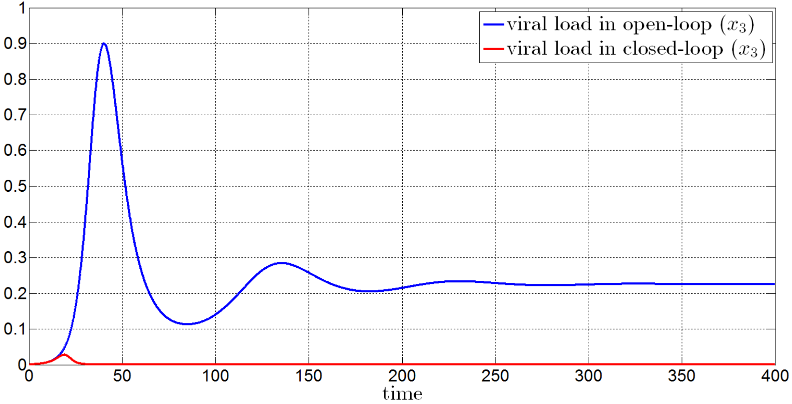
- Control of the predator-prey like model that describes the evolution of the HIV-1 dynamics when subjected to an external "medical agent"
- We do not take into account the constraints that are medically imposed

$$\begin{cases} \dot{x}_1 = s - dx_1 - (1-u_1)\beta x_1 x_3 \\ \dot{x}_2 = (1-u_1)\beta x_1 x_3 - \mu x_2 \\ \dot{x}_3 = (1-u_2)kx_2 - cx_3 \\ y = \begin{pmatrix} 0 & 0 & \gamma \end{pmatrix} x \end{cases}$$

Para-model control of the HIV-1 model

Control of the viral load

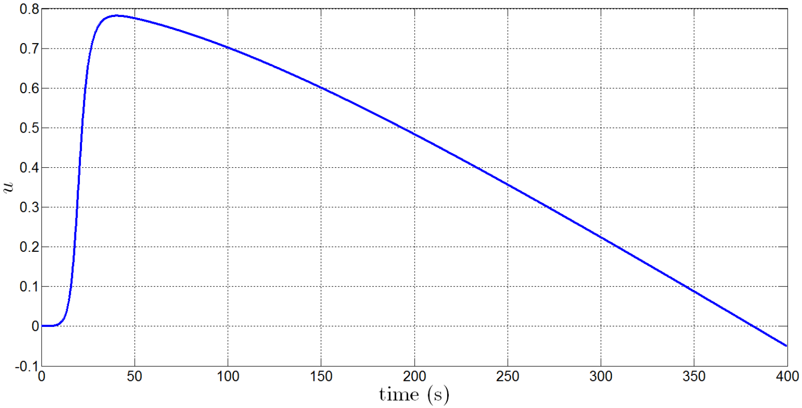
- Open-loop vs closed-loop



Para-model control of the HIV-1 model

Control of the viral load

- Evolution of the associated u variable "medical agent"



OUTLINE

- Presentation of the model-free control methodology
- Towards Para-Model control
- A preliminary study of the para-model of the HIV-1
- Para-model control of the HIV-1 epidemiological model

HIV-1 epidemiological model

(Silva, Torres - 2018)

Consider the SICAE mathematical model for HIV/AIDS transmission

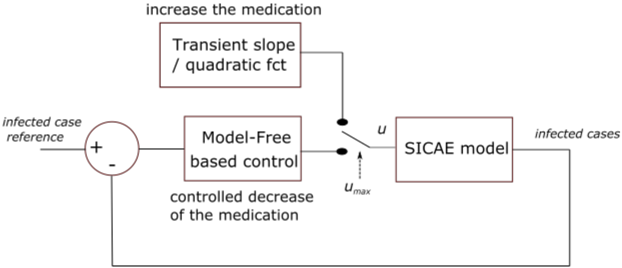
$$\begin{cases} \dot{S}(t) = \mu N - \frac{\beta}{N}(I(t) + \eta_C\, C(t) + \eta_A A(t))S(t) - \mu S(t) - S(t)u(t) + \theta E(t), \\ \dot{I}(t) = \frac{\beta}{N}(I(t) + \eta_C\, C(t) + \eta_A A(t))S(t) - (\rho + \phi + \mu)I(t) + \alpha A(t) + \omega C(t), \\ \dot{C}(t) = \phi I(t) - (\omega + \mu)C(t), \\ \dot{A}(t) = \rho\, I(t) - (\alpha + \mu)A(t), \\ \dot{E}(t) = S(t)u(t) - (\mu + \theta)E(t). \end{cases}$$

where u is the *driven* medication input and I is the *controlled* infected state

HIV-1 epidemiological model

Control of the viral load

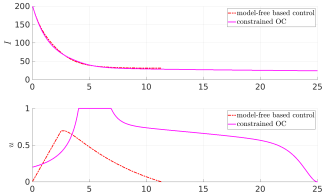
- Control sequence to drive the medication u in order to minimize the infected cases



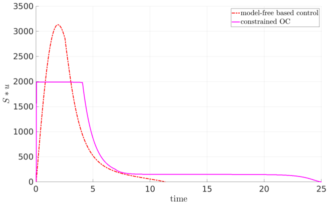
- The goal is to minimize the infected state I considering the SICAE model as a black box under the $Su \leq 2000$ constraint

Numerical results

Controlled SICAE model using a linear increasing transient



(a) Evolution of the infected state I versus the Time (year).

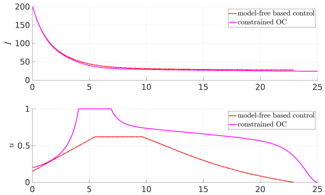


(b) Evolution of the controlled medication u versus the Time (year).

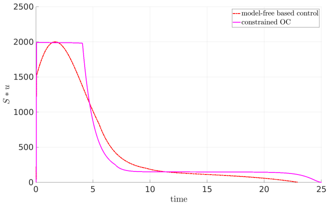
Evaluation of the **unconstrained** model-free based SICAE control

Numerical results

Controlled SICAE model using a linear increasing transient (I)



(c) Evolution of the infected state I versus the Time (year).

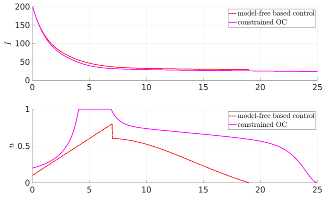


(d) Evolution of the controlled medication u versus the Time (year).

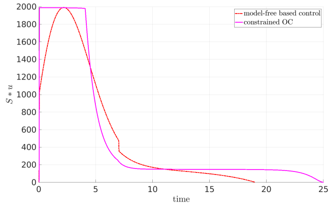
Evaluation of the **constrained** model-free based SICAE control (I)

Numerical results

Controlled SICAE model using a linear increasing transient (II)



(e) Evolution of the infected state I versus the Time (year).

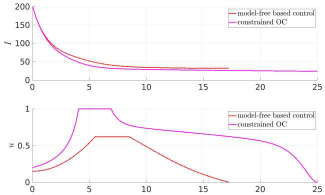


(f) Evolution of the controlled medication u versus the Time (year).

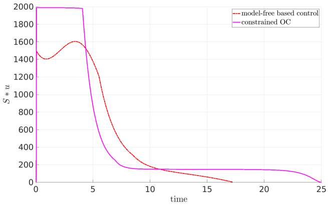
Evaluation of the **constrained** model-free based SICAE control (II)

Numerical results

Controlled SICAE model using a quadratic increasing transient (I)



(g) Evolution of the infected state I versus the Time (year).

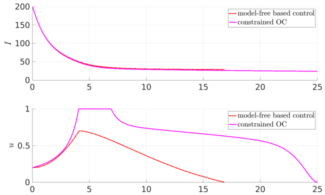


(h) Evolution of the controlled medication u versus the Time (year).

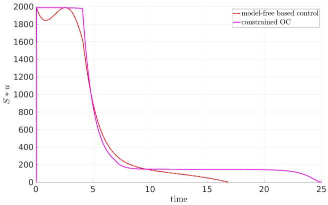
Evaluation of the **constrained** model-free based SICAE control (III)

Numerical results

Controlled SICAE model using a quadratic increasing transient (II)



(i) Evolution of the infected state I versus the Time (year).



(j) Evolution of the controlled medication u versus the Time (year).

Evaluation of the **constrained** model-free based SICAE control (IV)

Numerical results

Evaluation of the cost criteria

Case	T_e	J_{u+I}^{Te}	$I(T_e)$	$\max_{[0,t_e]} Su$	u_{max}
Unconst. model-free	11.3	1.1510^5	31.12	3129	0.70
Const. model-free - S (I)	19.0	2.3910^5	29.80	1990	0.80
Const. model-free - S (II)	22.9	2.8610^5	28.25	2000	0.62
Const. model-free - Q (I)	16.9	1.8310^5	29.12	1989	0.70
Const. model-free - Q (II)	17.2	2.3910^5	32.29	1604	0.62
Unconst. OC	25.0	1.6910^5	21.95	9750	1
Const. OC	25.0	2.7210^5	24.23	1989	1

The goal is to minimize the (time-ponderated) ITSE index:

$$J_{u+I}^{Te} = \int_0^{T_e} \tau \left(u^2 + I^2\right) \mathrm{d}\tau \qquad (1)$$

BFO-tuning of the Para-model control

Tuning of the control parameters

(Porcelli, Toint - 2015)

- DFO-based Brute Force Optimization (BFO) Matlab package
- For a given closed-loop, consider a performance index $\mathbb{P}$ (IAE, ISE, ITAE or ITSE) to minimize

PMA Tuning Optimization Procedure

Consider controlling an unknown system E over $[0, t]$. We expect to minimize a performance index $\mathbb{P}$ of the closed-loop:

$$\min_{K_i, K_p, k_\alpha, k_\beta} \mathbb{P} \quad \text{e.g.} \quad \min_{K_i, K_p, k_\alpha, k_\beta} \int_0^t (y - y^*)^2 \mathrm{d}\tau \qquad \text{(ISE)}$$

Conclusion and perspectives

- The asymptotic value of I may depend on both the initial medication condition u_0 as well as the max value u_{max} *Rules to tune the control sequence could be deduced*
- Modify the simulation experiments to better fit biological constraints and current treatments:
- Life-long combined therapy (vs. a single dose)
- Limited access to treatment: What percentage of population would need to be covered to see the effect on HIV neo-infections globally?
- Assess impact of disturbances on the output (e.g. super-infections, non-compliance to treatment)

Thank you for your attention !

L. Michel, A para-model agent for dynamical systems, arXiv:1202.4707

L. Michel, C.J. Silva, D.F.M. Torres, Model-Free based control of a HIV/AIDS prevention model, Mathematical Biosciences and Engineering, submitted.