

# Closing the Loops in Biomedical Informatics

## From Theory to Daily Practice

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### Summary

**Objectives:** This article presents the 2009 selection of the best papers in the special section dedicated to biomedical informatics and cybernetics.

**Method:** Synopsis of the articles selected for the IMIA yearbook 2009

**Results:** Five papers from international peer reviewed journals were selected for this section. Most of the papers have a strong practical orientation in clinical care. And this selection gives a good overview of what is done with "closing loop" approach, particularly during the year 2008.

**Conclusion:** While quite mature for some clinical applications such as mechanical ventilation, it remains a challenge where rules for the decision system could be difficult to identify due to the number of variables. More complex systems with greater Artificial Intelligence approaches will certainly be the next trend for closed-loop applications.

### Keywords

Closed-loop, clinical care, cybernetic, control theory, feedback

Yearb Med Informatics 2009: 37-9

## Introduction

Attempting to close loops is not something new in human history. Babylonians were controlling their irrigation systems by using flood gates and float in a feedback control mode [1, 2, 3]. When the water level became too low, the link between the float and sluice gate caused the gate to open wider. Nowadays, the most common example of closed-loop, known by everyone, is the interaction system between thermostat and a furnace to control a room temperature in an autonomous way. In the field of clinical use, the first application of closed-loop approach was identified for anesthesia in 1950 when Bickford used EEG signal to control the infusion of thiopental [1]. Currently more mature, closed-loop control is used daily in very practical applications, such as mechanical ventilation, blood pressure and anesthesia delivery. The most cited advantages of such closed-loop applications are the reactivity of the system, the safety of the treatment and the reduction of costs. However some barriers could still exist such as the changing responsibilities of clinicians and the reliability of the sensors used [4]. Apart from the clinical usage of closed-loop approach, there are numerous related research and applications in the domain of machine learning and fuzzy logic in biomedical informatics which can be used in decision system, text mining and data mining applications [5, 6]. But today, one of the most promising uses of controlled loop paradigm is certainly in the mobility context where the care is user oriented independently of the space and the time [7].

## About the Paper Selection

The selection of the best papers for the special section 'Closing the loops In Biomedical Informatics' follows the tradition of previous Yearbooks. Five papers were selected and a brief content summary can be found in the following appendix.

These five papers give an overview of the state of the art applications and research which use the closed-loop paradigm. Most of the paper are very practical and prove that this approach is very useful for daily usage and more particularly in the clinical domain. These also demonstrate a maturity of these applications. However some challenges still remain depending on the final medical application such as the promising artificial pancreas [8]. The first paper [9] is pragmatic and shows an interesting way to analyze the cost-benefit relationship of a closed-loop diabetes therapy. The next article [10] presents a patient-centered care application which is currently a very active field in health to prevent and better treat the patient anywhere at any time. The third paper [11] presents an original approach to enrich a protein knowledge base by also adding links to diseases. The fourth selected paper by Stead [12] gives a clear overview of closed-loop clinical applications, based on a well described model. The last article [13] describes an exhaustive evaluation of intelligent decision support systems for mechanical ventilation and, as a consequence, gives an overview of closed-loop approaches in this context.

## Conclusions and Outlook

Although the closed-loop approach is still open in terms of new medical applications and more complex decision systems, these five selected papers demonstrate the maturity of closed-loop approaches. They focus more on questions of cost or technological choices rather than on feasibility, efficiency and reliability of such a system. Some challenges still remain since new application domains require taking into account more heterogeneous variables. Patient-centered care at the age of mobile connectivity is one of these interesting challenges.

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**Table 1** Best paper selection of articles for the IMIA Yearbook of Medical Informatics 2009 in the section 'Closing the Loops in Biomedical Informatics'. The articles are listed in alphabetical order of the first author's surname.

Section
<b>Closing the Loops in Biomedical Informatics</b>
<ul style="list-style-type: none"> <li>▪ Bott OJ, Hoffmann I, Bergmann J, Gusew N, Schnell O, Gómez EJ, Hernando ME, Kosche P, von Ahn C, Mattfeld DC, Pretschner DP. HIS modelling and simulation based cost-benefit analysis of a telemedical system for closed-loop diabetes therapy. <i>Int J Med Inform</i> 2007 Dec;76 Suppl 3:S447-55.</li> <li>▪ Conley EC, Owens DR, Luzio SL, Subramanian M, Ali AS, Hardisty A, Rana O. Simultaneous trend analysis for evaluating outcomes in patient-centred health monitoring services. <i>Health Care Manag Sci</i> 2008 Jun;11(2):152-66.</li> <li>▪ Mottaz A, Yip YL, Ruch P, Veuthey AL. Mapping proteins to disease terminologies: from UniProt to MeSH. <i>BMC Bioinformatics</i> 2008 Apr 29;9 Suppl 5:S3.</li> <li>▪ Stead WW, Patel NR, Starmer JM. Closing the loop in practice to assure the desired performance. <i>Trans Am Clin Climatol Assoc</i> 2008;119:185-94; discussion 194-5.</li> <li>▪ Tehrani FT, Roum JH. Intelligent decision support systems for mechanical ventilation. <i>Artif Intell Med</i> 2008 Nov;44(3):171-82.</li> </ul>

- Stead WW, Pater NR, Starmer JM. Closing the loop in practice to assure the desired performance. *Trans Am Clin Climatol Assoc* 2008;119:185-94; discussion 194-5.
- Tehrani FT, Roum JH. Intelligent decision support systems for mechanical ventilation. *Artif Intell Med* 2008 Nov;44(3):171-82. Epub 2008 Sep 2.

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## Appendix: Content Summaries of Selected Best Papers for the IMIA Yearbook 2009, Section on Closing Loops in Biomedical Informatics\*

**Bott OJ, Hoffmann I, Bergmann J, Gusew N, Schnell O, Gómez EJ, Hernando ME, Kosche P, von Ahn C, Mattfeld DC, Pretschner DP**  
HIS modelling and simulation based cost-

\* The complete papers can be accessed in the Yearbook's full electronic version, provided that permission has been granted by the copyright holder(s).

### benefit analysis of a telemedical system for closed-loop diabetes therapy

*Int J Med Inform* 2007;76 Suppl 3:S447-55

Telemedical systems are often characterized by high investments and high regular costs. This article shows that an original telemedical system for closed-loop diabetes therapy has cost benefits compared with current standards of diagnosis or treatment. This paper focuses more on the HIS modeling and simulation based cost-benefit analysis than the closed-loop system (INCA) presented here.

The idea of INCA is that a Smart assistant controls the insulin pump using a closed-loop algorithm. This system is also supervised remotely (remote-loop) by a physician who monitors glucose metabolism. The authors have proven that it is possible to use modeling and simulation based approaches originally developed for system analysis and design to conduct cost analyses of telemedical systems. The presented approach produces an estimation of a lower limit for cost savings concerning diabetes treatment related complications within a 30-year time frame. However the authors note that further work is needed to include indirect and intangible costs in this study.

**Conley EC, Owens DR, Luzio SL,**

**Subramanian M, Ali AS, Hardisty A, Rana O**  
**Simultaneous trend analysis for evaluating**  
**outcomes in patient-centred health moni-**  
**toring services**

**Health Care Manag Sci 2008 Jun;11(2):152-66**

One interesting way to address patient-centred care is to use a closed-loop approach. At the age of mobile connectivity, this kind of approach is suitable and this paper argues in this direction. This article presents research of an information system, the Healthcare@home system. The goal of this system is to enable 'near real time' risk analysis for disease early detection and prevention. Here, the used model comes from inter-enterprise computing and is applied to healthcare situations which are patient centered and contiguous across clinic, home and mobile locations. The discussed closed-loop approach is shown as an improvement in healthcare intervention outcomes, patient safety, decision support, objective measurement of service quality and a way to provide inputs for quantitative healthcare modeling. This paper is also architecture oriented and the Service-Oriented Architecture is especially presented.

**Mottaz A, Yip YL, Ruch P, Veuthey AL**

**Mapping proteins to disease terminologies:**  
**from UniProt to MeSH**

**BMC Bioinformatics 2008 Apr 29;9 Suppl 5:S3**

This article presents a useful initiative in the domain of biomedical informatics. The keyword of this paper is certainly interoperability: it shows how the authors have created a possible gateway between the proteins from the UniProt KnowledgeBase and the medical resources. The presented system is able to map disease names extracted either from UniProtKB entry or from corresponding OMIM to the MeSH. The evaluation of 200 diseases shows that the mapping system obtains respectively 86% and 64% in terms of precision and recall. Applied on more than 3'000 diseases, the clinicians and researchers can navigate from disease to genes and from genes to diseases in an efficient way.

**Stead WW, Pater NR, Starmer JM**

**Closing the loop in practice to assure the de-**  
**sired performance**

**Trans Am Clin Climatol Assoc 2008;119:185-**  
**94; discussion 194-5**

This pedagogical paper gives a clear overview of closed-loop approaches in the healthcare domain. The original approach developed in this paper is made of 3 main components, 1/ an explicit "end-to-end" plan", 2/ a record of what is actually done as it is done and 3/ an instant display of the status of the patient against their plan. Fur-

thermore the specificity of the approach is to strongly integrate the clinical team into the closed-loop. The goal is to reach the point where this clinical team does in practice what they want to do 100% of the time. The instant feedback to the clinician is provided in the form of a process control dashboard. As a practical example, the author gives examples of this approach from the work done with ventilator management in Vanderbilt University Medical Center's intensive care units.

**Tehrani FT, Roum JH**

**Intelligent decision support systems for me-**  
**chanical ventilation**

**Artif Intell Med 2008 Nov;44(3):171-82**

Closed-loop approaches in mechanical ventilation system certainly represent the lion share of publications in the domain. And even if the author indicates a focus on Intelligent Decision Support Systems (IDSSs) instead of the closed-loop techniques, this paper gives an entire overview of the IDSSs history for mechanical ventilation from 1985 to the present and an interesting view of closed-loop approaches in this context. The presented taxonomy of the IDSS is composed of the basis structure (rules-based, model-based), ventilation models, patient types, optimized parameters and type of technology (open/closed-loop).