Closed Loop Anesthesia: Can We Make it Safe by Design?

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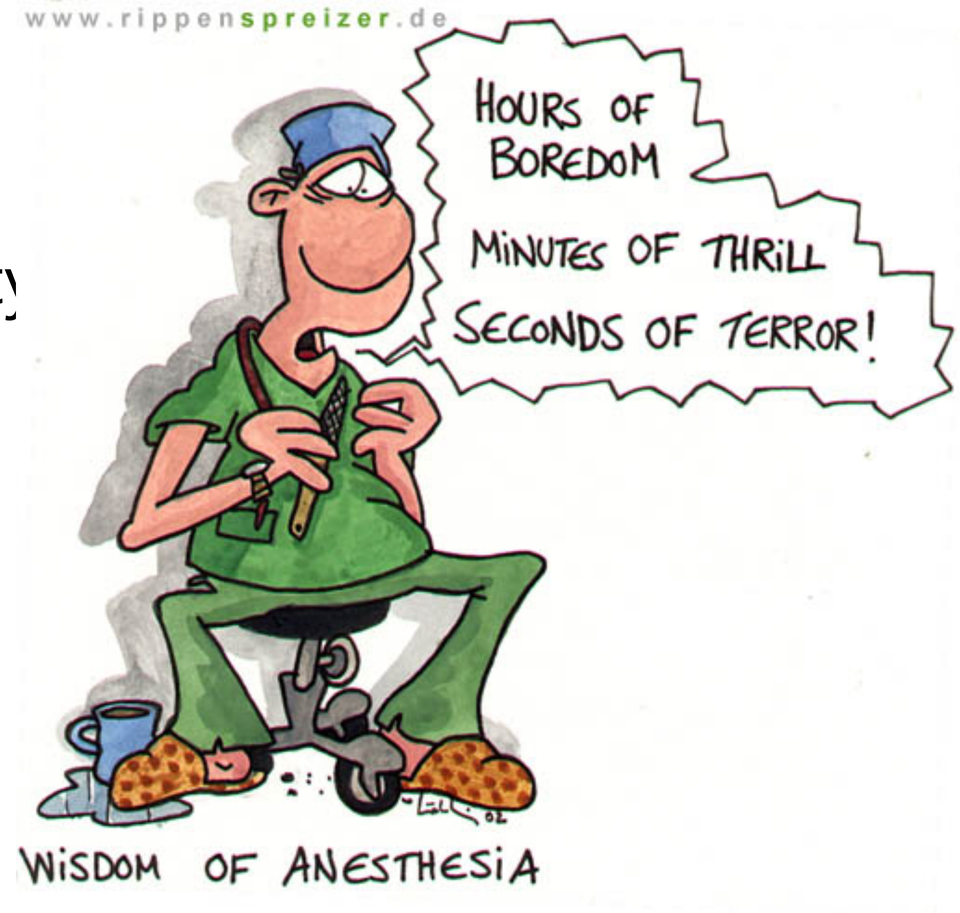
Disclosures

- Consulting activities
  - NeuroWave Systems
  - Bigfoot Medical
- Research grants
  - NeuroWave Systems
  - Medtronic
- Co-inventor of the NeuroSense monitor
- Co-founder and equity holder in LionsGate Medical Technologies

Automation of Anesthesia

- First attempts in 1950-51
- Complexity combined with variability
- Limits to human vigilance
- Information overdose
- Patient outcomes



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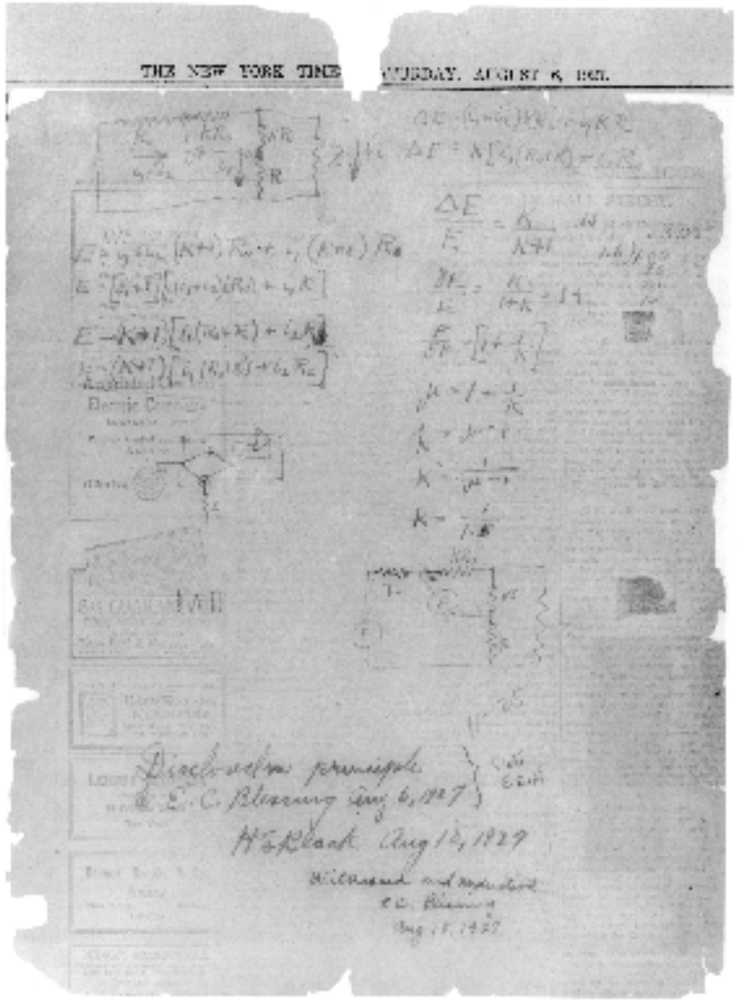
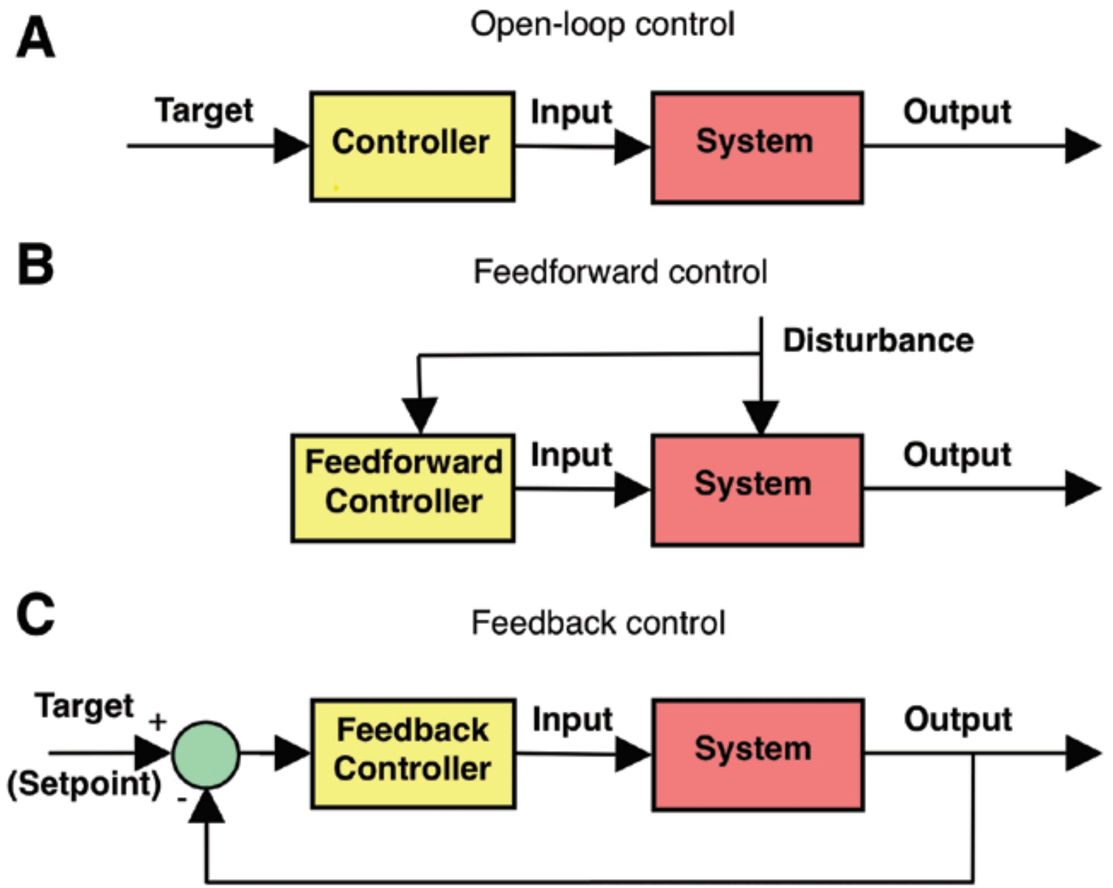
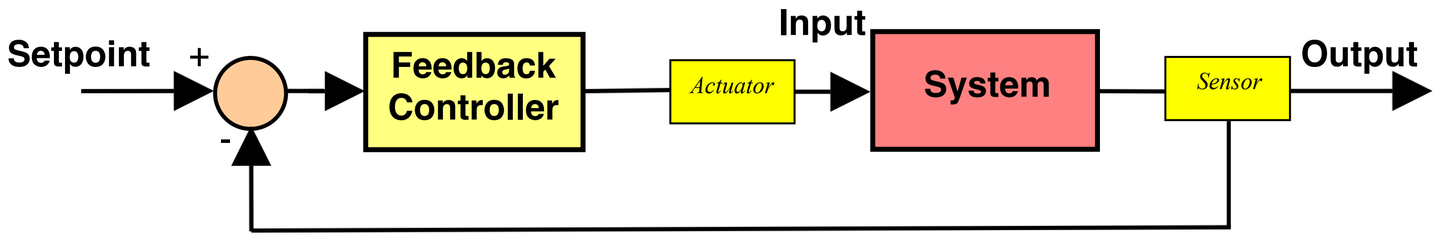
The Power of Feedback





Harold Black's 1927 invention of the negative feedback amplifier eliminated distortion over telephone lines, enabling long-distance telephony

Feedback



- Feedback is everywhere
- Feedback reduces the effect of uncertainties
- With feedback, one can build high-performance systems from imperfect, imprecise components, even imperfect models!
- Main danger with feedback is **instability!**

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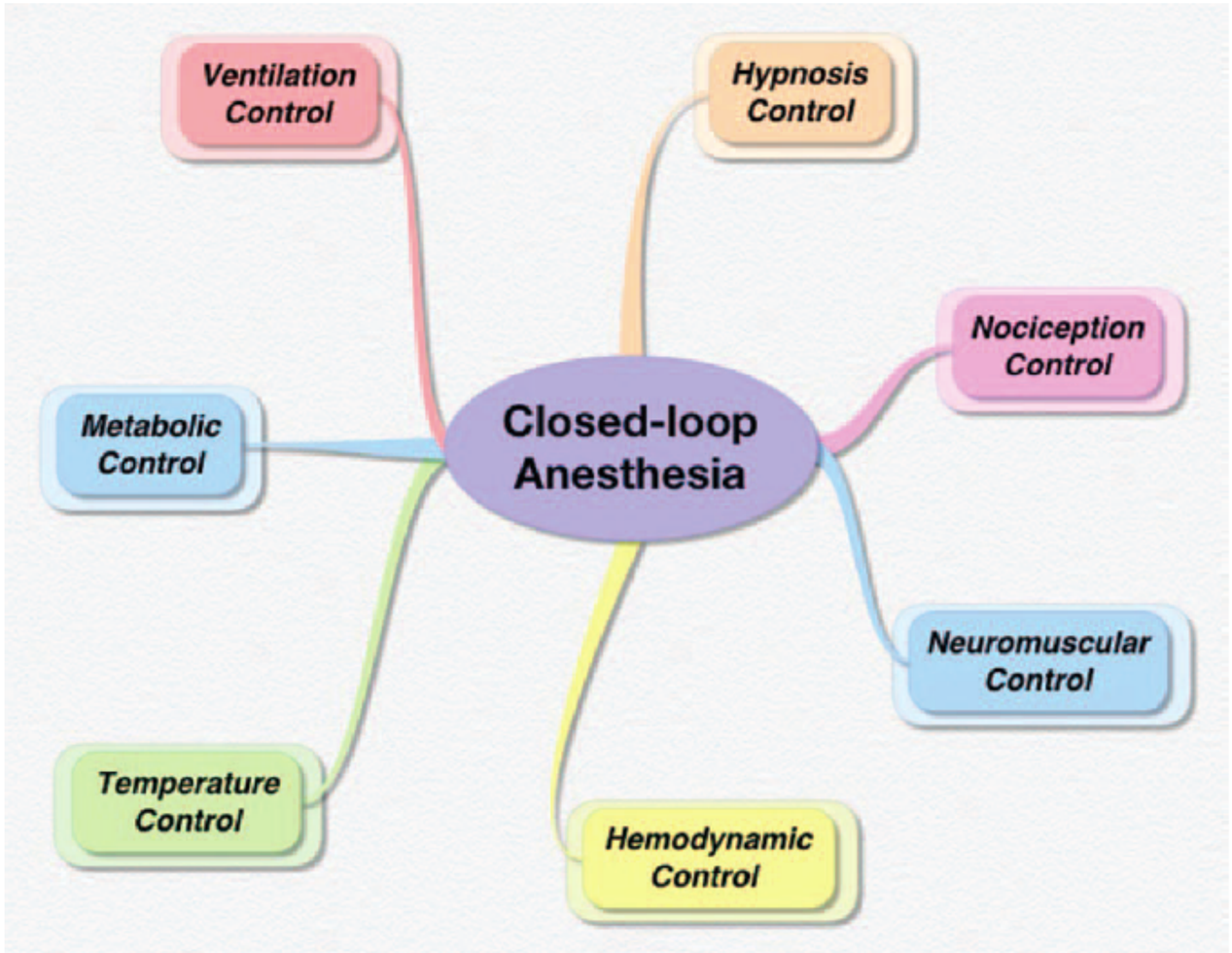
Complete System for Closed-Loop Control of Anesthesia



G.A. Dumont, J.M. Ansermino (2013), "Closed-loop Control of Anesthesia: A Primer for Anesthesiologists", *Anesthesia & Analgesia*, 110(5): 1130-8.

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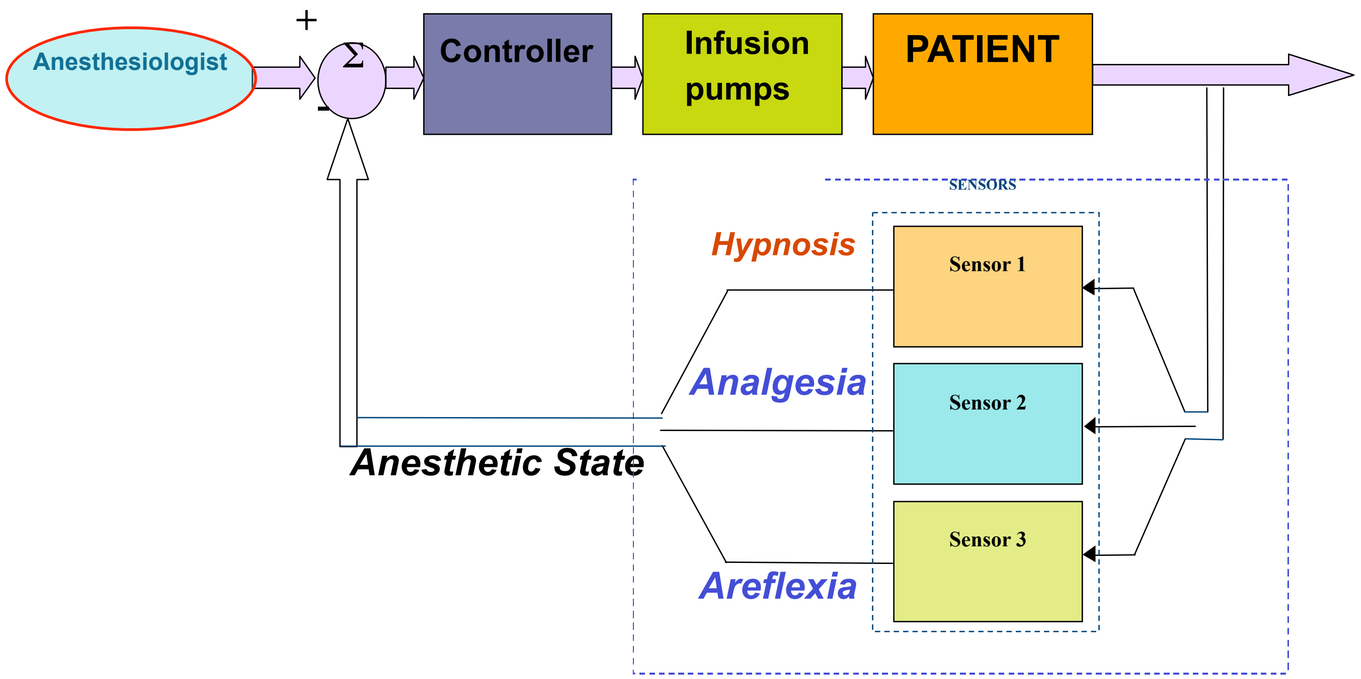
Automation in Intravenous Anesthesia



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Certification

- The entire system must be certifiable
  - Monitor/sensor
  - Actuator (infusion pumps)
  - Algorithms
  - User interface
  - Software
  - Implementation

B. Parvinian, C. Scully, H. Wiyor, A. Kumar, and S. Weininger, “Regulatory considerations for physiological closed-loop controlled medicaldevices used for automated critical care: Food and drug administrationworkshop discussion topics,” Anesthesia & Analgesia, 2017.

Certification

- Validation
  - Mathematical proofs
  - Simulations
  - Extensive clinical trials
- Risk analysis
- Knowledge and minimization of residual risks
- Clinical benefits

B. Parvinian, C. Scully, H. Wiyor, A. Kumar, and S. Weininger, “Regulatory considerations for physiological closed-loop controlled medicaldevices used for automated critical care: Food and drug administrationworkshop discussion topics,” Anesthesia & Analgesia, 2017.

Certification

Table 3. Concept of Level of Automation Applied to an Example of a Physiological Closed-Loop Controlled Medical Device

Medical Device LOA	Task	Example Neonatal Oxygen Therapy
1	Manual therapy. All decisions pertaining to care of the patient as related to a specific therapy are made by the clinician. The device does not provide decisions nor does it provide recommendations	Clinician determines oxygen therapy is needed. Makes Fio_2 adjustment for a hypoxemic patient based on vital signs, Spo_2 monitor, and overall status of the patient. Clinician decides when to wean
2	Partial automation. Clinician determines the type of therapy that is needed, determines the input target/range. The device actuates automatically to keep the patient on target or within the prescribed range. All set points are determined by clinician	Clinician determines the patient needs oxygen therapy, inputs the prescribed range of Spo_2 between 90% and 95%. Device senses Spo_2 of 80% and increases Fio_2 by 50% automatically to keep the patient Spo_2 between 90% and 95% as determined by clinician. Clinician decides when to wean
3	High automation. The clinician determines the type of therapy that is needed and prescribes the first target range or set point. Device actuates to keep the patient within target prescribed range but determines and adjusts the subsequent set points automatically. Clinician will have override capabilities to assume manual care at any time	Clinician determines the patient needs oxygen therapy. Device senses Spo_2 of 80% and increases Fio_2 by 50% autonomously to keep the patient Spo_2 between 90% and 95% as determined by the device algorithm. The clinician decides when and how to wean
4	Full automation. Device determines type of therapy. Determines the set points and course of oxygen delivery as well as initiation and rate of weaning. Clinician will have override capabilities to assume manual care at any time	Device determines oxygen therapy is needed and autonomously delivers oxygen to keep Spo_2 within a range of 90%–95% as determined by device. The device determines when and how the patient is going to be weaned from oxygen. Clinician can always intervene

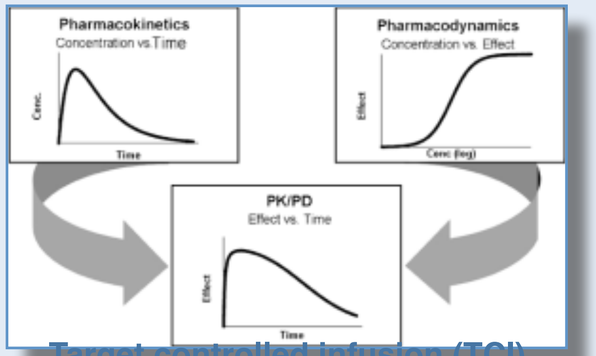
Abbreviations: Fio_2, fraction of inspired oxygen; LOA, levels of automation; Spo_2, peripheral capillary oxygen saturation.

B. Parvinian, C. Scully, H. Wiyor, A. Kumar, and S. Weininger, "Regulatory considerations for physiological closed-loop controlled medicaldevices used for automated critical care: Food and drug administrationworkshop discussion topics," Anesthesia & Analgesia, 2017.

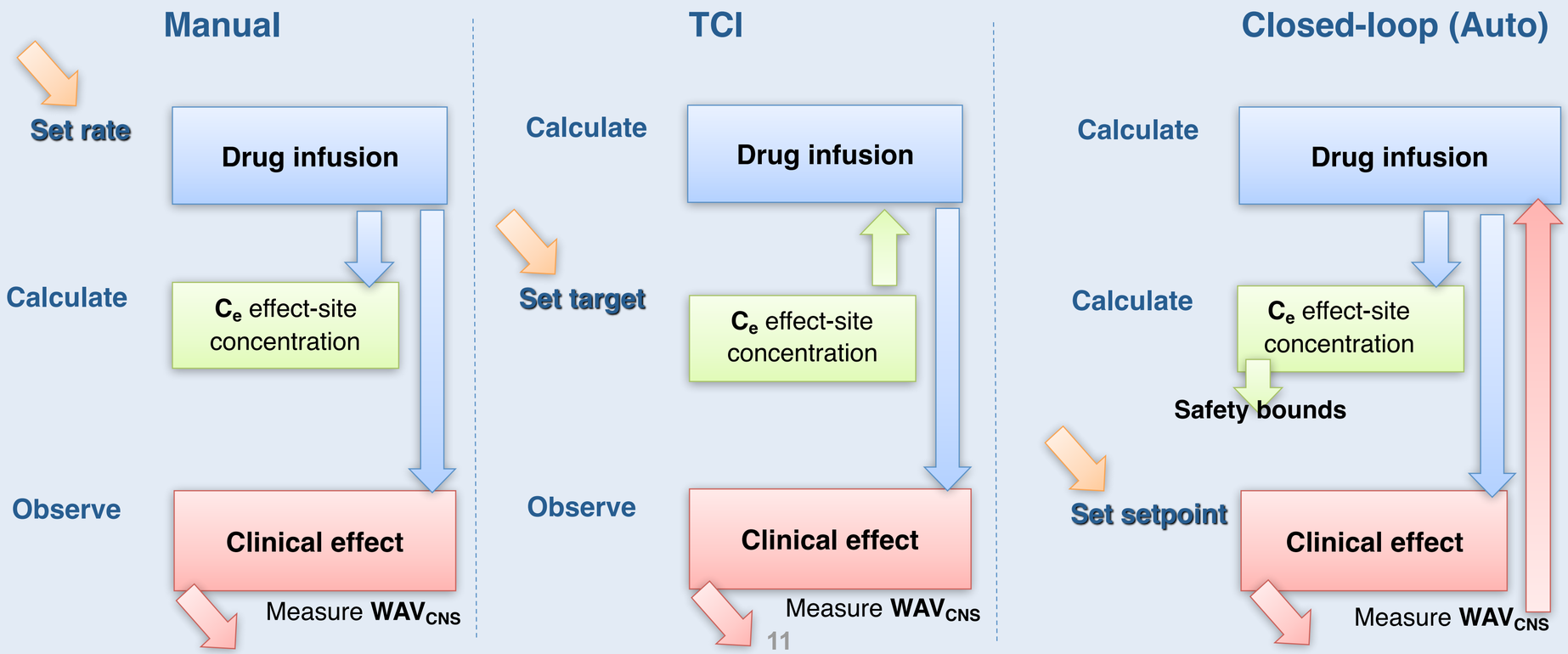
Control of Depth of Hypnosis

Principles

iControl allows **manual, TCI** and **closed-loop (Auto)** control of drug infusion



Target controlled infusion (TCI) based on PKPD models



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Challenges

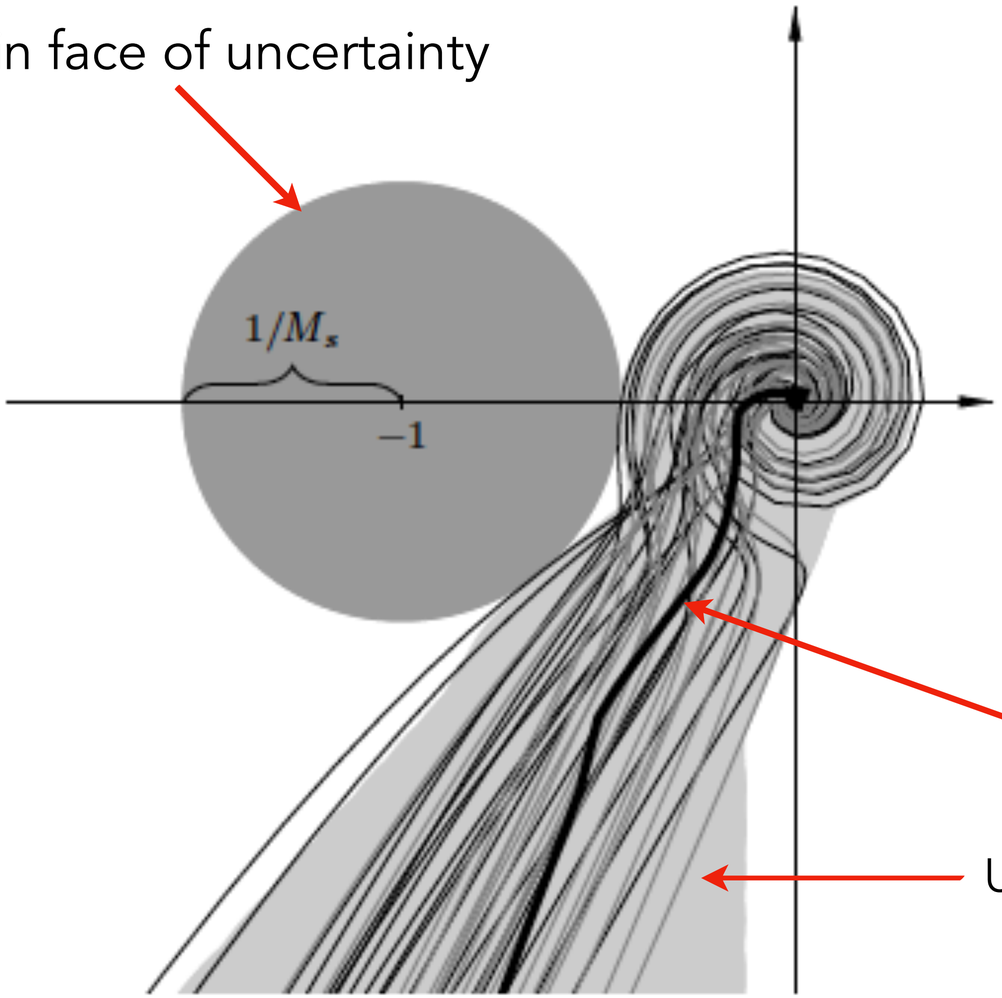
- Significant variability and uncertainty
- Lack of models, not fully understood mechanisms
- Potentially significant interactions
- Difficult to identify the patient model
- Measurements are difficult and often indirect

iControl

- Design based on rigorous control theory
- Stability and performance guarantees
- Clinician-defined safety constraints
- Safety guarantees using safe control theory
- Fallback modes
- Validated and verified software implementation
- Rigorous usability studies

Robust Control in Anesthesia

Garanteed stability in face of uncertainty



Nominal model

Uncertainty band

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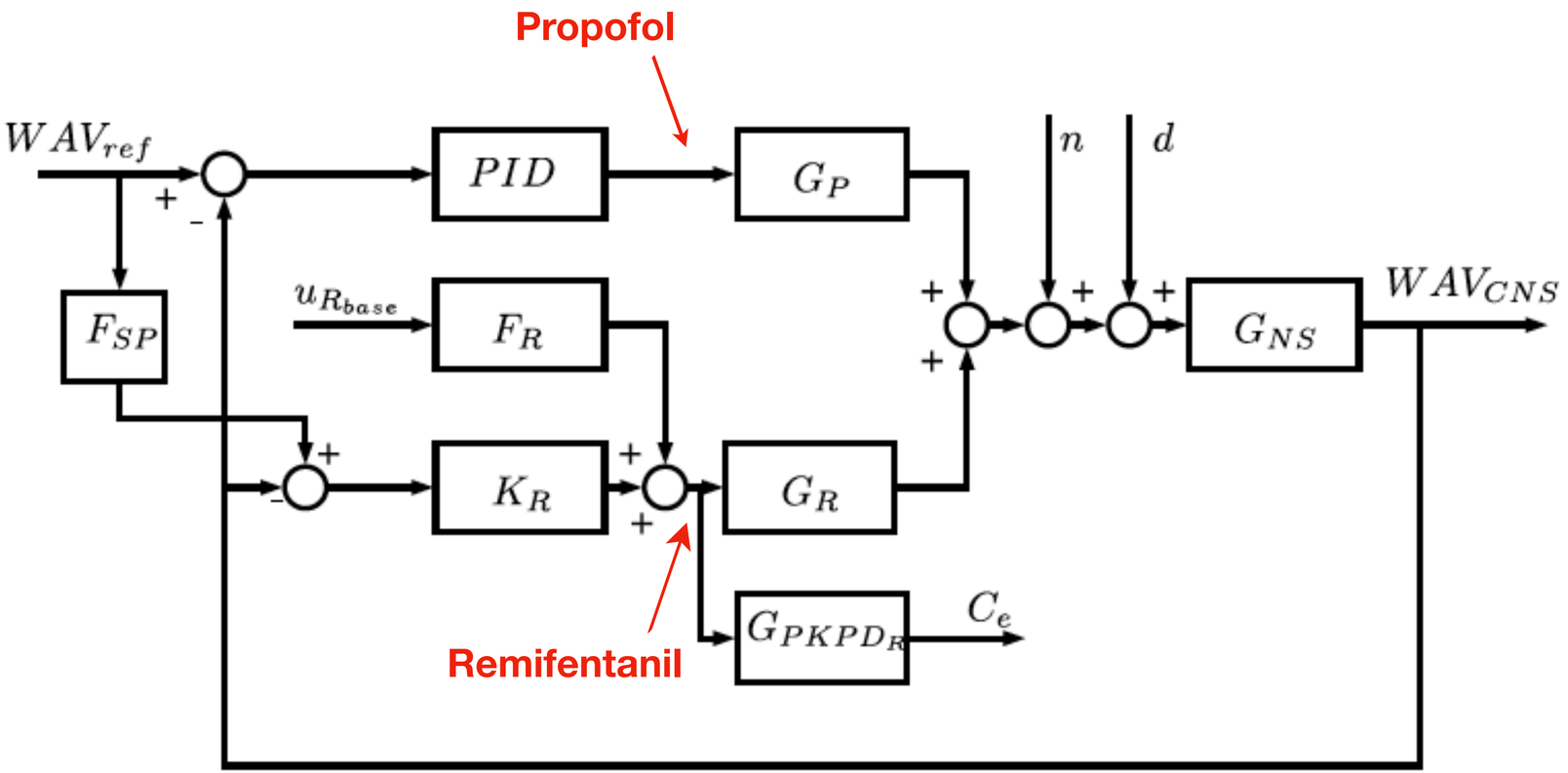
iControl-RP



vanHeusden K, Ansermino JM, Dumont GA (2017). Robust MISO control of propofol-remifentanil anesthesia guided by the NeuroSENSE monitor. IEEE Trans. On Control Systems Technology, Published online, Aug. 2017. DOI: 10.1109/TCST.2017.2735359

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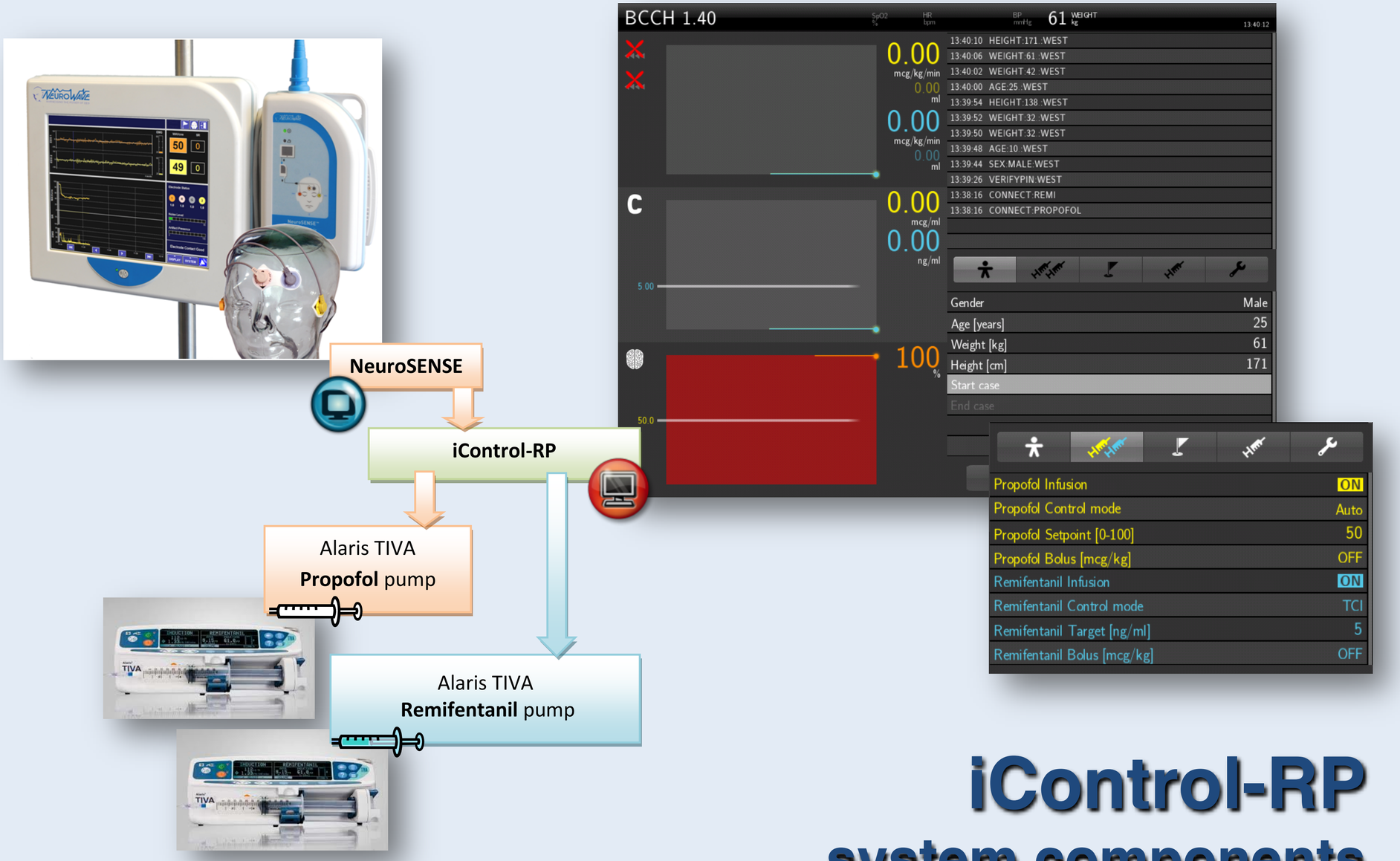
Software Implementation

- The iControl system was designed and implemented using rigorous validation requirements of high-risk medical instrumentation, including a detailed user and system requirements specification, hazard analysis, and system design specification:
  - Implemented as client-server system
  - Server on an embedded system running Linux
  - Main client on flat panel computer running Windows
  - Hardware-in-the-loop simulations
  - Usability studies and automated system tests

cartoonstock.com

iControl-RP



iControl-RP
system components

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iControl-RP

Clinical trials at Royal Columbian Hospital
New Westminster, BC, Canada

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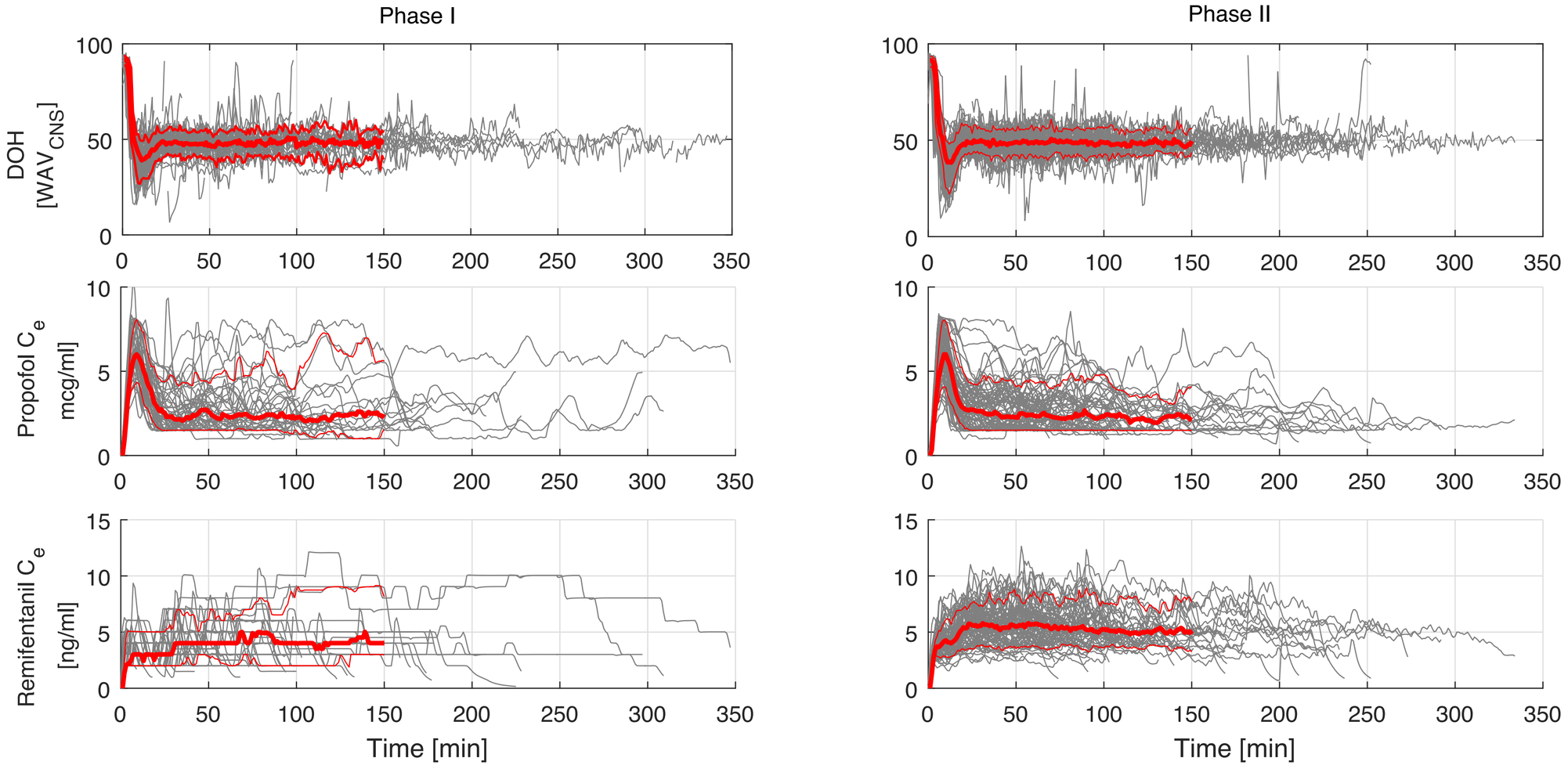
iControl-RP Trials



West N, vanHeusden K, Görges M, Brodie S, Petersen CP, Dumont GA, Ansermino JM, Merchant RM (2017). Design and evaluation of a closed-loop anesthesia system with robust control and safety system. Anesthesia & Analgesia, Published online, Nov 27, 2017. DOI: 10.1213/ANE.0000000000002663

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iControl-RP 37yr old male

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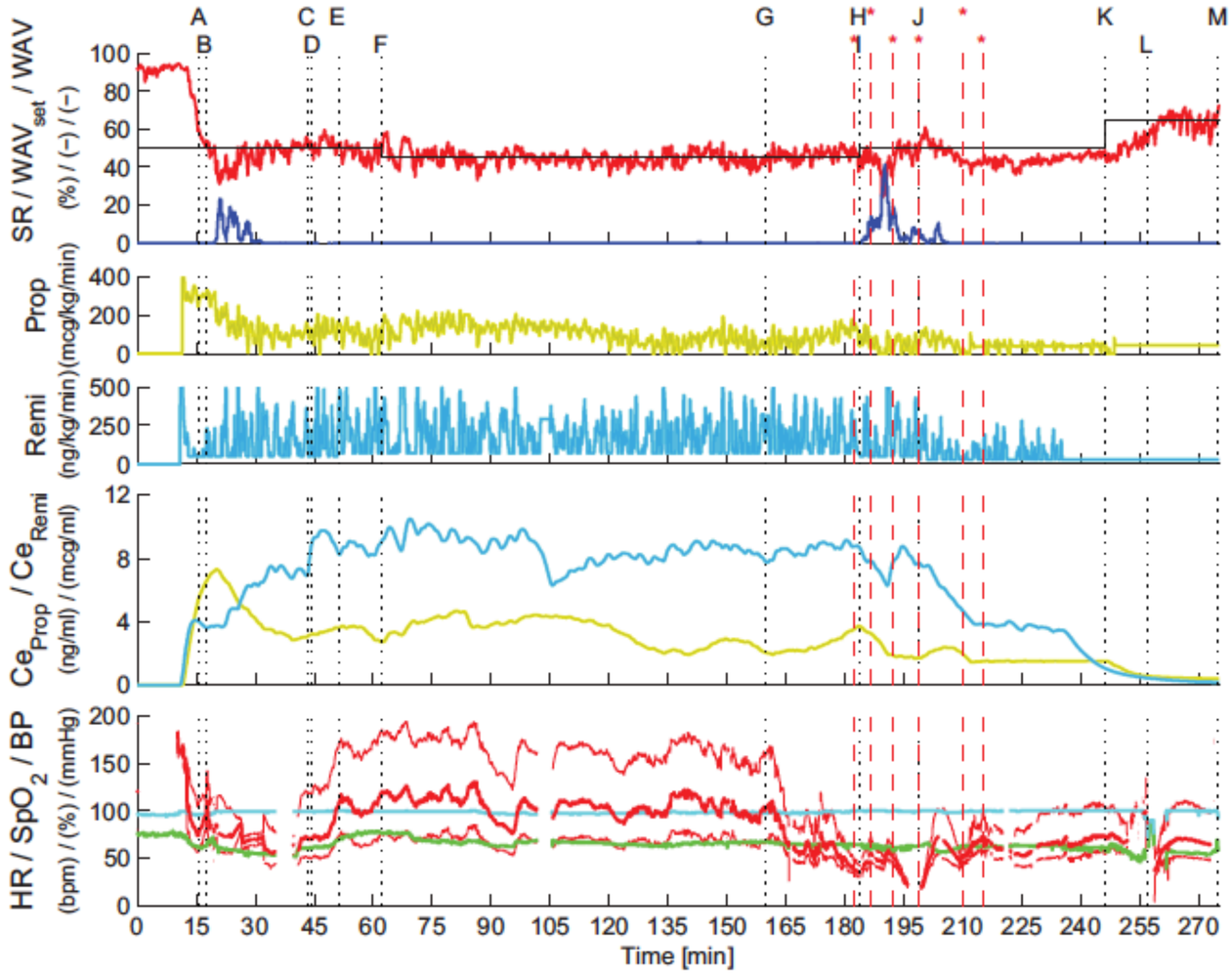
iControl-RP 79yr old male



Brodie S, Görges M, Ansermino JM, Dumont GA, Merchant R (2017). Closed-loop control of total intravenous anesthesia during significant intra-operative blood loss: A case report. Anesthesia & Analgesia Case Reports, Published online, July 17, 2017. doi: 10.1213/XAA.0000000000000576

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Oscillation Detection

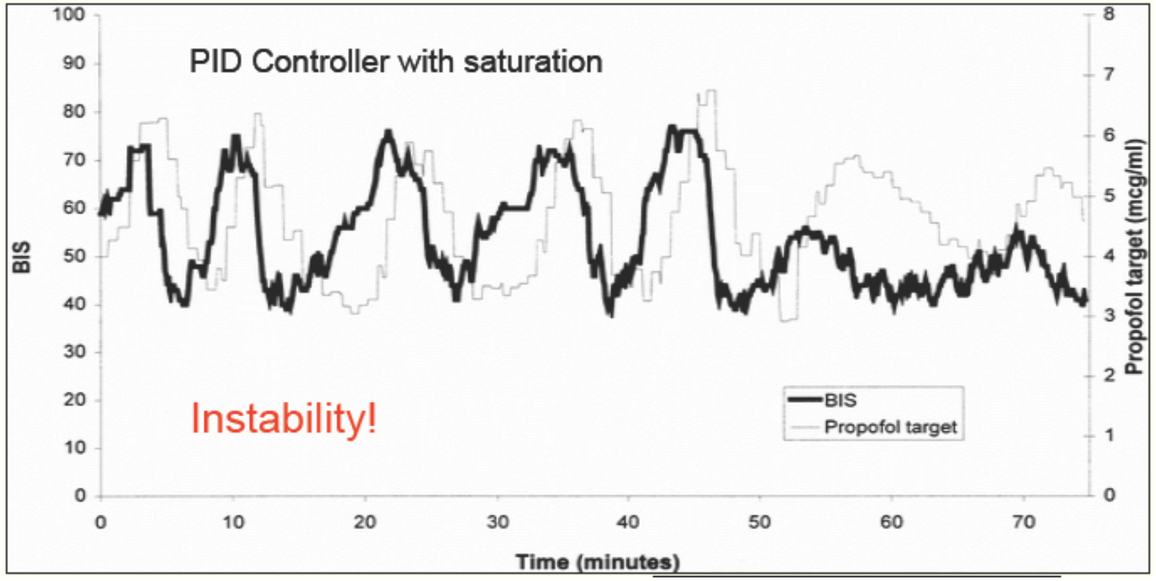
- Oscillations (at least for an isolated control loop are a signature of impending instability)

Anesthesiology 2002; 96:67–73
© 2002 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Closed-loop Control of Anesthesia Using Bispectral Index

Performance Assessment in Patients Undergoing Major Orthopedic Surgery under Combined General and Regional Anesthesia

Anthony R. Absalom, M.B.Ch.B., F.R.C.A., Nicholas Sutcliffe, M.B.Ch.B., M.R.C.P., F.R.C.A.,† Gavin N. Kenny, B.Sc.(Hons), M.D., F.R.C.A., F.A.N.Z.C.A.‡*



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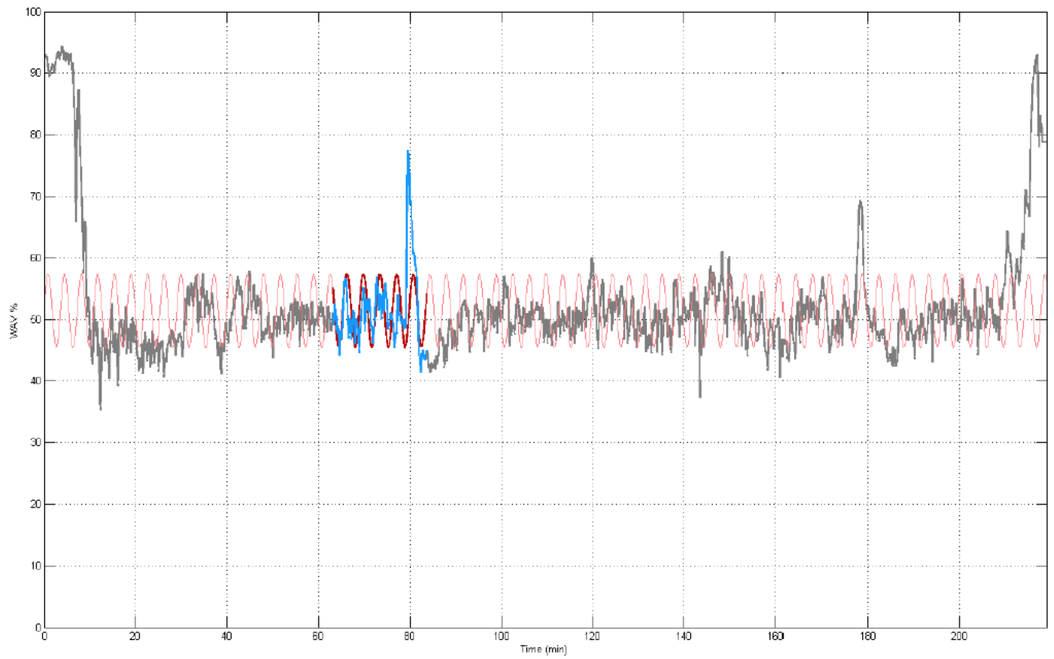
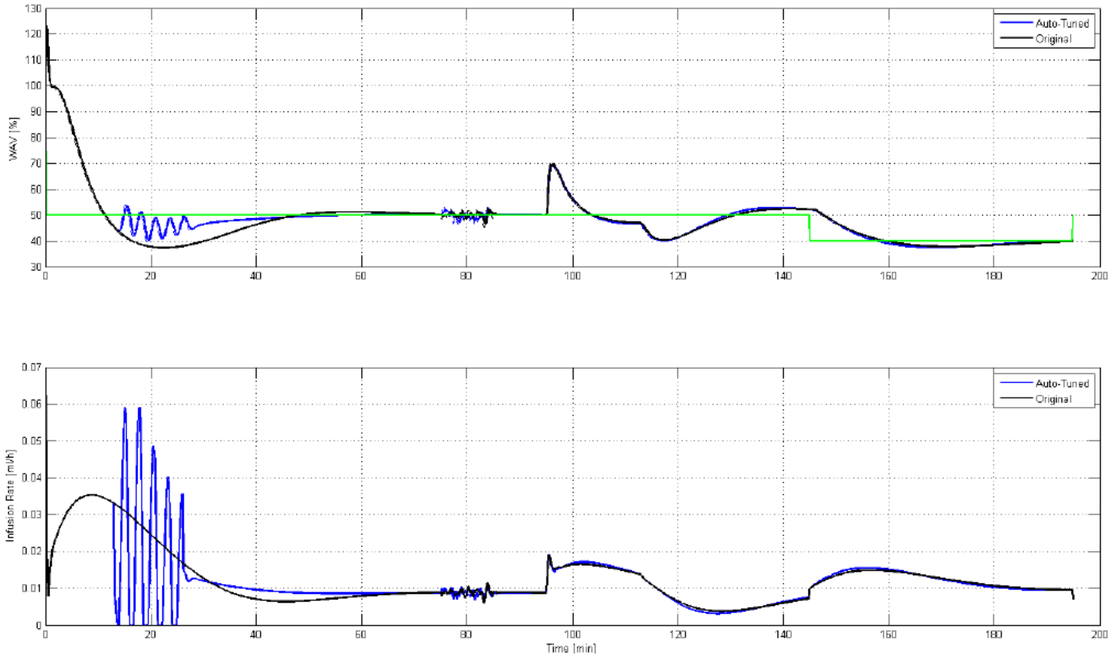
Oscillation Detection

- Automatic oscillation detection followed by controller retuning





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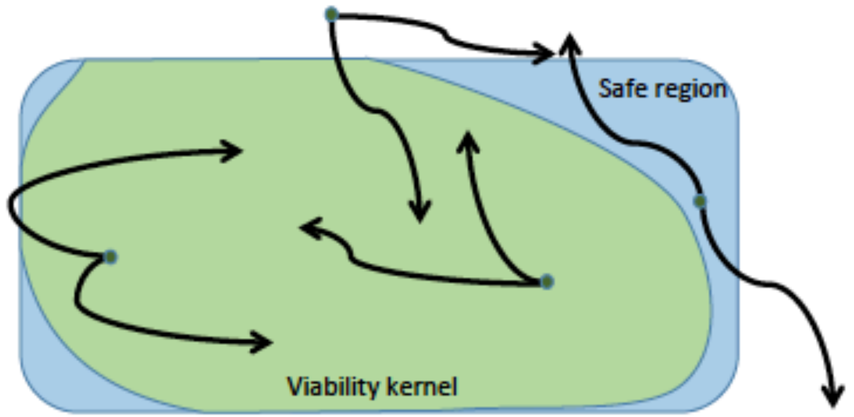
Safety Preserving Control

Viability kernel (guarantee of safety):

$$Viab_{[0,\tau]}(\mathcal{K},\mathcal{U}) = \{x(0) \in \mathcal{K} |\ \exists u(t) \in \mathcal{U}\ s.t.\ x(t) \in \mathcal{X},\ \forall t \in [0,\tau]\}.$$



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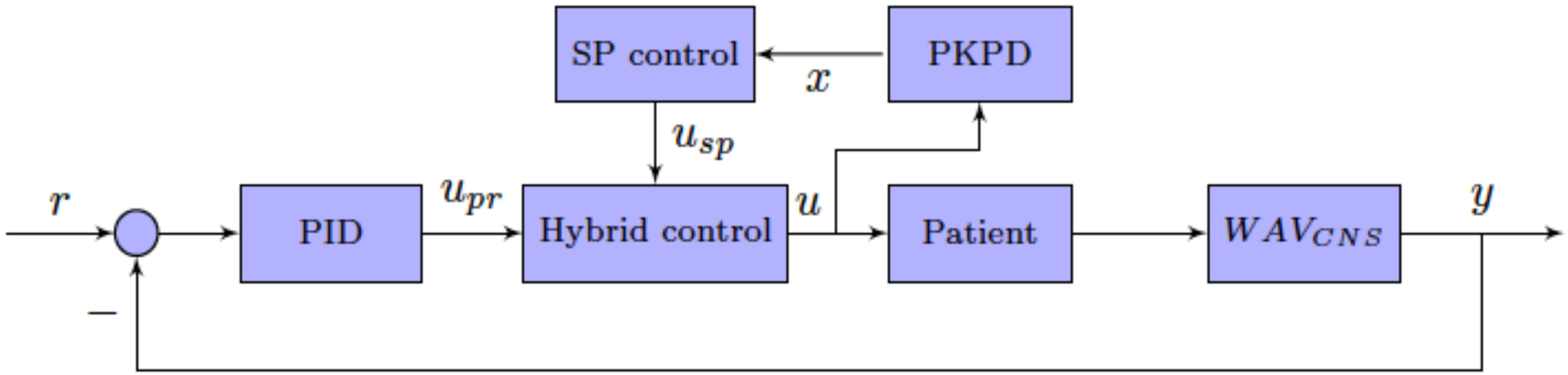
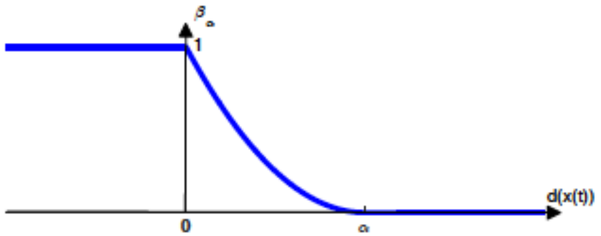
Safety Preserving Control





β_α as a function of $d(x(t))$.

$$u(t) = \begin{cases} u_{pr}(t), & x(t) \in \breve{Viab}_{[t,\tau]}(\mathcal{K}, \mathcal{U}, X); \\ u_{sp}(t), & x(t) \notin \breve{Viab}_{[t,\tau]}(\mathcal{K}, \mathcal{U}, X). \end{cases}$$

$$u(t) = (1 - \beta_\alpha) u_{pr}(t) + \beta_\alpha u_{sp}(t).$$

We specify β_α as follows:

$$\beta_\alpha = \begin{cases} 0 & , \quad \alpha < d(x(t)); \\ \left(\dfrac{\alpha - d(x(t), t)}{\alpha} \right)^2 & , \quad 0 < d(x(t)) \leq \alpha; \\ 1 & , \quad d(x(t)) \leq 0; \end{cases}$$

Yousefi M, vanHeusden K, Mitchell I, Ansermino JM, Dumont GA,"A Formally-Verified Safety System for Closed-Loop Anesthesia ", 20th IFAC World Congress, Toulouse, France, July 9-14, 2017.

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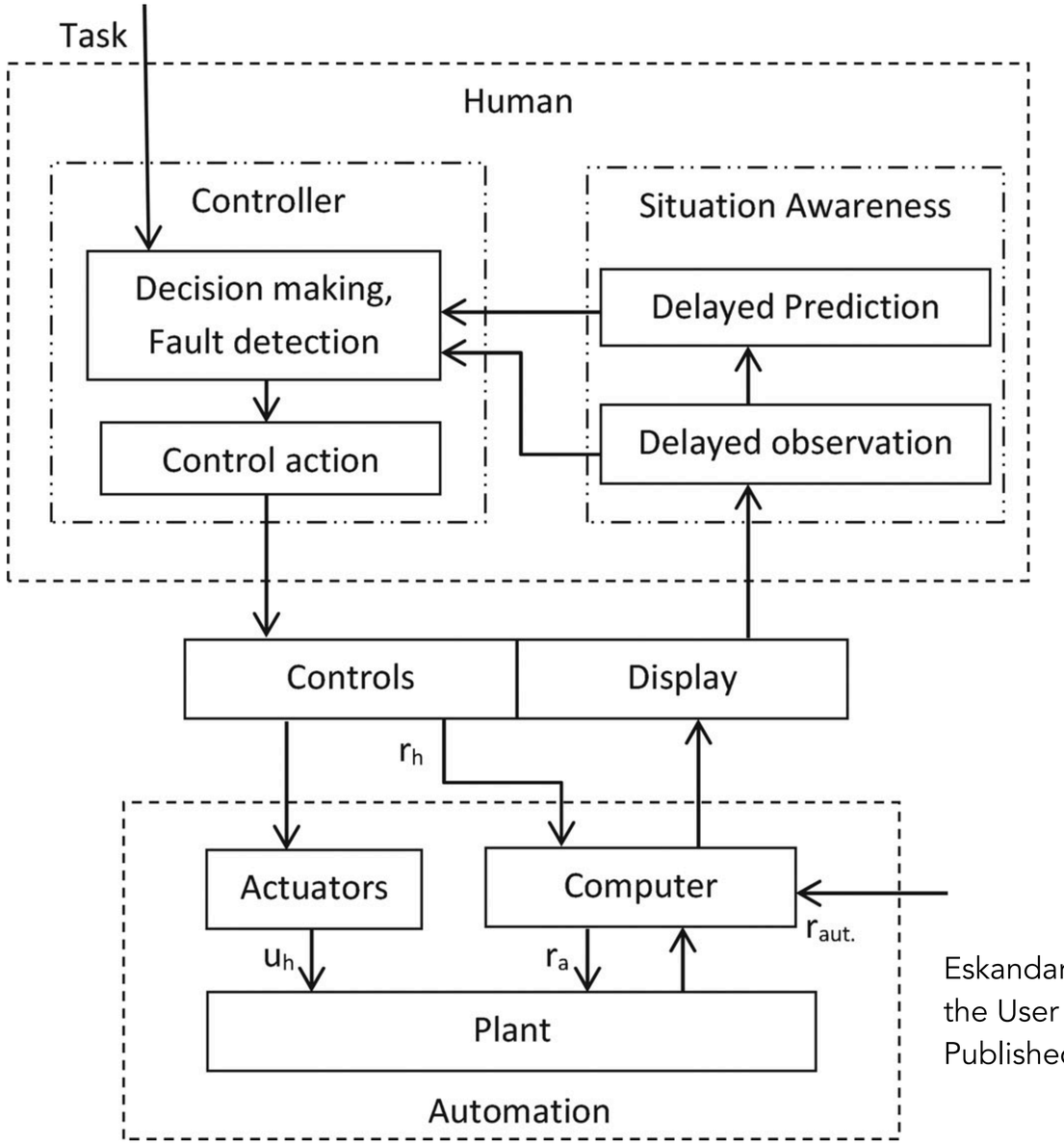
Ensuring Situational Awareness



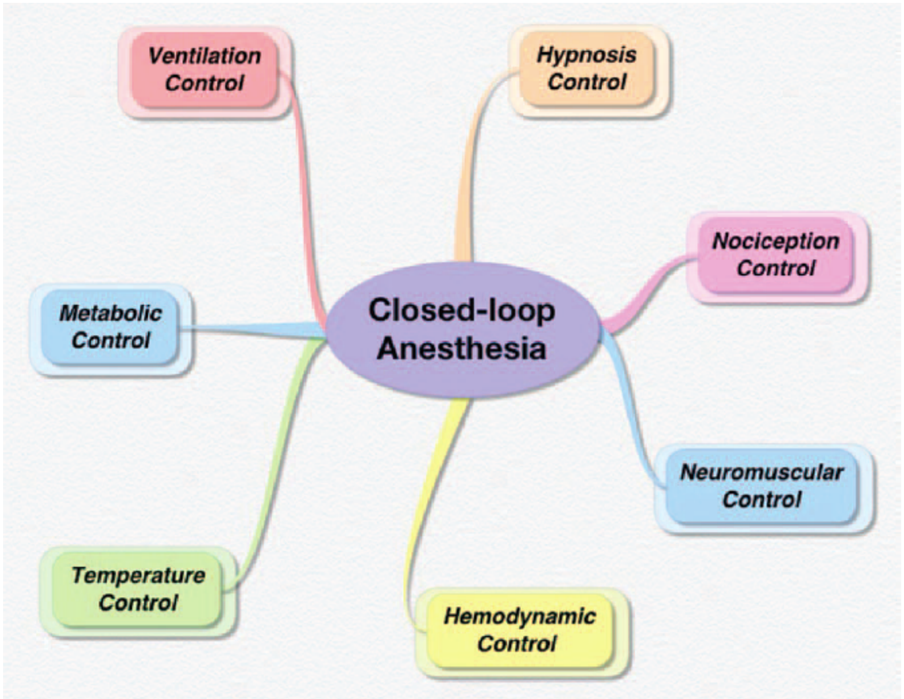
- Determining the information that needs to be displayed to ensure situational awareness
- Modelling the human observer
- Using theory of functional observers
- Again **uncertainty** poses major challenges

Eskandari N, Dumont GA, Wang ZJ (2014). An Observer/Predictor-Based Model of the User for Attaining Situation Awareness. IEEE Trans. on Human-Machine Systems, Published online, Nov. 2014. DOI: 10.1109/THMS.2014.2382475

Conclusions

- Automatic, safe closed-loop induction and maintenance technically feasible
- Robustly tuned PID gives adequate control performance for control of depth of hypnosis in children and adults
- Use of formal methods for design of safety systems (fallback modes)
- Rigorous hardware/software integration & software engineering

Future Development



- Multi-drug, multi-loop systems
- Integration and interoperability issues
- Need to reflect clinical priorities
- Human-in-the-loop issues: anesthesiologist as co-pilot
- Interactions, **emergent behaviours** in “cyberphysiological systems” can be counterintuitive and need to be understood

Thank you!

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