caOBNET: Objective Bayesian Nets for Integrating Cancer Evidence: A Systems Biology Approach

A collaboration between the University of Kent Centre for Reasoning and the University College London Cancer Institute

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Cancer treatment decisions should be based on all available evidence. But this evidence is complex and varied: it includes not only the patient's symptoms and expert knowledge of the relevant causal processes, but also clinical databases relating to past patients, databases of observations made at the molecular level, domain knowledge embodied in medical ontologies, and knowledge encapsulated in medical informatics systems such as argumentation systems. What is needed is a principled way of integrating these evidence sources.

Objective Bayesian nets offer a principled path to evidence integration. Objective Bayesianism is a theory that models evidence using probabilities. These probabilities – e.g. the probability of recurrence of a patient's cancer; the probability that the patient will respond to treatment – are invaluable for making treatment decisions. An objective Bayesian net is a practical device for representing and calculating these probabilities. By building an objective Bayesian net one can integrate disparate evidence sources.

The goal of this project is to implement this approach and to analyse its performance. We are particularly keen to investigate the way in which objective Bayesian nets can be used to combine:

- qualitative and quantitative knowledge: the integration of quantitative statistical evidence with qualitative ontological, argumentative and common sense evidence is an important goal from the point of view of the knowledge engineer;
- molecular and clinical knowledge: the integration of different levels of analysis is an important goal from the systems biology perspective.

People

Team Members

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Writing

Lorenzo Casini, Phyllis McKay Illari, Federica Russo and Jon Williamson: **Models for prediction, explanation and control: recursive Bayesian networks**, Theoria 26(1):5-33, 2011.

> *The Recursive Bayesian Net (RBN) formalism was originally developed for modelling nested causal relationships. In this paper we argue that the formalism can also be applied to modelling the hierarchical structure of mechanisms. The resulting network contains quantitative information about probabilities, as well as qualitative information about mechanistic structure and causal relations. Since information about probabilities, mechanisms and causal relations is vital for prediction, explanation and control respectively, an RBN can be applied to all these tasks. We show in particular how a simple two-level RBN can be used to model a mechanism in cancer science. The higher level of our model contains variables at the clinical level, while the lower level maps the structure of the cell's mechanism for apoptosis.*

Talks

Phyllis McKay Illari: **Recursive Bayesian networks for prediction, explanation and control in cancer science: a position paper**, International Conference on Bioinformatics (Bioinforatics 2010), Valencia, 20-23 January 2010;

Matt Williams: `**Bayesian and Argumentative approaches: Promises & Pitfalls**', at Evidence, Medical Decision Making and Policy: Trials and Tribulations LSE, 16 May 2007.

Jon Williamson: **Epistemic complexity from an objective Bayesian perspective**, at Epistemic complexity, scientific invariants and cultural evolution, Rome Tor Vergata University, 6-7 October 2006.

Sylvia Nagl: `**Objective Bayesian nets for integrating cancer knowledge: a systems biology approach**', at the Workshop on Probabilistic Modeling and Machine Learning in Structural and Systems Biology (Tuusula, Finland, 17-18 June 2006. Video of the talk.

Lorenzo Casini, Phyllis McKay Illari, Federica Russo and Jon Williamson: **Recursive Bayesian networks for prediction, explanation and control in cancer science: a position paper**, Proceedings of the International Conference on Bioinformatics, Valencia, 20-23 January 2010;

> *The Recursive Bayesian Net formalism was originally developed for modelling nested causal relationships. In this paper we argue that the formalism can also be applied to modelling the hierarchical structure of physical mechanisms. The resulting network contains quantitative information about probabilities, as well as qualitative information about mechanistic structure and causal relations. Since information about probabilities, mechanisms and causal relations are vital for prediction, explanation and control respectively, a recursive Bayesian net can be applied to all these tasks.*
>
> *We show how a Recursive Bayesian Net can be used to model mechanisms in cancer science. The highest level of the proposed model will contain variables at the clinical level, while a middle level will map the structure of the DNA damage response mechanism and the lowest level will contain information about gene expression.*

Sylvia Nagl, Matt Williams and Jon Williamson: **Objective Bayesian nets for systems modelling and prognosis in breast cancer**, in Dawn Holmes and L.C. Jain (eds): `Innovations in Bayesian Networks: Theory and Applications', Springer 2008, pp. 131-168.

Cancer treatment decisions should be based on all available evidence. But this evidence is complex and varied: it includes not only the patient's symptoms and expert knowledge of the relevant causal processes, but also clinical databases relating to past patients, databases of observations made at the molecular level, and evidence encapsulated in scientific papers and medical informatics systems. Objective Bayesian nets offer a principled path to knowledge integration, and we show in this chapter how they can be applied to integrate various kinds of evidence in the cancer domain. This is important from the systems biology perspective, which needs to integrate data that concern different levels of analysis, and is also important from the point of view of medical informatics.

Sylvia Nagl, Matt Williams, Nadjet El-Mehidi, Vivek Patkar and Jon Williamson: `**Objective Bayesian nets for integrating cancer knowledge: a systems biology approach**', in Juho Rousu, Samuel Kaski and Esko Ukkonen (eds): Proceedings of the Workshop on Probabilistic Modeling and Machine Learning in Structural and Systems Biology (Tuusula, Finland, 17-18 June 2006), Helsinki University Printing House, 2006, pp. 44-49. Video of the talk.

> *According to objective Bayesianism, an agent's degrees of belief should be determined by a probability function, out of all those that satisfy constraints imposed by background knowledge, that maximises entropy. A Bayesian net offers a way of efficiently representing a probability function and efficiently drawing inferences from that function. An objective Bayesian net is a Bayesian net representation of the maximum entropy probability function. In this paper we apply the machinery of objective Bayesian nets to breast cancer prognosis. Background knowledge is diverse and comes from several different sources: a database of clinical data, a database of molecular data, and quantitative data from the literature. We show how an objective Bayesian net can be constructed from this background knowledge and how it can be applied to yield prognoses and aid translation of clinical knowledge to genomics research.*

Matt Williams and Jon Williamson: `**Combining argumentation and Bayesian nets for breast cancer prognosis**', presented at the Second Workshop on Combining Probability and Logic (Progic2005), 6th-8th July 2005, and in the Journal of Logic, Language and Information, 2006.

Sylvia Nagl: `**Objective Bayesian approaches to biologi-**

cal complexity in cancer‘, the Second Workshop on Combining Probability and Logic (Progic2005), 6th-8th July 2005.

Related Work

Scipath: Systems complexity interface for *pathways* project

Sylvia Nagl: `**Cancer Bioinformatics: From Therapy Design to Treatment**‘, Wiley 2006. Details

Jon Williamson: `**Objective Bayesian nets**‘, in S. Artemov, H. Barringer, A. S. d’Avila Garcez, L. C. Lamb, and J. Woods (eds.): We Will Show Them: Essays in Honour of Dov Gabbay, Vol 2., pp. 713-730, College Publications, 2005.

Jon Williamson: `**Bayesian nets and causality: philosophical and computational foundations**‘, Oxford University Press 2005. Details