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MODEL-BASED DESIGN OF CLOSED-LOOP NEUROMODULATION DEVICES

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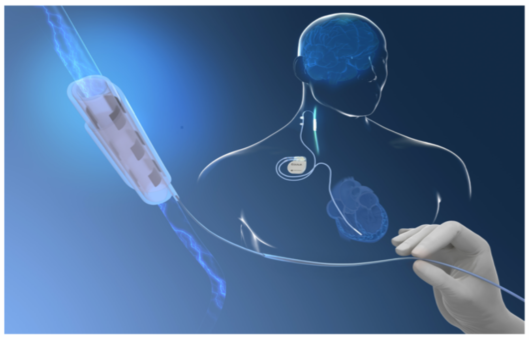
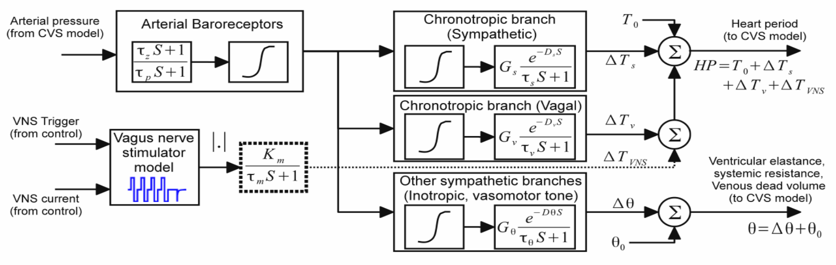
Context and objective

- Vagus nerve stimulation (VNS) has been identified as a potential therapeutic approach in different clinical applications, such as epilepsy, supra ventricular arrhytmias and heart failure (HF).
- Adaptive closed-loop approaches may be necessary in order to optimize the therapy and minimize side effects.
- However, due to the lack of observability *in-vivo* and the complexity of the underlying physiological mechanisms, the control methods employed are usually simple, and based on heuristics.
- Objective: To propose and evaluate a model-based control design framework adapted to the design of closed-loop medical devices.



Method: Model Based Design

1) Create a model of the plant

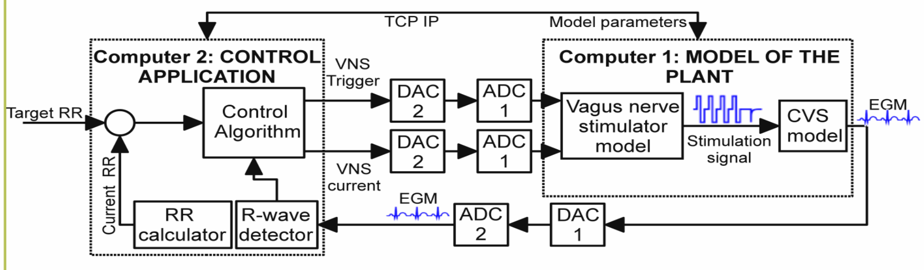


Model: circulation+baroreflex+neurostimulator (see Ojeda et al. 2015).

2) Define the controller

$$\textbf{PID:}\; u(t) = k_p\left(e(t) + \frac{1}{T_i}\int e(t)dt + k_d\frac{de(t)}{dt}\right)$$

3) Couple model and controller



4) Identify optimal parameters

Performance criteria:

- **Rise time (tr)**. The time required for the waveform to go from 0.1 of the final value to 0.9 of the final value.
- **Percent overshoot (%OS)**. The amount that the waveform overshoots the steady-state expressed as a percentage of the steady-state value.
- **Mean squared error (MSE)** during steady-state error. Is the MSE measured when the system dynamic reaches the steady state.

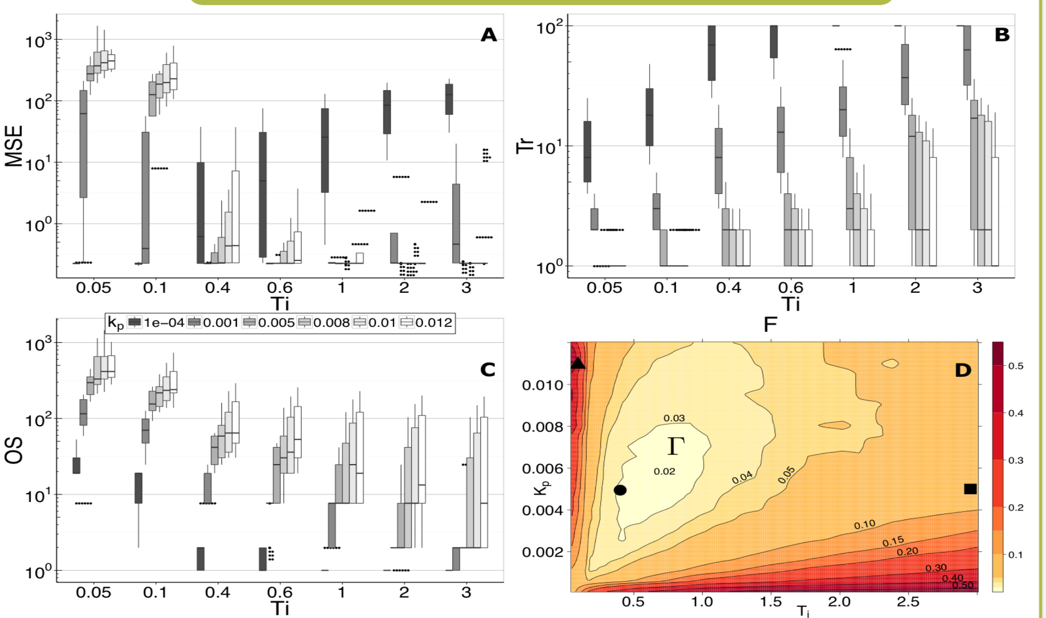
$$e(t) = \text{Target RR} - \text{RR}(t) \qquad \text{MSE} = \frac{1}{N}\sum_{t=1}^{N} e^2(t)$$

- Global criterion leading a good balance between accuracy and speed of convergence

$$\text{F} = 0.25\frac{\overline{\text{MSE}}}{\max(\overline{\text{MSE}})} + 0.25\frac{\overline{\%\text{OS}}}{\max(\overline{\%\text{OS}})} + 0.5\frac{\overline{T_r}}{\max(\overline{T_r})}$$

Performance measures are evaluated, on a "virtual population", for a set of control parameters.

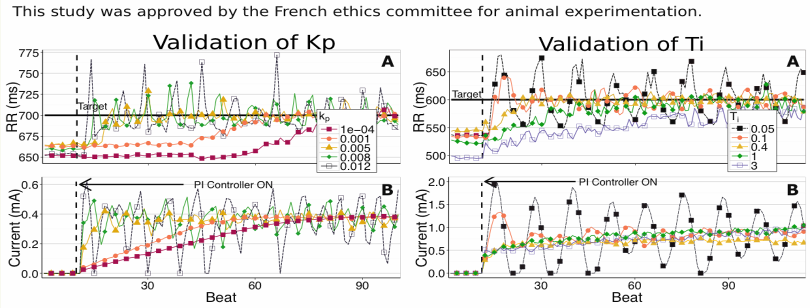
Results on virtual population



[EMBC 2014, NER 2015, TBME 2016,2017,2018, PlosOne 2016,2017]
Patents: US2015223746, US2016375250, US2016375251, US2016375252, US2016375253

Experimental validation

This study was approved by the French ethics committee for animal experimentation.



Two steps:

1) Sheep anesthetized with Propofol and a morphine bolus. A bipolar pacemaker lead containing an intracardiac accelerometer was placed in the right ventricle (SonRTipTM lead, Sorin CRM, Clamart, France) and a cuff-type VNS electrode (Cuff electrode C4D3-1, Obelia) was implanted on the right vagus nerve, at a cervical site.
2) Sheep anesthetized by Etomidate and Isoflurane. After verification stage of the implanted instrumentation the control tests were started.

The surface ECG, the intracadiac ElectroGraMs (EGM), the left intra-ventricular pressure and the body temperature (37°C) were monitored during the whole procedure. Breathing was artificially controlled at 0.3 Hz.

Conclusions

- A **model-based control design framework**, which is adapted to the design of medical devices was proposed.
- Design of PID controllers for regulating the heart rate, using a physiological model (representing the cardiovascular system of a sheep), including the cardiac response to VNS.
- Better understanding on the way of tuning the kp and Ti parameters of a PID controller.
- Other control methods and devices have been evaluated using the proposed approach.

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