

Ryan Koehler, Ph.D.

Happy Valley, OR 97086

503-964-0810

ryan@verdascend.com

Computational Scientist

Biotechnology, Bioinformatics, Genomics, Data analysis, Software, Molecular design, University-level curriculum development and instruction.

CORE EXPERTISE

- **Broad science background.** Bioinformatics, molecular biology, assay & genomic technologies, data analytics, computer science, computer chemistry.
- **Inventor & leadership roles.** Work has directly led to commercial product lines, publications, trade secrets, patents. Managed groups doing data analysis, machine learning, developing software systems in chemical and biology domains.
- **Software development.** Python, C, Perl, R, Linux (scripting / admin), databases, web. Computational pipelines, algorithms, process automation, testing.
- **Collaboration.** Engage with scientists, engineers, customers, contributing domain expertise, support, troubleshooting. Effectively enable use of new technologies.
- **Teacher and trainer.** University-level course development, custom content & illustration. Classroom and on-line formats targeting technical and lay audiences.
- **Business proprietor,** client interfacing, requirements gathering, project proposals, project management, documentation, reports and technical writing.

PROFESSIONAL EXPERIENCE

- | | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|-----------------------|
| Principal & Owner | VerdAscend Sciences | 2009-Present |
| <ul style="list-style-type: none">• Consultant, focused on biotechnology, design, analytics, software projects.• Bioinformatics: Oligo & assay design, troubleshooting. Machine learning & modeling.• Software: Automation scripts, design & analysis pipelines, software testing. | | |
| Principal Scientist, Bioinformatics | TOMA Biosciences | 2015...Present |
| <ul style="list-style-type: none">• Design and refine probes for targeted NGS somatic (cancer) variant detection system.• Assay, tool and pipeline development, including simulations and machine learning.• Drive bioinformatics (scoring, software) toward CLIA / CAP accredited diagnostic. | | |
| Staff Scientist, Bioinformatics | QuantaLife / Bio-Rad | 2010-2013 |
| <ul style="list-style-type: none">• Designed hundreds of custom assays, building ddPCR content and streamlining R&D experiments. Wide range of targets and customer applications.• Computational process development. Thermodynamic models via machine learning.• Patent applications, publications, customer presentations. QuantaLife Droplet Award. | | |
| Staff Scientist, Bioinformatics | Applied Biosystems | 2000-2009 |
| <ul style="list-style-type: none">• Architect and bioinformatics lead for assay design pipelines (TaqMan and SNPlex). Systems have generated millions of quality assays and millions of dollars in revenue.• Scientific manager, mentor (5+ years). My group focused on software tool development, experimental data analysis, sequence-based pattern classification and rule discovery.• Improved development efficiencies and robustness of multiple, highly complex genomic assay systems using data analysis coupled with experimental design.• Invented algorithms and software addressing nucleotide thermodynamics, tag sequence selection, multiplex partitioning, sequence analysis and data mining challenges.• Numerous invention disclosures, DNA awards, Trade Secret of the Year Award. | | |
| Scientist, Computational Chemistry | Terrapin / Telik | 1995-1999 |
| <ul style="list-style-type: none">• Supported drug discovery with molecular modeling, target analysis, database and virtual screening, compound prioritization. Built web interface to company databases.• Devised a general framework for chemical library design, modeled affinity fingerprints via molecular docking and multivariate statistics. Derived anti-cancer QSAR models. | | |

TEACHING EXPERIENCE

Instructor **University of California San Diego Extension** **2009-Present**

- *Genomic Sequencing Technologies*. Developed and teach on-line course covering sequencing chemistries & platforms, common work-flows (e.g. variant discovery), bioinformatics, traditional and emerging applications (e.g. personalized medicine).
- *Bioinformatics*. Developed and teach on-line course covering literature and database searches, classic and newer alignment algorithms, comparative genomics, phylogenetics, next-gen sequencing applications.

Associate Professor **California State University East Bay** **2004-2005**

- *Advanced Bioinformatics / Chemoinformatics*. Drug discovery focus covering structural biology, molecular modeling, database similarity searching, physico-chemical property calculation, metabolite predictions. Developed curriculum and content.

Teaching Assistant **University of California Santa Cruz** **1990-1995**

- Organic Chemistry discussion & lab. Lead study sections, authored quizzes.

Mentor **University of Maryland University College** **2010-Present**

- Share academic and career advice with students in biotechnology certificate program.

CORE COMPETENCIES / TECHNICAL SKILLS

Professional Competencies

- Excellent verbal, written and graphic communication skills.
- Coordination of projects, balancing priorities, managing customer expectations.
- Easily approachable, friendly, forthright with concerns and amenable to criticism.
- Adept translator of scientific and technical complexities into lay terms and specifications.
- Independent or team contributor, collaborations via phone, email, on-line meetings.
- Scientific manager & mentor (5+ years managing PhD scientists, software developers).

Scientific & Engineering

- Broad background in bioinformatics, biotechnology, molecular biology, genomics, genetics, drug discovery, chemistry & cheminformatics, data and computer science.
- Bioinformatics databases & tools including NCBI, UCSC, aligners, oligo and PCR design, genome browsers. Knowledge of implementation use cases.
- Analytics methods and programming (Python, pandas, scikit-learn, R), machine learning (e.g. clustering, classifiers, predictive models), data mining, feature extraction and selection. Experimental design and analysis strategies.
- Next-generation sequencing technologies, tools and work-flows, variant discovery, annotation and file manipulations. Experience with tools, databases, platforms: bwa, samtools, bedtools, ExAC, COSMIC, etc. Workflow design, running and troubleshooting on DNAnexus. Aware of algorithm trade-offs, limitations and issues.
- Computational chemistry, structure based design, virtual screening, structural biology.

Software Development

- **Languages:** Expert programmer in C, Python, Perl, Unix shell (bash, awk, sed); Experienced with R, C++, MySQL (database design & use); Working web skills with LAMP (configure & admin), WordPress, HTML, PHP, CSS, JavaScript.
- **Applications:** Command line utilities & tools (e.g. sequence property calculations: <https://github.com/ryantkoehler/vertools>). Integrated data processing pipelines, including database & third party code. Code snippets, data visualization (Jupyter notebooks).
- **Platforms:** Linux, including system admin of users, software, Apache and database servers, networking, backup demons; Amazon EC2. Capable on Mac and Windows.
- **Life cycle:** System analysis, requirements gathering, design constraints; Architecture, prototyping, implementation and deployment; Quality assurance, algorithm validation, unit testing; Support, troubleshooting, training, technical documentation.
- **Best practices:** Standardized naming, comments; Modular design, code re-usability, testing; Experience with agile development, version control (git, bitbucket).

EXAMPLE PROJECT ACCOMPLISHMENTS

- **Designed suite of ddPCR assays.** Created several hundred custom assays for droplet digital PCR system with success rate > 95%. Applications included SNP genotyping, rare mutation detection, copy number determination, quantitative gene expression. Targets included human, animal, microbe, viral and plant; Several publications.
- **Machine learning for thermodynamic modeling.** Implemented a genetic algorithm to optimize oligo thermodynamic parameters based on training set data. This effectively reverse engineered unpublished models, allowing accurate T_m predictions.
- **Parameter-file-driven expert system.** Author of TaqMan PCR assay design tool (C code) for genomic sequence data. This tool remains the core of several commercial bioinformatics pipelines used for multiple variations of commercial assay products.
- **Multiplex design and ordering system.** Architect and author of SNPlex genotyping assay design pipeline. XML interfaces to ordering & sales database. Addresses input checking, genome specificity screening, thermodynamic probe design, priority balancing.
- **Analytics, experimental design & rule improvement.** Applied feature selection and machine learning to identify molecular attributes associated with assay performance as deduced from experimental results (pass or fail, robust or fragile, etc). Designed experiments to confirm models, and invent or adjust design rules accordingly.
- **Classification algorithms.** Invented diversity-directed chemical structure library design methodology, biasing toward favorable properties and away from suspect motifs. General, extensible framework deployed for drug discovery; Several publications.

EDUCATION / TRAINING

Ph.D. Chemistry, University of California Santa Cruz

1995

- Created de novo molecular design software. Chemical structure evaluation and scoring, novel graphics and visualization methodologies. Teaching and research fellowships.

B.S. Biochemistry, University of California Davis.

1989

- Dean's certificate for tutoring. Senior research project in organic synthesis.

Additional Training and Courses

- **Software:** S-PLUS; Matlab; Python; Web technologies, Startup engineering.
- **Science:** Bioinformatics (array) data analysis; Machine learning.
- **Management:** Project management; People management.

PUBLICATIONS

Google Scholar: <http://scholar.google.com/citations?user=X4YvzvMAAAAJ&hl=en>

A Vilborg, Y Bouhlal, **R Koehler**, D Mendoza, F Goodsaid, Y Pouliot, F De La Vega, M Lucero, HP Ji, A So. TOMA OS-Seq: A Novel Capture-Based Library Preparation Platform with Minimal PCR-Dependency for Detecting Clinically Relevant Mutations Using NGS. *Journal Of Molecular Diagnostics*. **18**. 1027-1027, 2016.

Francisco De La Vega, **Ryan Koehler**, Yannick Pouliot, Yosr Bouhlal, Austin So, Federico Goodsaid, Sean Irvine, Len Trigg, Lincoln Nadauld. Joint somatic mutation and germline variant identification and scoring from tumor molecular profiling and ct-DNA monitoring of cancer patients by high-throughput sequencing. *Cancer Research*. **76**. 2712-2712, 2016.

J.F. Regan, N. Kamitaki, T. Legler, S. Cooper, N. Klitgord, G. Karlin-Neumann, C. Wong, S. Hodges, **R. Koehler**, S. Tzonev, S. McCarroll. A rapid molecular approach for chromosomal phasing. *PLoS One*. **10**. 2015.

G.P. McDermott, et al. Multiplexed target detection using DNA-binding dye chemistry in droplet digital PCR. *Anal. Chem*. **85**.11619-27, 2013.

P. Belgrader, S.C. Tanner, J.K. Regan, **R.T. Koehler**, B.J. Hindson, A.S. Brown. Droplet Digital PCR Measurement of HER2 Copy Number Alteration in Formalin-Fixed Paraffin-Embedded Breast Carcinoma Tissue. *Clin. Chem.* **59**, 991-4, 2013.

N.J. Heredia, P. Belgrader, S. Wang, **R.T. Koehler**, et al. Droplet Digital™ PCR quantitation of HER2 expression in FFPE breast cancer samples. *Methods.* **59**, 183-6, 2013.

H White, A So, **R Koehler**, et al. Ultra-sensitive detection of somatic mutations by droplet digital PCR with conventional TaqMan assays. *J. Med. Genetics.* **49**, S55-S55, 2012.

B.J. Hindson, et al. High-throughput droplet digital PCR system for absolute quantitation of DNA copy number. *Anal Chem.* **83**, 8604-10, 2011.

R.T. Koehler, H. Issac, N. Cloonan, S.M. Grimmond. The Uniqueome: A Mappability Resource for Short-tag Sequencing. *Bioinformatics.* **27**, 272-274, 2011.

R.T. Koehler, N. Peyret. Effects of DNA Secondary Structure on Oligonucleotide Probe Binding Efficiency. *Computational Biology and Chemistry.* **29**, 393-7, 2005.

R.T. Koehler, N. Peyret. Thermodynamic Properties of DNA sequences: Characteristic Values for the Human Genome. *Bioinformatics.* **16**, 3333-9, 2005.

F.M. De La Vega, et al. The Linkage Disequilibrium Maps of Three Human Chromosomes Across Four Populations Reflect Their Demographic History and A Common Underlying Recombination Pattern. *Genome Res.* **15**, 454-62, 2005.

A.R. Tobler, et al. The SNPlex Genotyping System: a Flexible and Scalable Platform for SNP Genotyping. *J Biomol Tech.* **16**, 398-406, 2005.

R.T. Koehler, H.O. Villar. Design of Screening Libraries Biased for Pharmaceutical Discovery. *J. Comp. Chem.* **21**, 1145-52, 2000.

H.O. Villar, **R.T. Koehler**. Comments on the Design of Chemical Libraries for Screening. *Molecular Diversity.* **5**, 13-24, 2000.

R.T. Koehler, H.O. Villar. Statistical Relationships Among Docking Scores for Different Protein Binding Sites. *J. Computer Aided Molecular Design.* **14**, 23-37, 2000.

H.O. Villar, **R.T. Koehler**. Amino acid preferences of small naturally occurring polypeptides. *Biopolymers.* **53**, 226-32, 2000.

R.T. Koehler, S.L. Dixon, H.O. Villar. LASSOO: A Generalized Directed Diversity Approach to the Design and Enrichment of Chemical Libraries. *J. Med. Chem.* **42**, 4695-4704, 1999.

S.L. Dixon, **R.T. Koehler**. The Hidden Component of Size in 2D Fragment Descriptors: Side-Effects on Sampling in Bioactive Libraries. *J. Med. Chem.* **42**, 2887-2900, 1999.

R.T. Koehler, H.O. Villar, K.E. Bauer, D.L. Higgins. Ligand-Based Protein Alignment and the Specificity of Glutathione S-Transferase Inhibitors. *Proteins, Structure, Function and Genetics.* **28**, 202-16, 1997.

PATENTS / PATENT APPLICATIONS

S. Saxonov, et al. Library characterization by digital assay. US patent application WO 2013019751 A1. July 2011.

K. Lao, et al. Universal-tagged oligonucleotide primers and methods of use. US patent application WO 2003097794 A2. Jan 2007.

C.R. Scafe, et al. Methods for searching polynucleotide probe targets in databases. US patent US 7085652 B2. Aug 2006.

R.T. Koehler, et al. Methods for placing, accepting, and filling orders for products and services. US patent application US 20080228589 A1. Jan 2002.

B. Rosenblum, et al. Polynucleotide sequence detection assays and analysis. US patent application EP 1572974 A2. Nov 2003.