

## PM11: ISMB 2006 Tutorial

### Title:

Computational Biology of Post-transcriptional Gene Regulation: At the Interplay of Genomes, Networks and Evolution

### Topic Area:

- Sequence Analysis (40%)
- Comparative Genomics (30%)
- Systems Biology (including Pathways and Networks) (15%)
- Machine Learning and Artificial Intelligence (15%)

### Main Presenter:

- Uwe Ohler, PhD
- Assistant Professor, Duke University
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- Recent Teaching Experience:
  - Duke University: Section on RNA sequence analysis in the Genome Informatics graduate class in the Computational Biology Program (Spring 2005).
  - Massachusetts Institute of Technology (MIT): undergraduate advanced seminar on *Genomics and Bioinformatics of Gene Expression* (Spring 2003).
- Earlier tutorial presentations:
  - MIT Independent Activities Period: Tutorial on *What can computers tell me about my gene and protein* (Spring 2003);
  - Contributor, ISMB 1999 Tutorial on *The annotation of a complex eukaryotic genome*. Presenters: Martin Reese and Suzi Lewis.

### Second presenter:

- Dirk Holste, PhD
- Group Leader Computational Biology, Research Institute of Molecular Pathology and Ludwig Boltzmann Institute of Functional Genomics
- Dr Bohr Gasse 3-5, A-1030, Vienna, Austria
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- Teaching experience:
  - MIT Postdoctoral Association Vice President for Research Activity: Facilitator for *Research Practice Seminar* (Spring 2005).
  - MIT Independent Activities Period: Tutorial on *The Postdoctoral Scholar's Experience* (Spring 2005).

- Humboldt University: undergraduate courses in bioinformatics, dynamical systems, and stochastic processes (1999-2002).

**50-word abstract:**

To control gene expression under diverse contexts, it is exerted as a complex network at the level of both transcription and post-transcription. We propose an integrated tutorial on the biology of and current computational approaches for post-transcriptional gene regulation, with a focus on (alternative) splicing of mRNAs, an essential step of RNA processing in metazoans.

**Tutorial level:**

Intermediate level.

**Prior knowledge required:**

- No previous experience in the specialty area required.
- Because of the range of topics addressed, it helps if people have a basic knowledge of either sequence analysis (i.e., “What is a motif?”) or relevant aspects of molecular biology.

**Suitability of this tutorial for ISMB:**

- The field of post-transcriptional gene regulation (PTGR) has gained a lot of attention in recent years, including alternative pre-mRNA splicing, micro-RNAs, and RNA-binding proteins. All these areas of research have a much broader effect on gene regulation than previously anticipated, and we are now in the situation to have a wealth of data at our disposition. This is therefore a current growth area and an exciting field for computational biology.
- We will provide an overview of different aspects of PTGR affecting the messenger RNA, with a focus on splicing and alternative splicing. This should allow attendees to “get the bigger picture” as well as to go in-depth in one particular aspect. We do not intend to give a comprehensive literature review, but rather to look at exciting recent examples.
- The tutorial will be aimed at computational biologists who are new to or interested in this exciting area, as well as computer literate biologists who want to understand more about the computational aspects. The audience is expected to consist of a cross-section of graduate students and researchers.
- Both main and second presenters have been actively working in this area for several years, in part jointly as postdoctoral associates in one of the top computational RNA labs (Chris Burge’s lab at MIT), and are able to provide first-hand insights and examples of up to date research.

**Profile of Main Presenter**

- Assistant Professor in Computational Biology at Duke University’s Institute for Genome Sciences and Policy, with a current group of 1 postdoc, 2 graduate students, 2 graduate rotation students, and one staff bioinformatician.
- More than eight years of progressive experience in pattern recognition and machine learning, sequence analysis, comparative genomics, evolution and computational-biological modelling.
- Lectured undergraduate computer science machine learning classes (1997-1999) and undergraduate and graduate computational biology seminars (1999,

2003, 2005); supervision of undergraduate and graduate research projects in computational biology of sequence analysis and comparative genomics (1999-current).

- Demonstrated abilities to abstract, structure and present complex facts, as stated in publication record in international journals and conferences and invited presentations. Guest associate editor for PLoS Computational Biology.
- Active member of ISCB (since 1999), the ISMB program committee (in 2005), the curriculum and student advisory committees of the Duke Graduate Program in Computational Biology and Bioinformatics (since 2005), and of the program committee for the International Workshop on Genome Annotation Analysis and Alternative Splicing (Berlin, 2004).

### **Profile of Second Presenter**

- Group leader in genomics and computational molecular biology with more than six years of progressive experience in genome and transcriptome quantitative analysis, comparative genomics, evolution and mathematical-biological modelling.
- Lectured undergraduate and graduate block-seminar courses (1999-2002); supervision of undergraduate and graduate research projects in computational biology of RNA sequence analysis and comparative genomics (2003-2005).
- Demonstrated abilities to abstract, structure and present complex facts, as stated in publication record in international journals and conferences.
- Active member of ISCB (since 2001), of MIT's Computational Systems Biology Initiative (since 2005), and of organizing committee for International Workshop on Biophysics and Bioinformatics (Berlin, 2001).

### **Tutorial Outline:**

- **Introduction:** Eukaryotic gene structure and levels of gene regulation (*15 mins*)
- **Relevant computational methodology** (*total 30 mins*)
  - RNA Secondary Structure Prediction
  - Sequence Analysis and Machine Learning
- **Concepts of experimental methodology** (*total 15 mins*)
  - Gene level: Mutagenesis, RT-PCR. Northern Blotting, Sequencing
  - Genome-wide: Expression Arrays and Splicing-specific Arrays
- **RNA Splicing and Alternative Splicing** (*total 1.5 hrs*)
  - Biology and Signals (15 mins)
  - Alternative pre-mRNA Splicing (30 mins)

*Break*

- Sequence Alignments and Databases (*15 mins*)
- Transcript-based Prediction of (Alternative) Splicing (*30 mins*)
- Available Resources
- **Overview of other mechanisms** (*total 30-45 mins*)
  - UTRs and RNA-binding Proteins (*15 mins*)
  - Micro-RNAs: Genes and Targets (*15 mins*)
  - Connections and Networks (*15 mins*)
- **Discussion** (*total 15-30 mins*)