

BIOGRAPHICAL SKETCH

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NAME: Ann Loraine

eRA COMMONS USER NAME (credential, e.g., agency login): aloraine

POSITION TITLE: Associate Professor of Bioinformatics and Genomics

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Texas, Austin	B.A.	05/89	Plan II (Liberal Arts)
University of Texas, Austin	B.S.	12/89	Zoology
University of California, Berkeley	Ph.D.	12/96	Molecular and Cell Biology
University of California, Berkeley	Postdoc	12/98	Bioinformatics

A. Personal Statement

I have 18+ years experience designing and developing visualization software for genomics, starting with my postdoctoral work at the Berkeley Drosophila Genome Project (BDGP), where I wrote visualization applets in Java for the BDGP Web site and FlyBase. Following my postdoc, I worked as a software engineer at Neomorphic, founded by BDGP alumni, where I designed and wrote the Gene Editor component of Annotation Station, which The Institute for Genomic Research used to annotate the Arabidopsis genome. When Affymetrix bought Neomorphic in 2001, I re-joined the company as a Bioinformatics Scientist. At Affymetrix, I published articles on probe set annotation, alternative splicing, and genome data visualization. After returning to academia in 2004, I worked with former colleagues at Affymetrix to launch the open source GenoViz project, which included Integrated Genome Browser and its graphics library the GenoViz Software Development Kit. In 2008, funding from the National Science Foundation enabled my team and me to develop and support IGB, transforming it from an Affymetrix-focused product into a general-purpose, desktop genome browser with thousands of users. Further funding from the NIH enabled us to continue developing the software and supporting IGB users. Maintaining and developing Integrated Genome Browser is a major focus of my research group. In addition, we are interested in understanding and developing best practices for building software for expert users – research biologists.

1. Mall T, Eckstein J, Norris D, Vora H, Freese NH, Loraine AE. ProtAnnot: an App for Integrated Genome Browser to display how alternative splicing and transcription affect proteins. *Bioinformatics*. 2016 Apr 7. pii: btw068. [Epub ahead of print] PubMed PMID: 27153567.
2. Freese, N.H., Norris, D.C., & Loraine, A.E. (2016) Integrated Genome Browser: Visual analytics platform for genomics. *Bioinformatics*. 2016 Mar 16. pii: btw069. [Epub ahead of print] PubMed PMID: 27153568.
3. Nicol, J.W., Helt, G.A., Blanchard, S.G., Raja, A., & Loraine, A.E. (2009). The Integrated Genome Browser: free software for distribution and exploration of genome-scale datasets. *Bioinformatics* 25: 2730-2731. PMID: PMC2759552
4. Helt, G.A., Nicol, J.W., Erwin, E., Blossom, E., Blachard, S.G., Chervitz, S.A., Harmon, C., Loraine, A.E. (2009). GenoViz Software Development kit: Java toolkit for building genomics visualization applications. *BMC Bioinformatics* 10: 266. PMID: PMC2746221
5. Helt, G.A., Lewis, S., Loraine, A.E., & Rubin, G.M. (1998). BioViews: Java-based tools for genomic data visualization. *Genome Research*, 8: 291-305. PMID: PMC148103

B. Positions and Honors

Positions

1997-1998	Post-doc, Berkeley Drosophila Genome Project, UC Berkeley
1998-1999	Programmer/Analyst, Berkeley Drosophila Genome Project, UC Berkeley
1999-2000	Bioinformatics Software Engineer, Neomorphic, Inc., Berkeley, CA
2000-2003	Bioinformatics Scientist, Affymetrix, Inc., Emeryville, CA
Spring, 2004	Instructor for Introduction to Statistics for Bioinformatics, Cal State Hayward
Summer, 2004	Consultant, Affymetrix, Inc., Emeryville, CA
2004-2008	Assistant Professor of Genetics, University of Alabama at Birmingham
2004-2008	Assistant Professor of Biostatistics, Section on Statistical Genetics, UAB
2004-2008	Associate Scientist, UAB Comprehensive Cancer Center
2007-2008	Assistant Adjunct Professor, Computer and Information Sciences, UAB
2008-	Associate Professor, Dept. of Bioinformatics and Genomics, UNC Charlotte

C. Contribution to Science

- 1. Visualization software for genomics.** Software that displays genomic data in interactive formats can help biologists understand data better. My work is based on the premise that maximizing interactivity, navigation speed, ease of use, feature diversity, and extensibility help researchers achieve deeper, more accurate insight into vast datasets from genomics – and avoid costly mistakes. As a postdoctoral trainee at the Berkeley Drosophila Genome Project and FlyBase, I used the newly released Java programming language and an early version of the GenoViz SDK to create interlinked, interactive chromosome and physical map viewers. These were among the first interactive tools in bioinformatics to apply overview-plus-detail and semantic zooming to the display of genome maps. At Neomorphic and Affymetrix I continued this work, contributing to design and development of Integrated Genome Browser and other tools. I continue this work today as leader of the Integrated Genome Browser project. Through my work developing IGB and supporting its thousands of users, my group and I have contributed indirectly to discoveries in diverse fields. More recently, we are contributing to science by transforming IGB into a visual analytics platform that will make it easy for developers to create, test, and deploy new methods for genomic data visualization.
 - a. FlyBase Consortium. (1999). The FlyBase database of the Drosophila Genome Projects and community literature. *Nucleic Acids Res*, 27: 85-88. PMID: PMC148103
 - b. Loraine, A.E. & Helt, G.A. (2002). Visualizing the genome: techniques for presenting human genome data and annotations. *BMC Bioinformatics*. 3: 19. PMID: PMC119855
 - c. Loraine, A.E., Blakley, I.C., Jagadeesan, S., Harper, J., Miller, G., Firon, N. (2015) Analysis and visualization of RNA-Seq expression data using RStudio, Bioconductor, and Integrated Genome Browser. *Methods Mol Biol* 1284:481-501. PMID: 25757788
 - d. Integrated Genome Browser – <http://www.bioviz.org>, <https://bitbucket.org/lorainelab/integrated-genome-browser>
- 2. Alternative splicing and gene function.** Most protein-coding genes in higher eukaryotes contain introns, sequences that are removed from the primary transcript via RNA splicing. In alternative splicing, different regions are removed depending on the cellular context. While a scientist at Affymetrix, I investigated the effects of alternative splicing on protein sequence using mRNA alignments from human and mouse genomes. I found that alternative splicing, promoters, or 3-prime end processing deleted or remodeled conserved regions in around 1/3 of multi-variant genes in high-quality mouse and human datasets. These results, along with requests from customers, prompted Affymetrix to develop “exon arrays” able to detect differential expression of splice variants. To visualize results, I designed a prototype protein domain viewer (ProtAnnot) that shows protein motifs and gene models in the same view. Recently, my group updated and released ProtAnnot as a new IGB App.
 - a. Loraine, A.E., Helt, G.A., Cline, M.S., Siani-Rose, M. (2003). Exploring alternative transcript structure in the human genome using BLOCKS and InterPro. *Journal of Bioinformatics and Computational Biology*. 1(20): 289-306.

- b. Cline, M.S., Shigeta, R., Wheeler, R.L., Siani-Rose, M., Kulp, D., & Loraine, A.E. (2004). The effects of alternative splicing on transmembrane proteins in the mouse genome. *Pac Symp Biocomput*: 17-28.
 - c. Loraine, A.E., McCormick, S., Estrada, A., Patel, K., Qin, P (2013). RNA-Seq of Arabidopsis pollen uncovers novel transcription and alternative splicing. *Plant Physiol* 162: 1092-1109. PMID: PMC3668042
 - d. Mall, T., Eckstein, J., Norris, D.C., Vora, H., Freese, N.H., & Loraine, A.E. (2015) ProtAnnot: an Integrated Genome Browser App for visualizing how alternative splicing and transcription affect proteins. In press at Bioinformatics. Preprint at BioRxiv: <http://www.biorxiv.org/content/early/2015/09/03/025924.1>
3. **Splicing and environmental stress in plants.** Understanding how plants acclimate to environmental stress is critical to maintaining human and animal food supplies in the face of ongoing climate change. My group studies how plant RNA splicing pathways adapt to daily and seasonal fluctuations in temperature, light, and water availability. Toward this end, we study regulation of alternative splicing, estimated to affect between 20 and 50 percent of plant genes. We developed an analysis method that uses RNA-Seq and EST alignments to detect differential splice site use between samples. By applying this method to multiple datasets from our lab and others, we learned that alternative splicing patterns are remarkably uniform across sample types and experimental conditions. For most pairs of alternative splice sites, one site predominates, with the less frequently used site supported by less than 10% of available data. However, we also identified a subset of alternatively spliced genes that are frequently differentially spliced in many experimental settings. Many encode predicted RNA-binding proteins or plant homologs of known splicing regulators in other species. We hypothesize that regulated alternative splicing of these genes help maintain splicing stability in plants, and are testing this idea using genetic approaches in model plant *Arabidopsis thaliana*.
 - a. English, A.C., Patel, K.S., & Loraine, A.E. (2010). Prevalence of alternative splicing choices in *Arabidopsis thaliana*. *BMC Plant Biology* 10:102. PMID: PMC3017808
 - b. Loraine, A.E., McCormick, S., Estrada, A., Patel, K., Qin, P (2013). RNA-Seq of Arabidopsis pollen uncovers novel transcription and alternative splicing. *Plant Physiol* 162: 1092-1109. PMID: PMC3668042
 - c. Liu, R., Loraine, A.E., & Dickerson, J.A. (2014). Comparisons of computational methods for differential alternative splicing detection using RNA-Seq in plant systems. *BMC Bioinformatics* 15; 364. PMID: PMC4271460
 - d. Gupta, V., Estrada, A., Blakley, I., Reid, R., Patel, K., Meyer, M., Anderson, S., Brown, A., Lila, M.A., & Loraine, A.E. (2015). RNA-Seq analysis and annotation of a draft blueberry genome assembly identifies candidate genes involved in fruit ripening, biosynthesis of bioactive compounds, and stage-specific alternative splicing. *Gigascience* 4:5 PMID: PMC4379747
4. **Co-expression to predict gene function.** Public databases contain data from thousands of DNA microarray experiments conducted over many years. These data make it possible to identify groups of genes that are co-expressed at similar levels across many experiments. These co-expressed genes often encode proteins with related functions, such as enzymes in the same metabolic pathway or multi-subunit complex. I used co-expression analysis to investigate coordinate regulation of genes encoding metabolic pathway enzymes in the model plant *Arabidopsis thaliana*. I showed that genes from the same metabolic pathways are highly co-expressed, and that this correlation can identify previously unknown members of the pathway and transcription factors that regulate their expression.
 - a. Wei, H., Persson, S., Mehta, T., Srinivasasainagendra, V., Chen, L., Page, G.P., Somerville, C., Loraine, A.E. (2006). Transcriptional coordination of the metabolic network in *Arabidopsis*. *Plant Physiol* 142:762-774.
 - b. Srinivasasainagendra V., Page, G.P., Mehta, T., Coulibaly, I., & Loraine, A.E. (2008). CressExpress: a tool for large-scale mining of expression data from *Arabidopsis*.
 - c. Loraine, A.E. (2009). Co-expression analysis of metabolic pathways in plants. *Methods Mol Biol* 553:247-264. PMID: PMC1586052
 - d. CressExpress <http://cressexpress.org/> and CressExpress 2.0 prototype <http://test.cressexpress.org/web/> (featuring new data imported from Gene Expression Omnibus, re-designed interface using JavaScript and Apache Lucene for search)

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/ann.loraine.1/bibliography/42894909/public/?sort=date&direction=descending>

D. Research Support

NIH 5R01GM103463-04

07/01/11 - 06/30/16

Continued maintenance and development of software: Integrated Genome Browser and the GenoViz SDK, visualization software for next-generation genomics.

This project develops the Integrated Genome Browser (IGB) and its foundation library of genomics visualization software components, the GenoViz SDK.

Role: Principal Investigator

NSF 1238051

Kieber (PI)

10/01/12 - 09/30/16

Genomic approaches to understanding cytokinin signaling and function in rice.

This project uses integrative genomic and bioinformatics approaches to illuminate how the plant hormone cytokinin influences the number and size of grains that rice plants produce.

Role: Co-Principal Investigator

NSF 1354452

Krizek (PI)

05/01/14 - 04/30/19

Regulation of floral growth and patterning in *Arabidopsis*.

This project investigates the role of conserved, DNA-binding proteins ANT and AIL6 in determining the position and growth pattern of floral organs, using *Arabidopsis* as a model.

Role: Co-Principal Investigator

Completed Research Support

NSF 1022053

Kieber (PI)

09/01/10 - 08/31/15

Arabidopsis 2010: Analysis of the cytokinin-regulated transcriptional network.

Cytokinins in plants govern many aspects of cell growth and division in plants. This project uses integrative genomic approaches to dissect regulatory networks underlying cytokinin responses in plant cells.

Role: Co-Principal Investigator

NSF 0955431

Loraine (PI)

03/01/10 - 02/28/15

Collaborative research: Research Coordination Network in integrative pollen biology.

This project developed a coordinated forum for the pollen research community, facilitating resource sharing, tools development, information exchange, and collaboration.

Role: Principal Investigator