

Report on the
**1st Workshop on Biological Networks:
Theory and Applications**

Edinburgh, Friday 8th October 2010
Informatics Forum, School of Informatics
University of Edinburgh

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The First SICSA Workshop on Biological Networks took place in Edinburgh on 8 October 2010. The aim of the workshop was to provide an opportunity for researchers from informatics and related disciplines and from the life sciences to discuss current activities, progress and research opportunities in the area of computational and mathematical analysis of biological networks. With a programme of short talks and breakout discussions, we aimed at creating an informal, friendly atmosphere that would enhance communication between disciplines and ideally initiate new cooperation. The workshop was jointly sponsored by the Scottish Informatics and Computer Science Alliance (SICSA), the Scottish Bioinformatics Forum (SBF). The Scottish Universities Life Sciences Alliance (SULSA) and the Roslin Institute supported the event by advertising it to their members. Through these arrangements, we hoped to be able to reach both the Scottish computing and life science communities.

During planning, we anticipated to have around 25 participants, and to include 8 contributed presentations (15 minutes plus 5 minutes discussion time) as well as one invited lecture. To our surprise and delight, the workshop had 60 registrations (the room capacity), and several more attended during the day, indicating a strong interest in this area. We received a total of 13 submissions for presentations, of which we were able to include ten into the final programme.

The affiliations of the registered participants break down as follows: University of Edinburgh: 35; Heriot-Watt University: 4; University of Dundee: 3; Roslin Institute: 3; University of Strathclyde: 3; Edinburgh Napier University: 2; University of Glasgow: 2; BioSS: 2; University of St Andrews: 2; University of Stirling: 1; University of Aberdeen: 1; MRC Human Genetics Unit: 1; Pfizer: 1.

The ten short talks covered a broad range of topics, including new methods for network analysis, modelling and applications in areas ranging from protein interactions to brain networks. In the first presentation, Dirk Husemeier introduced recent developments in Dynamic Bayesian Networks for inferring regulatory networks, and the potential of synthetic biology to provide ground truth data for algorithm evaluation. Next, Rainer Breitling presented applications of network inference tools for metabolic networks from mass spectrometry data, and highlighted the challenges in the analysis of the complicated resulting structures. In the last talk in the first session, Clare Lee presented a technique for network reordering based on non-negative matrix factorisation. The second session started with Julien Ollivier, who introduced a rule-based simulation method that offers reduced complexity over traditional methods in situations where the configuration space becomes very large. Then, Seymour Knowles-Barley

talked about current research on drosophila brain networks ranging from protein networks in individual neurons to the networks connecting whole brain areas, and the challenge in connecting these different levels. The second session ended with a talk by Ernesto Estrada on a method to quantify heterogeneity in networks. In the final session, Hongwu Ma presented a very efficient method for network decomposition. Then, Emma Hart introduced her work on immune system networks, and posed the question how network topology could be related to its function. Next, Desmond Higham introduced a method for the analysis of directed networks. An inspiring talk on the philosophy of modelling by Derek Gatherer concluded the short talks sessions.

Overall, we feel the workshop was very successful and achieved its main aims. This is supported by the very positive feedback we received (see section 2). There is definitely a need for this kind of event, and we plan to repeat the workshop on a yearly basis. These future events will try to draw an even stronger participation from researchers in biology, as was recommended several times in the feedback forms, to further strengthen links between the computational and biological communities.

1 Breakout discussions

During the break out discussions (see programme in section 3) the workshop participants were randomly split into five groups and given the following questions as material for discussion:

1. What are the main limiting factors in collaborations between theoreticians and experimental biologists on network problems? How could these be avoided?
2. What important problems theoreticians should attempt to tackle, and how could these be solved in collaborations with biologists?
3. Has this workshop exposed new interesting scientific questions or methodologies you may work on/use in future, or let to new potential collaborations?

During the feedback session, the following responses were collected:

Group 1 :

1.
 - Access to data can be difficult as biologists can be quite protective.
 - Data can be qualitative in nature and may contain substantial noise.
 - Communication is a limiting factor as the different communities have different languages.
 - Modellers don't necessarily understand their own artifacts well enough to communicate effectively with biologists.
 - Theoreticians may desire impossibly long or expensive experiments in order to validate models.
 - Trust takes time to establish, and experimentalists would like to see results to be convinced of the utility of modelling.

- Can biology be like Physics, where theory often precedes experiments? Perhaps yes, but this depends on the specific area.
2. Disease modelling and dynamic networks were found to be important areas.

Group 2 :

1.
 - Language problem, e.g. as between statisticians and machine learners. This was found to be even harder between CS and biology.
 - Concepts from CS are very abstract from biological perspective and biological problems are too vague from CS perspective.
 - How to tackle this? Education, e.g. at conferences. Communities should help each other to appreciate particular methodologies and problems. At University level, 1st year of PhD can be used to train CS and biologists in the other discipline.
 - Obstacles are also that the complexity of the other discipline are not appreciated, and impatience results: e.g. data analysis does not just take a few minutes.
2. Important problems are application-based, e.g. disease. A general problem is network inference, trying to be constrained by the physics of the system. Collaboration between biologists and theoreticians are important, but it is possible that theoretical concepts are not developed without a critical mass of theoreticians. Focussing on a collaboration may not give best results. Blue sky research is important.
3. Yes

Group 3 :

1.
 - Again the problem of language, terms, definitions was noted, and the need to find a common tongue was emphasised, but it was found that this takes time.
 - Also intimidation by lack of knowledge of other discipline may pose a problem.
 - How to avoid this? Interdisciplinary education. Even basic understanding of biology for CS can be helpful. Mutual trust, respect are necessary.
2. Can there be a true answer to this question? The important question is the one that we are working on. Dynamic networks, structural properties of networks were mentioned. Biologists propose a problem, and theoreticians hopefully find it interesting enough to work on.
3. Yes

Group 4 :

1.
 - Chasing data. Biologists not happy to share data until publication.
 - Tools are available but not always user-friendly.
 - It is hard to get experimental biologists to go to a meeting like this.
 - Biologists tend to like to use tried-and-tested tools

- Solutions: Education. Not just collaboration, but people trained in both disciplines. Also, theoreticians seem to be on the receiving end. They depend on data, but are not involved in writing grants. Perhaps they could outsource data collection?
2. Disease. Any disease is multi-scale, e.g. Diabetes, which has daily changes in variables, but also longer term ones.
 3. (1) The metabolite presentation. Ideas of using mass-spec to identify how metabolites are interacting. (2) Idea of breaking networks down.

Group 5 :

1. A difference of mentalities was noted:
 - Biologists don't always provide quantitative descriptions.
 - Lack of understanding, e.g. biologists are not aware of capabilities and limitations of computational methods.
 - Most of time, biologists lead projects
2. Theoreticians should focus on theoretical part of work, not necessary be at the service of biological problems.
3. An explosion of questions and methodologies was noted, and the group was optimistic about collaborations.

2 Feedback report

In the feedback form, participants were asked to judge the workshop content and organisation, to comment on a potential future workshop and to suggest other workshop themes. Ratings were given on a scale from 1 (poor/strongly disagree) to 5 (excellent/strongly agree). We received 27 completed feedback forms.

Overall, the workshop was judged very positively. A median score of 4 was given in response to the question *Has the workshop fulfilled your expectations?*. The scientific content was judged with median score 4, and the organisation with a median score of 5. All 27 returned forms indicated that the workshop should be repeated next year. Several comments suggested that it would be useful to have more attendees from biology in a future event.

Regarding a future workshop, we asked several questions how the programme should be modified. There was strong support for including posters, software demonstrations and to have more collaborative activities (median scores 4). A longer workshop, more invited speakers, longer talks or an international workshop were judged as less relevant (median scores 2, 3, 3 and 3, respectively).

Eleven participants wished to have more specialised workshops in addition. The following suggestions were made:

- Genetics and inference
- Gene or protein/protein interaction modelling and epidemiological networks
- Disease

- Network analysis, tools and algorithms, including other fields: sociology, ecology
- A more introductory workshop focusing on basic mathematical and computational language and problems in biological networks
- Larger networks, epidemiology/social
- Proteomics
- Machine learning/probabilistic modelling/large scale statistics
- Connectome networks in neuroscience
- Darwinian evolution of networks

3 Final workshop programme

09:00-09:20 registration and coffee (G.03)

9:20 welcome

09:30-09:50 Dirk Husmeier, Biomathematics and Statistics Scotland (BioSS)

Inferring gene regulatory networks with non-stationary dynamic Bayesian networks

09:50-10:10 Rainer Breitling, University of Glasgow

Inferring metabolic networks from high-accuracy metabolomics

10:10-10:30 Clare Lee, University of Strathclyde

Reordering multiple networks simultaneously

10:30-11:00 coffee (G.03)

11:00-11:20 Ollivier Julien, McGill / University of Edinburgh

Scalable rule-based modelling of allosteric proteins and biochemical networks

11:20-11:40 Seymour Knowles-Barley, University of Edinburgh

Fruit Fly Brain Networks

11:40-12:00 Ernesto Estrada, University of Strathclyde

On heterogeneity of biological networks

12:00-13:30 lunch (Mini Forum 1) and coffee (G.03)

13:30-13:50 Hongwu Ma, University of Edinburgh

A new method for the decomposition of biological networks

13:50-14:10 Emma Hart, Edinburgh Napier University

Topological constraints on the function of immune networks

14:10-14:30 Desmond Higham, University of Strathclyde

Computational Methods in Network Science

14:30-14:40 Derek Gatherer, University of Glasgow, MRC Centre for Virus Research

Modelling versus Realization: Rival Philosophies of Computational Theory in Systems Biology

14:40-15:20 break out discussions

15:20-15:50 plenum discussion

15:50-16:10 coffee break

16:10-17:10 Lecture by Anne Smith, University of St Andrews

Using Bayesian networks to explore complex biological systems: genes, brains, and ecosystems