Top Computational biology Resources

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12 websites to learn computation and many others!

- 1. coursera https://www.coursera.org/ The first website I used. I took a data science Specialization https://www.coursera.org/specializations/jhu-data-science and https://www.coursera.org/learn/bioinformatics
- 2. edx https://www.edx.org/ I took this one first https://www.edx.org/professional-certificate/harvardx-data-analysis-for-life-sciences and https://www.edx.org/course/statistical-learning and recently some management classes
- 3. udactiy https://www.udacity.com/ I took R courses, ggplot2,github and intro to ML
- 4. udemy https://www.udemy.com/ I took several python courses there.
- 5. MIT opencourseware https://ocw.mit.edu/ 1806 linear algebra and many others!
- 6. harvard CS50 https://pll.harvard.edu/course/cs50-introduction-computer-science?delta=0
- 7. youtube channel 3blue1brown https://www.youtube.com/channel/UCYO_jab_esuFRV4b17AJtAw blow you away with Crystal clear explanations. I watched the linear algebra series
- 8. Khan academy https://www.khanacademy.org/
- 9. free code camp https://www.freecodecamp.org/
- 10. Josh Starmer's Statquest for machine learning. The best ever https://www.youtube.com/channel/UCtYLUTtgS3k1Fg4y5tAhLbw
- 11. EBML-EBI training https://www.ebi.ac.uk/training/online/ bioinformatics courses
- 12. skillup https://www.simplilearn.com/skillup-free-online-courses this is new to me as well.

10 courses to get you started with bioinformatics

- 1. http://rafalab.dfci.harvard.edu/pages/harvardx.html by Rafa Irizarry at Dana-Farber.
- 2. https://github.com/quinlan-lab/applied-computational-genomics#course-lecture-slides

by Aaron Quinlan, the creator of bedtools and many other cool tools.

- 3. https://www.bioinformaticsalgorithms.org/ You can find the video classes on Coursera
- 4. http://www.personal.psu.edu/iua1/courses/2014-BMMB-852.html by Istvan Albert, the creator of biostars.

5. Introduction to Bioinformatics and Computational Biology https://liulab-dfci.github.io/bioinfocombio/ by @XShirleyLiu

glad to contribute a little myself.

6. data carpentry workshops https://datacarpentry.org/lessons/#genomics-workshop I am honored to serve as the curriculum committee chair

7. Computational Genomics: Applied Comparative Genomics https://github.com/schatzlab/appliedgenomics2018

- 8. Introduction to Computational Biology https://biodatascience.github.io/compbio/ by Mike Love
- 9. MIT Computational Biology: Genomes, Networks, Evolution, Health Fall 2018 6.047/6.878/HST.507 by Manolis Kellis
- 10. An introduction to Applied Bioinformatics https://github.com/applied-bioinformatics/iab2 Very nice book with python code.

16 resources for re-analyzing public expression data.

- 1. https://rnama.com/docs/search-evaluation RNA meta Analysis has ~26,700 studies (5,717 RNA-Seq and 20,955 Microarray)
- 2. refine.bio will have harmonized over 60,000 gene expression experiments
- 3. BioJupies https://maayanlab.cloud/biojupies/
- 4. Recount2-FANTOM Recounting the FANTOM Cage Associated Transcriptome. Long non-coding RNAs.
- 5. Recount3 https://rna.recount.bio/
- 6. dee2 Digital Expression Explorer 2. Digital Expression Explorer 2 (DEE2) is a repository of uniformly processed RNA-seq data mined from public data obtained from NCBI Short Read Archive. By Ziemann Mark et.al! Version 2 of dee.
- 7. Extracting allelic read counts from 250,000 human sequencing runs in Sequence Read Archive https://www.biorxiv.org/content/10.1101/386441v1?rss=1
- 8. MetaSRA: normalized sample-specific metadata for the Sequence Read Archive
- 9. ARCHS4: Massive Mining of Publicly Available RNA-seq Data from Human and Mouse ARCHS4 provides access to gene counts from HiSeq 2000, HiSeq 2500 and NextSeq 500 platforms for human and mouse experiments from GEO and SRA.
- 10. DEP-reads: Uniformly processed public RNA-Seq data Read counts data for 5,470 human and mouse datasets from ARCHS4 v6 and 12,670 datasets from DEE2 for 9 model organisms by steven Ge.
- 11. SRA-explorer This tool aims to make datasets within the Sequence Read Archive more accessible.
- 12. intropolis is a list of exon-exon junctions found across **21,504** human RNA-seq samples on the Sequence Read Archive (SRA) from spliced read alignment to hg19 with Rail-RNA.
- 13. batch recompute ~20,000 RNA-seq samples from larget sequencing project such as TCGA, TARGET and GETEX. Used hg38 and gencode v21 as annotation.
- 14. A cloud-based workflow to quantify transcript-expression levels in public cancer compendia used kallisto for TCGA/CCLE datasets and gencode v24 as annotation.

- 15. MiPanda is an online resource for the interrogation and visualization of gene expression data from the myriad of publicly available cancer and normal next generation sequencing datasets.
- 16. Curation of over 10,000 transcriptomic studies to enable data reuse

5 websites to analyze GEO RNAseq data without a single line of code

- 1. GEOdiver https://www.geodiver.co.uk/
- 2. shinyGEO https://gdancik.shinyapps.io/shinyGEO/
- 3. scanGEO http://scangeo.dartmouth.edu/ScanGEO/
- 4. GREIN: GEO RNA-seq experiments interactive navigator for re-analyzing GEO RNA-seq data https://hub.docker.com/r/ucbd2k/grein/
- 5. ImaGEO: Integrative Meta-Analysis of GEO Data https://imageo.genyo.es/
- 6. Gemma https://gemma.msl.ubc.ca/home.html

12 web tools to explore genomics data

- 1. cbioportal https://cbioportal.org explore genomic datasets at the tips of your fingers
- 2. xena https://xena.ucsc.edu, a UCSC effort. Everyone needs to learn how to use UCSC genome browser https://genome.ucsc.edu
- 3. depmap portal https://depmap.org/portal/interactive/ Cancer Cell Line Encyclopedia
- 4. TCGA RNA fusion portal https://tumorfusions.org
- 5. http://gepia2.cancer-pku.cn/#index Gene expression profile interactive analysis
- 6. Tumor Immune Syngeneic MOuse (TISMO) database http://tismo.cistrome.org
- 7. PDX models https://lnkd.in/ezby9kns
- 8. http://tide.dfci.harvard.edu/login/ Tumor Immune Dysfunction and Exclusion
- 9. http://timer.cistrome.org TIMER is a comprehensive resource for systematical analysis of immune infiltrates across diverse cancer types
- 10. genePattern https://genepattern.org
- 11. https://epiviz.github.io/index.html Epiviz is an interactive visualization tool for functional genomics data.
- 12. draw mutation for a protein https://pecan.stjude.cloud/proteinpaint/TP53/

6 links on workflow to make your life easier

Bioinformatics analysis involves a lot of steps, 6 links on workflow to make your life easier:

- 1. over hundreds of workflow tools and engines https://github.com/pditommaso/awesome-pipeline
- 2. see also from the CWL wiki https://github.com/common-workflow-language/common-workflow-language/wiki/Existing-Workflow-systems

- 3. A review of bioinformatic pipeline frameworks https://academic.oup.com/bib/article/18/3/530/2562749
- 4. discussion on biostars https://www.biostars.org/p/115745/
- 5. two papers by Titus Brown Ten simple rules and a template for creating workflows-as-applications
- 6. Streamlining Data-Intensive Biology With Workflow Systems https://dib-lab.github.io/2020-workflows-paper/

8 links to bookmark for better data visualization

Data visualization is a critical step in data analysis, 8 links to bookmark for better data visualization :

- 1. Nature Methods point of view data visualization http://blogs.nature.com/methagora/2013/07/data-visualization-points-of-view.html the columns on color mapping and heatmap are very nice.
- 2. Ten simple rules to colorize biological data visualization https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1008259
- 3. data visualization resources https://sabahzero.github.io/dataviz/resources
- 4. Fundamentals of Data Visualization https://clauswilke.com/dataviz/
- 5. Data Visualization https://socviz.co/ by Kieran Healy. I've read book and 4 and 5.
- 6. R Graphics Cookbook by Winston Chang.
- 7. ggplot2: Elegant Graphics for Data Analysis by Hadely Wickham.

5 tools to visualize genomic datasets

- $1. \ Karyoploter \ https://bernatgel.github.io/karyoploter_tutorial/Tutorial/PlotCoverage/PlotCoverage. \\ html I used that to plot single-cell ATACseq tracks https://github.com/crazyhottommy/scATACutils/#plot-atacseq-tracks-for-each-cluster-of-cells, more examples https://rpubs.com/crazyhottommy/scATAC_tracks$
- 2. plotgardener is a genomic data visualization package for R. Using grid graphics, plotgardener empowers users to programmatically and flexibly generate multi-panel figures

https://github.com/PhanstielLab/plotgardener

3. The goal of **g(r)osling** https://github.com/gosling-lang/grosling is to help you build interactive genomics visualizations with Gosling. This package uses reticulate to provide an interface to the Gos Python package. https://github.com/gosling-lang/grosling

 ${\it 4.} Intervene: a tool for intersection and visualization of multiple gene or genomic region sets $$https://bitbucket.org/CBGR/intervene/src/master/$$

5. https://42basepairs.com/ saw it yesterday by @RobAboukhalil

8 links to BETTER understand principal component analysis (PCA)

- 1. https://divingintogeneticsandgenomics.rbind.io/post/pca-in-action/ PCA in action, my blog post to calculate SVD and PCA with #rstats
- 2. https://www.youtube.com/watch?v=rYz83XPxiZo MIT 1806 linear algebra on SVD
- 3. https://peterbloem.nl/blog/pca-4 THE SINGULAR VALUE DECOMPOSITION (SVD)
- 4. http://rafalab.github.io/pages/harvardx.html High Dimension data analysis, week 2.
- 5. https://towardsdatascience.com/why-pca-looks-triangular-a642daac721a why PCA looks triangular.
- 6. https://www.nxn.se/valent/2017/6/12/how-to-read-pca-plots How to read PCA plots for single-cell data.
- 7. https://twitter.com/AedinCulhane/status/1007110262187544577 PCA horseshoe artifact
- 8. https://www.youtube.com/watch?v= UVHneBUBW0 by Josh Starmer

9 tools for interactive exploring single-cell RNAseq data

- 1. cellxgene https://github.com/chanzuckerberg/cellxgene
- 2. cellar https://github.com/euxhenh/cellar
- 3. scSVA: an interactive tool for big data visualization and exploration in single-cell omics https://www.biorxiv.org/content/10.1101/512582v1
- 4. ASAP: a web-based platform for the analysis and interactive visualization of single-cell RNA-seq data https://academic.oup.com/bioinformatics/article/33/19/3123/3852081?login=false
- 5. iSEE Provides functions for creating an interactive Shiny-based graphical user interface for exploring data stored in SummarizedExperiment objects, including row- and column-level metadata
- 6. VISION A high-throughput and unbiased module for interpreting scRNA-seq data.
- 7. DISCO: Deep Integration of Single-Cell Omics. Want to visual millions of cell online and annotate cell type automatically? Try it!!! Make single cell easier and make life easier!
- 8. TISCH Tumor Immune Single-cell Hub (TISCH) is a scRNA-seq database focusing on tumor microenvironment (TME).
- 9. CancerSCEM To date, CancerSCE version 1.0 consists of 208 cancer samples across 28 studies and 20 human cancer types

12 resources to bookmark for reproducible computational research

- 1. a reproducible workflow. https://www.youtube.com/watch?v=s3JldKoA0zw This two minute video will change your mind on reproducible research
- 2. Parallel sequencing lives, or what makes large sequencing projects successful https://academic.oup.com/gigascience/article/6/11/gix100/4557140?login=false
- $3. \ \ Common-sense \ approaches \ to \ sharing \ tabular \ data \ alongside \ publication \ https://www.sciencedirect.\\ com/science/article/pii/S2666389921002300$
- 4. A Reproducible Data Analysis Workflow with R Markdown, Git, Make, and Docker https://psyarxiv.com/8xzqy/

- 5. Practical Computational Reproducibility in the Life Sciences https://www.cell.com/cell-systems/fulltext/S2405-4712(18)30140-6
- 6. A video by Dr.Keith A. Baggerly from MD Anderson The Importance of Reproducible Research in High-Throughput Biology highly recommended.
- 7. Ten Simple Rules for Reproducible Computational Research http://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1003285)
- 8. Good Enough Practices in Scientific Computing http://arxiv.org/abs/1609.00037
- 9. Best Practices for Scientific Computing https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1001745
- 10. A Quick Guide to Organizing Computational Biology Projects http://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.100042 A must read for computational biologists!
- 11. Reproducibility of computational workflows is automated using continuous analysis https://www.nature.com/articles/nbt.3780
- 12. Five selfish reasons to work reproducibly https://genomebiology.biomedcentral.com/articles/10.1186/s13059-015-0850-7

7 FREE Books to learn data science

- 1. Data science: A first introduction https://datasciencebook.ca/
- 2. Introduction to Data Science http://rafalab.dfci.harvard.edu/dsbook/
- 3. Agile Data Science with R https://edwinth.github.io/ADSwR/index.html
- 4. Tidy Modeling with R https://www.tmwr.org/
- 5. Feature Engineering and Selection: A Practical Approach for Predictive Models https://bookdown.org/max/FES/
- 6. Another Book on Data Science https://www.anotherbookondatascience.com/ compare R and python side by side
- 7. Research Software Engineering with Python https://merely-useful.tech/py-rse/

7 Books for you to learn bioinformatics

- 1. Data Analysis for the Life Sciences https://leanpub.com/dataanalysisforthelifesciences You can get it for free!
- 2. practical computing for biologist https://practicalcomputing.org/ My first ever book to start learning computational biology.
- 3. A Primer for Computational Biology https://open.oregonstate.education/computationalbiology/
- 4. Computational Genomics with R http://compgenomr.github.io/book/
- 5. The Biologist's Guide to Computing https://book.biologistsguide2computing.com/en/stable/
- 6. Bioinformatics Data Skills https://www.oreilly.com/library/view/bioinformatics-data-skills/9781449367480/ A must read to upgrade your bioinformatics skills once you know the basics.
- 7. Bioinformatics Workbook: A tutorial to help scientists design their projects and analyze their data. https://bioinformaticsworkbook.org/#gsc.tab=0

8 Resources to study Transcription factor binding, enhancers and histone modification distribution

- 1. ENCODE https://www.encodeproject.org/
- 2. The International Human Epigenome Consortium (IHEC) epigenome data portal http://epigenomesportal.ca/ihec/index.html?as=1
- 3. Blueprint epigenome http://dcc.blueprint-epigenome.eu/#/home
- 4. EpiFactors http://epifactors.autosome.ru/ is a database for epigenetic factors, corresponding genes and products.
- 5. CistromeDB http://cistrome.org/db/#/ by Shirley Liu group
- Remap https://remap2022.univ-amu.fr/ is a large scale integrative analysis of DNA-binding experiments for Homo sapiens, Mus musculus, Drosophila melanogaster and Arabidopsis thaliana transcriptional regulators.
- 7. ChIP-Atlas http://chip-atlas.org/ An integrative, comprehensive database to explore public Epigenetic dataset, including ChIP-Seq, DNase-Seq, ATAC-Seq, and Bisulfite-Seq data: ChIP-Atlas covers almost all public data archived in Sequence Read Archive of NCBI, EBI, and DDBJ with over 224,000 experiments.
- 8. Fantom5 https://fantom.gsc.riken.jp/5/

8 R/command line tools to deal with excel, tsv and csv files

R packages:

- readxl
- tidyxl
- janitor

command line tools:

- VisiData is an interactive multitool for tabular data. It combines the clarity of a spreadsheet, the efficiency of the terminal, and the power of Python, into a lightweight utility which can handle millions of rows with ease.
- csvkit
- csvtk a cross-platform, efficient and practical CSV/TSV toolkit.
- Miller is a command-line tool for querying, shaping, and reformatting data files in various formats including CSV, TSV, JSON, and JSON Lines.
- eBay's TSV Utilities

6 training resources for data management

- Best Practices for Biomedical Research Data Management https://learn.canvas.net/courses/1854
- Research Data Management Librarian Academy (https://rdmla.github.io/)
- DataONE Data Management Skillbuilding Hub (https://dataoneorg.github.io/Education)
- Data Management Training Clearinghouse (https://dmtclearinghouse.esipfed.org/)
- Research data management open training materials Zenodo Community (https://zenodo.org/communities/dcc-rdm-training-materials)
- Consortium of European Social Science Data Archives (CESSDA) Training Resources (https://www.cessda.eu/Training-Resources)

Bonus:

Learn from TCGA # Collaborative Genomics Projects: A Comprehensive Guide https://www.sciencedirect.com/book/9780128021439/collaborative-genomics-projects-a-comprehensive-guide

7 links to deeply understand heatmap

Making a heatmap is an essential skill for a bioinformatician. Just check how many figures are heatmap or heatmap variants in the genomics or single cell paper.

But you probably do not understand heatmap. 7 reading resources to understand heatmap!

- 1. Mapping quantitative data to color https://www.nature.com/articles/nmeth.2134
- 2. Heat map from Nature Method column https://www.nature.com/articles/nmeth.1902
- 3. A tale of two heatmap functions https://rpubs.com/crazyhottommy/a-tale-of-two-heatmap-functions An old post by me.
- 4. Heatmap demystified https://rpubs.com/crazyhottommy/heatmap_demystified yet another post by me
- 5. understand color mapping is key https://jokergoo.github.io/ComplexHeatmap-reference/book/a-single-heatmap.html#colors
- 6. understand rastering https://jokergoo.github.io/2020/06/30/rasterization-in-complexheatmap/

7.what happens when you have a huge matrix 20,000 rows/genes x 50 columns to plot? https://gdevailly.netlify.app/post/plotting-big-matrices-in-r/

I learned so much from Zuguang Gu, thanks for his awesome Complexheatmap package https://jokergoo.github.io/ComplexHeatmap-reference/book/index.html . it is my go-to tool for making heatmaps.

23 tools to work with (single-cell) TCR/BCR-seq immune repertoire data

- 1. immunarch
- 2. scRepertoire
- 3. dandelion python package for analyzing single cell BCR/TCR data from 10x Genomics 5' solution!

- 4. TRUST4 developed in Shirley Liu's group. Use it to extract TCR/BCR information from bulk RNAseq or 5' scRNAseq data.
- 5. a dramatic speedup for one of the core computations for adaptive immune receptor repertoire (AIRR) analysis the discovery and counting of receptors that overlap between repertoires! Check out CompAIRR. With 10^4 repertoires of 10^5 sequences each, CompAIRR ran in 17 minutes while the fastest existing tool took 10 days, amounting to a ~1000x speedup
- 6. ClusTCR: a Python interface for rapid clustering of large sets of CDR3 sequences with unknown antigen specificity;
- 7. GLIPH2
- 8. GIANA allows computationally-efficient TCR clustering and multi-disease repertoire classification by isometric transformation from Bo Li.
- 9. tcrdist3 is a python API-enabled toolkit for analyzing T-cell receptor repertoires
- 10. TCRex: a web tool for the prediction of TCR-epitope recognition
- ImRex TCR-epitope recognition prediction using combined sequence input represention for convolutional neural networks.
- 12. NetTCR 2.0 Sequence-based prediction of peptide-TCR binding
- 13. CellaRepertorium
- 14. enclone from 10x. we should give this a try if we want to cluster TCR and BCR clonotypes.
- 15. migec: A RepSeq processing swiss-knife.
- 16. MiXCR is a universal software for fast and accurate analysis of T- and B- cell receptor repertoire sequencing data.
- 17. ImReP is a computational method for rapid and accurate profiling of the adaptive immune repertoire from regular RNA-Seq data.
- 18. TcellMatch: Predicting T-cell to epitope specificity. cellMatch is a collection of models to predict antigen specificity of **single T cells** based on CDR3 sequences and other single cell modalities, such as RNA counts and surface protein counts
- 19. scirpy: A scanpy extension for single-cell TCR analysis.
- 20. Tessa is a Bayesian model to integrate T cell receptor (TCR) sequence profiling with transcriptomes of T cells. Enabled by the recently developed single cell sequencing techniques, which provide both TCR sequences and RNA sequences of each T cell concurrently, Tessa maps the functional landscape of the TCR repertoire, and generates insights into understanding human immune response to diseases.
- 21. DeepTCR Deep Learning Methods for Parsing T-Cell Receptor Sequencing (TCRSeq) Data

 $https://twitter.com/John_Will_I_Am/status/1570837756787691527\\ https://www.science.org/doi/10.1126/sciadv.abq5089$

- 22. Integrating T cell receptor sequences and transcriptional profiles by clonotype neighbor graph analysis (CoNGA)
- 23. Echidna: Integrated simulations of single-cell immune receptor repertoires and transcriptomes

15 tools/papers for multi-sample multi-group single-cell RNAseq differential expression analysis

- 1. An Empirical Bayes Method for Differential Expression Analysis of Single Cells with Deep Generative Models scVI-DE
- 2. muscat
- 3. Confronting false discoveries in single-cell differential expression "These observations suggest that, in practice, pseudobulk approaches provide an excellent trade-off between speed and accuracy for single-cell DE analysis." One needs to consider biological replicates, pseudobulk works well.
- 4. Modelling group heteroscedasticity in single-cellRNA-seq pseudo-bulk data
- 5. BSDE: barycenter single-cell differential expression for case-control studies
- 6. distinct Both are from Mark Robinson group.
- 7. nebula https://www.biorxiv.org/content/biorxiv/early/2020/09/25/2020.09.24.311662.full.pdf
- 8. Fast identification of differential distributions in single-cell RNA-sequencing data with waddR https://github.com/goncalves-lab/waddR
- 9. CoCoA-diff: counterfactual inference for single-cell gene expression analysis
- 10. Bias, robustness and scalability in single-cell differential expression analysis From Mark Robinson group.
- 11. Comparative analysis of differential gene expression analysis tools for single-cell RNA sequencing data "We observed that current methods designed for scRNAseq data do not tend to show better performance compared to methods designed for bulk RNAseq data."
- 12. Tree-based Correlation Screen and Visualization for Exploring Phenotype-Cell Type Association in Multiple Sample Single-Cell RNA-Sequencing Experiments TreeCorTreat is an open source R package that tackles this problem by using a tree-based correlation screen to analyze and visualize the association between phenotype and transcriptomic features and cell types at multiple cell type resolution levels.
- 13. Quantifying the effect of experimental perturbations in single-cell RNA-sequencing data using graph signal processing read this thread https://twitter.com/krishnaswamylab/status/1328876444810960896?s=27
- 14. Causal identification of single-cell experimental perturbation effects with CINEMA-OT

github https://github.com/vandijklab/CINEMA-OT

15. IDEAS: individual level differential expression analysis for single-cell RNA-seq data

10 tips for learning git

1. Several basic commands will serve you a long way:

```
git clone
git add
git commit -m
git push
```

Those are enough to get you started. To be honest, those are still the most frequent commands I use.

- 2. understand git and github. You use git to track files locally, and github can host your repos. You can start with the github skill page https://buff.ly/3tO2iaf gitlab https://buff.ly/3JlGA69 is an alternative to github
- 3. software carpentry git workshop is a nice resource to learn git https://buff.ly/3kUhqB7
- 4. An open source game about learning Git! https://buff.ly/2ZPXUrX
- 5. Learn it for free on Udemy https://buff.ly/3RvTCA9
- 6. The best interactive tutorial for learing git branching https://buff.ly/2tQTJN4 I had a lot of fun playing it.
- 7. https://buff.ly/2w5p9zi Oh Shit, Git!?! You know, sometimes it messed up so much locally I just delete my local copy and do a fresh git clone :)
- 8. https://buff.ly/2U9C8hC How to use git with R.
- 9. git cheatsheet https://buff.ly/3H2PrWa
- 10. if you collaborate with others, you need to understand the github flow https://buff.ly/3CcvTio