

Packages, ecosystems, and services:  
Software resources and strategies for multimodal  
single-cell genomics

Vince Carey  
BIRS Meeting June 2020

## *Road map*

- "Chat race" game to warm up a little
- A triangular schema defining context of relevant work
- Brief review of scalability, divide and conquer, and the software ecosystem concept
- Some aspects of the Bioconductor ecosystem
- Some prospects for productive evolution of ecosystem management - an illustration with S. Davis' GHA workflow-4-workshop infrastructure

## ***Chat races***

Given: a "sub-quote" - a notorious phrase to which certain substitutions are applied

To win points, be the first to chat the name of the author of the original phrase

Example:

**Notorious phrase:** To consult the statistician after an experiment is finished is often merely to ask him to conduct a post mortem examination. He can perhaps say what the **experiment** died of.

**Sub-quote for game:** To consult computer scientists after a program has been coded is often merely to provoke them to propose that a different language be used. They can perhaps say why the original choice was a fatal one.

The answer here would be: Ronald A. Fisher

## ***First race***

Sub-quote: All programs are wrong; some are more useful than others

To whom is the original remark on which this is based attributed? Be the first to put their name in the chat

## ***Second race***

Sub-quote: Bioconductor is the most successful genomic analysis platform. Those who ignore it are condemned to reinvent it.

To whom is the original remark on which this is based attributed?

## ***Third race***

It takes a software ecosystem to raise a compelling analysis in multimodal single cell genomics

Who popularized the proverb from which this is derived?

## ***Fourth race***

I shall not today attempt to define "compelling analysis in multimodal single-cell genomics" but I know it when I see it.

What is the name of the Supreme Court justice who wrote the original quote in the context of an obscenity trial?



## ***Fifth race***

To create a Bioconductor package

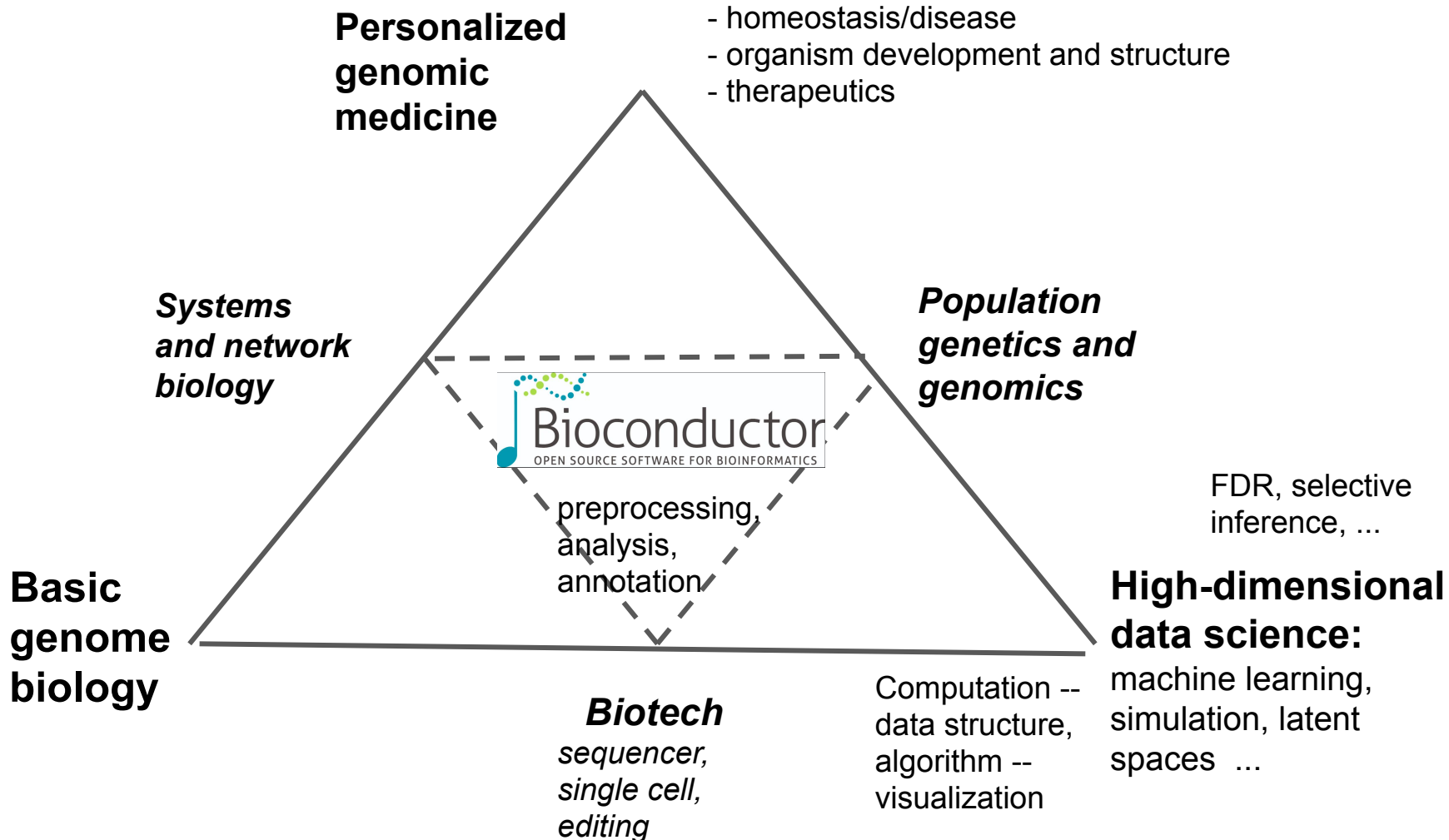
is to battle with trolls in the vaults of WRE and the build system

To run BiocCheck over one's package

is to sit in judgment over oneself

THE GAME ... I HOPE YOU ENJOYED THE GAME ... I HOPE

It was not pure frivolity. Is "all models are wrong" true, but "all programs are wrong" false? Should Bioconductor be reinvented? What is a software ecosystem? What makes a multimodal single cell analysis compelling/reliable -- can we define it? And what about BiocCheck? Where did its criteria for warning or error come from?



# Some connections to ongoing discussions

- From benchmarking section:
  - Leverage single cell eQTL? (e.g. doi: 10.1038/s41467-020-14457-z) **Through GTEx**, we have a large set of known tissue and cell-type-specific eQTL to benchmark methods. We should expect to find relationships at single cell level when we see them in bulk.
    - **What's a good representation/API for GTEx?**
- From spatial/scProteomics:
  - Reuse concepts and structures in atmospheric modeling/GIS
    - **How do we coordinate global efforts on integrative data structure design and analysis methods?**
- **Can we plan first and then act, or do we always need to experiment first and then refine/synthesize?**
  - Example of [TreeSummarizedExperiment](#)

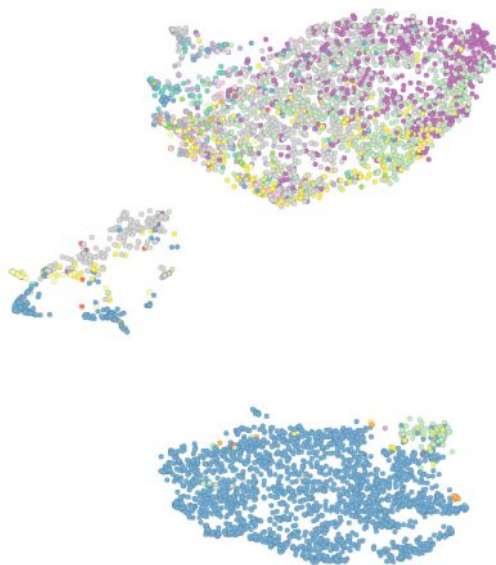
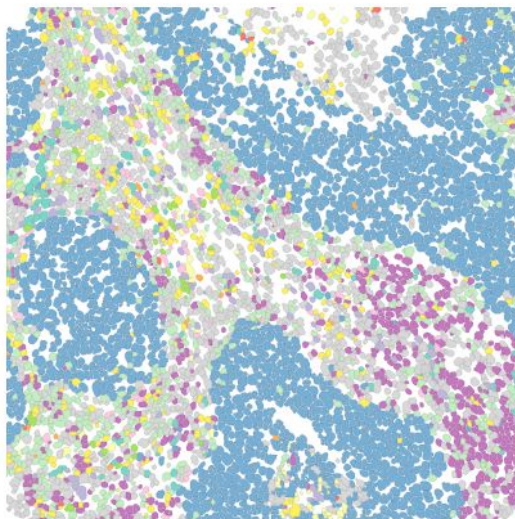
# Interesting innovation in dynamic visualization: Kris

- Neighboring cells can have relatively different U-Map projections, at least with the current transformation / channels
- Immune cells at the boundary between tumor and immune have noticeably different expression (and lay elsewhere on the map)

The code to prepare the data is [here](#).

The tumor clusters (from the original rda object) are 4, 7, 10, 17.

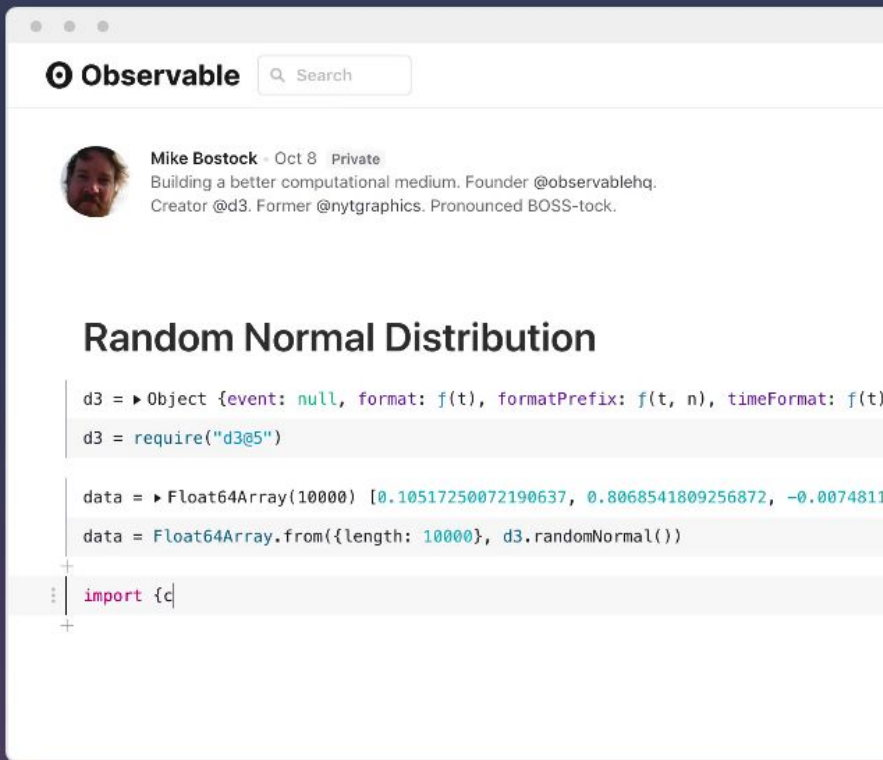
The immune clusters are 1, 2, 3, 4, 8, 10, 11, 12.



Feature

## Learn and reuse

- Designed from the ground up to **share ideas**.
- Code has never been easier to **find and reuse**.
- **Thousands of notebooks** to learn from and fork.
- Turn any notebook into a little library by **importing cells**.



The screenshot shows a web browser window with the Observable logo and a search bar. Below the header is a user profile for Mike Bostock, dated Oct 8, Private. The notebook title is "Random Normal Distribution". The code is as follows:

```
d3 = ▶ Object {event: null, format: f(t), formatPrefix: f(t, n), timeFormat: f(t)}
d3 = require("d3@5")

data = ▶ Float64Array(10000) [0.10517250072190637, 0.8068541809256872, -0.0074811]
data = Float64Array.from({length: 10000}, d3.randomNormal())

import {c}
```

# Basic facts

- It takes an ecosystem to make an analysis
- It takes an ecosystem to make an ecosystem
- Where do you begin?
  - Functions, packages, data structures, ... ?
- Claim: Two elements are fundamental
  - Ecosystem builder
  - Evolutionary strategy
- Fun fact: software ecosystem health assessment is a thing!

# Reviewing the Health of Software Ecosystems – A Conceptual Framework Proposal

Konstantinos Manikas and Klaus Marius Hansen

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**Abstract.** The health of a **software ecosystem** is an indication of how well the ecosystem is functioning. The measurement of health can point to issues that need to be addressed in the ecosystem and areas for the ecosystem to improve. However, the **software ecosystem** field lacks an applicable way to measure and evaluate health. In this work, we review the literature related to the concept of software ecosystem health and the literature that inspired the **software ecosystem** health literature (a total of 23 papers) and (i) identify that the main source of inspiration is the health of business ecosystems while also influenced by theories





# Community Health Analytics Open Source Software

LEARN MORE

Screenshot

CHAOSS is a Linux Foundation project focused on creating analytics and metrics to help define community health. [Learn More](#)

Get to know the CHAOSS community and learn how to [participate](#).



## CHAOSS Working groups

The goal of the working groups is to refine the metrics and to work with software implementations. The workgroups are built around the four categories of metrics that CHAOSS has identified.

The working groups are:

- [Common Metrics](#)
- [Diversity and Inclusion](#)
- [Evolution](#)
- [Risk](#)
- [Value](#)



🔍 Search for one of your repos ( \*repo group name\*/ \*repo name\* )

Insights

Bioconductor / IRanges

Repos

Groups

Recent views  
for this repo:

Overview

Risk Metrics

Compare from your  
repos:

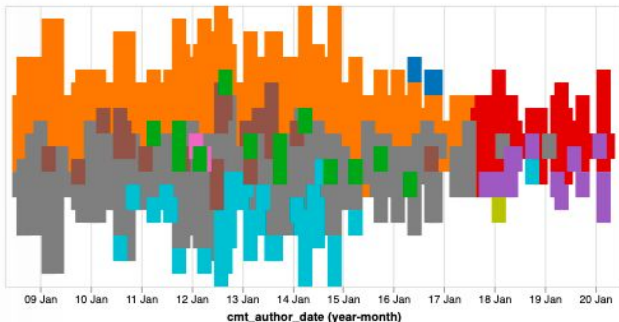
Select Group

Select Repo

Apply Reset

Screenshot

### Lines of code added by the top 10 authors as Percentages - By Time Period



#### cmt\_author\_email

- Lori.Shepherd@RoswellPark.org
- biocbuild@malbec1.roswellpark.org
- dtenenba@taipan.fhrc.org
- hpages@fredhutch.org

### License Coverage

0.4%

Total Files 247

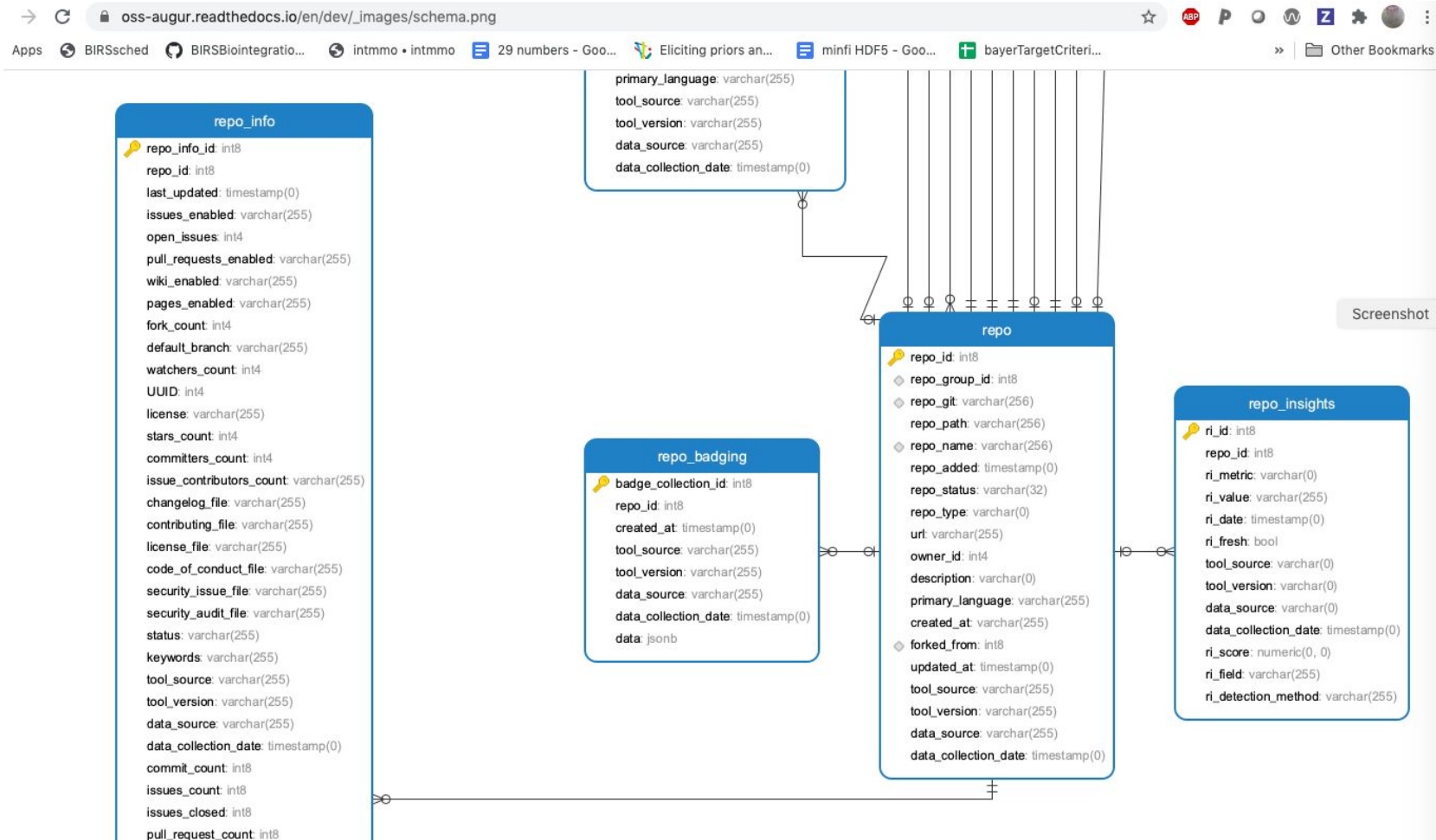
Files with Declared Licenses 1

Files without Licenses 246

### Lines of code added by the top 10 authors

Author	2008	2009	2010	2011	2012	2013	2014
biocbuild@malbec1.roswellpark.org	0	13164	2874	9645	14746	7745	111
jrodriguez@um.es	0	19114	5604	0	0	0	1
michafila@gene.com	0	3780	1732	831	1688	2525	12

# CHAOSS obtains metadata about project management such as licensing, issue longevity, CoC, ...



Screenshot

# What does Bioconductor need to be a superb platform for multimodal single-cell genomics?

- Support development of efficient data containers/data services
- Support software developers in achievement of scalability in their tools
- Support end-users in adoption and successful use

# Some themes

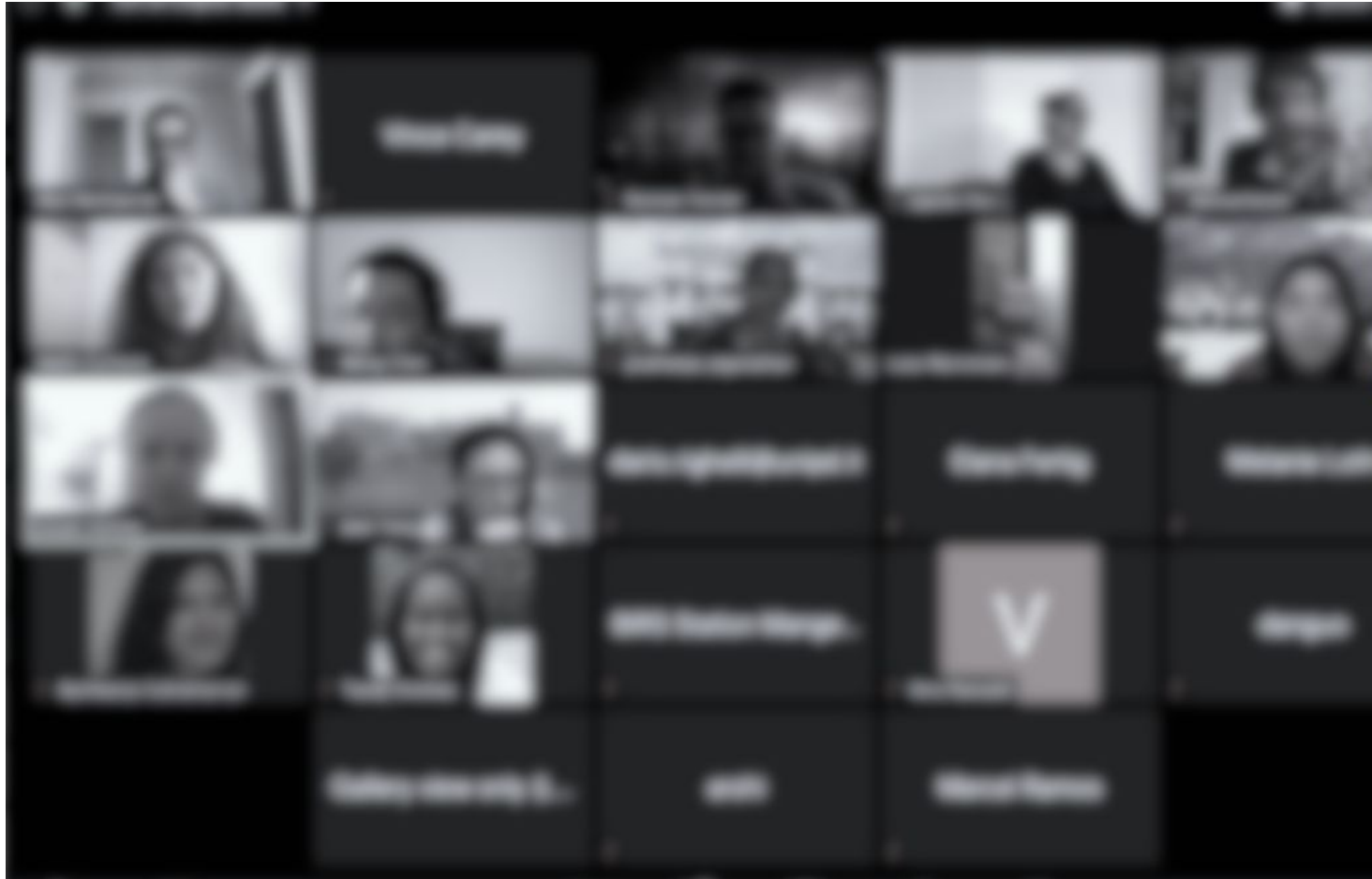
- A system is scalable if its throughput can be increased through cost-effective additions to its "capacity"
  - Adding cores or RAM **is preferred to** reformatting data **is preferred to** refactoring/ rewriting code
- Designing new methods for scalability is intrinsically hard and unstable IT and rapid change in biotechnology makes it harder
- All the components of a software ecosystem need to be jointly tested in realistic settings
  - We are all engaged in continuous integration/continuous distribution(CI/CD), **whether we like it or not**, and components and underlying platforms at developer, tester/builder, or user end can **change at any time**

# Personal thoughts

- "Divide and conquer" is a reasonable strategy for achieving scalability for various common tasks in genomic data science
  - Decomposable (random-access) data representations; programming for data access, sparsity, fault tolerance, ...
  - "Divide and conquer" seems hard to implement in social coding and organic software ecosystem development
- "Mileage" is a useful concept: use "high-mileage" tools that have been found reliable and robust in practice
- For very new biotechnologies, with emphasis on speed of deployment, these principles can be hard to adopt
- Containerization and automated CI/CD are helpful but have their own costs

Socializing divide and conquer is challenging: Brainstorm comment: Everyone thinks their problem/method is unique, so tools proliferate, even though they may implement very similar algorithms

...



# "Bioconductor" centrality: bio-biotech-data science-...

- ~20 years of R-based solutions to problems arising in genome-scale assays
  - Preprocessing: parsing idiosyncratic formats, deriving quantifications, bias assessment, single-sample and multisample transformations for comparability
  - Object designs: increasing reliability through tight binding of metadata to assay data:  $\mathbf{X}[\mathbf{G}, \mathbf{S}]$  endomorphisms
  - Annotation: platforms, genomes, pathways, ontologies, easily joined to assays
  - Visualization and analysis: capitalizing on R/CRAN, and extending the package and repository concepts



# Package

A package is a set of functions and documents that includes a collection of tests of function correctness and adequacy, and passes these tests

The tests should exercise all the functions in realistic ways. Tests should include random inputs and requests -- repeating the same tests over and over again should be avoided, although this has some value when the underlying platform is changing over time

A package may have the capacity to be usable on different technological platforms. When this is achieved, the package is called "portable".

A package may require the existence of other packages

# Virtues and costs of software packages

- Virtues
  - Modularity: address a limited class of tasks
  - Protocols for documentation and testing; issue tracking
  - Management, maintenance, portability systematized
- Costs
  - Dilemmas:
    - dependency on other packages vs. self-sufficiency
    - between maintaining stability for users vs. rapid introduction of new features and improvements
  - Management, maintenance, portability become obligations requiring effort in addition to research progress

# Ecosystem

A software ecosystem is a collection of packages that includes a collection of package interoperability tests, and passes the tests

An ecosystem can be deployed on one or more technological platforms (e.g., operating systems or cloud computing systems) and co-evolves with different platforms that are changing at different rates

# Giotto's implicit cross-language support (user consents)

```
> VC_small <- createGiottoObject(raw_exprs = expr_path, spatial_locs = loc_path)
```

```
Consider to install these (optional) packages to run all possible Giotto  
commands:  MAST trendsceek multinet RTriangle FactoMiner
```

```
Giotto does not automatically install all these packages as they are not  
absolutely required and this reduces the number of dependenciesInstall a  
miniconda Python environment for Giotto? (Yes/no/cancel) yes
```

```
|---- install giotto environment ----|
```

```
Collecting package metadata (current_repodata.json): done
```

```
Solving environment: done
```

```
## Package Plan ##
```

```
environment location: /Users/stvjc/Library/r-miniconda/envs/giotto_env
```

```
added / updated specs:
```

```
- python
```

# Two strategic approaches to consider for R+python

- 1) [basilisk](#) (Aaron Lun): Infrastructure support for Bioc-python interoperation -- a base conda environment is stored in user cache area, keyed to current Bioc/basilisk version; *client packages* specify **exact name and version** of python modules desired, which are acquired and cached as needed
- 2) [BiocSklern](#) and other basilisk-client packages to expose numerical and statistical components of interest
  - > Be precise about versions
  - > Don't go it alone!

# Core packages installed with basilisk

```
> library(basilisk)
1/8 packages newly attached/loaded, see sessionInfo() for details.
> listPackages()

```

	full	package
1	asn1crypto==1.3.0	asn1crypto
2	certifi==2020.4.5.2	certifi
3	cffi==1.14.0	cffi
4	chardet==3.0.4	chardet
5	conda==4.8.3	conda
6	conda-package-handling==1.6.0	conda-package-handling
7	cryptography==2.8	cryptography
8	idna==2.8	idna
9	pycosat==0.6.3	pycosat
10	pycparser==2.19	pycparser
11	pyOpenSSL==19.1.0	pyOpenSSL
12	PySocks==1.7.1	PySocks
13	requests==2.22.0	requests
14	ruamel-yaml==0.15.87	ruamel-yaml
15	six==1.14.0	six
16	tqdm==4.42.1	tqdm
17	urllib3==1.25.8	urllib3

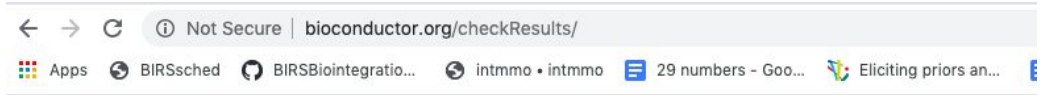
```
\ ■
```



Claim: the heart of the ecosystem is its build system/build governance

Bioconductor's principles:

- Three platforms (linux, windows, mac)
- Two streams: release, devel
- Track R's versioning (devel Oct-March, release April-Sept)
- Fast enough for biotech (point release every 6 months)
- Limited back-compatibility (to drop a component, deprecate for one release, then defunct)
- Software, annotation, and experiment packages are all first-class citizens
- Package dependencies limited to CRAN and Bioconductor



## Bioconductor build/check results

[Build System RSS Feeds](#)

### Bioconductor 3.12 (devel)

Latest results

- Software packages (daily): [browse](#), [download](#)
- Annotation packages (Wednesdays): [browse](#), [download](#)
- Experimental data packages (Mondays, Thursdays): [browse](#), [download](#)
- Workflow packages (Tuesdays, Fridays): [browse](#), [download](#)
- Long Tests (Saturdays only): [browse](#), [download](#)

### Bioconductor 3.11 (release)

Latest results

- Software packages (daily): [browse](#), [download](#)
- Annotation packages (Wednesdays): [browse](#), [download](#)
- Experimental data packages (Mondays, Thursdays): [browse](#), [download](#)
- Workflow packages (Tuesdays, Fridays): [browse](#), [download](#)
- Long Tests (Saturdays only): [browse](#), [download](#)



To support 1844 Bioc software packages, need 3862 total packages (including CRAN)

## Multiple platform build/check report for BioC 3.12

This page was generated on 2020-06-18 14:45:04 -0400 (Thu, 18 Jun 2020).

Approx. Package Snapshot Date (git pull): **2020-06-17 16:50:45 -0400 (Wed, 17 Jun 2020)**

Hostname	OS	Arch (*)	Platform label (**)	R version	Installed pkgs
<a href="#">malbec1</a>	Linux (Ubuntu 18.04.4 LTS)	x86_64	x86_64-linux-gnu	4.0.0 RC (2020-04-19 r78255) -- "Arbor Day"	<a href="#">3862</a>
<a href="#">tokay1</a>	Windows Server 2012 R2 Standard	x64	mingw32 / x86_64-w64-mingw32	4.0.0 (2020-04-24) -- "Arbor Day"	<a href="#">3634</a>
<a href="#">merida1</a>	macOS 10.14.6 Mojave	x86_64	x86_64-apple-darwin18.7.0	4.0.0 (2020-04-24) -- "Arbor Day"	<a href="#">3638</a>

Click on any hostname to see more info about the system (e.g. compilers) (\*) as reported by 'uname -p', except on Windows and Mac OS X (\*\*) as reported by 'gcc -v'

Screenshot

### Package status is indicated by one of the following glyphs

- TIMEOUT** INSTALL, BUILD, CHECK or BUILD BIN of package took more than 40 minutes
- ERROR** Bad DESCRIPTION file or INSTALL, BUILD or BUILD BIN of package failed, or CHECK produced errors
- WARNINGS** CHECK of package produced warnings
- OK** INSTALL, BUILD, CHECK or BUILD BIN of package was OK
- skipped** CHECK or BUILD BIN of package was skipped because the BUILD step failed
- NA** BUILD, CHECK or BUILD BIN result is not available because of an anomaly in the Build System

Click on any glyph in the report below to access the detailed results.

- Use the check boxes to show only packages
- with the
- selected status types.

### Package propagation status is indicated by one of the following LEDs

- YES: Package was propagated because it didn't previously exist or version was bumped
- NO: Package was not propagated because of a problem (impossible dependencies, or version lower than what is already propagated)
- UNNEEDED: Package was not propagated because it is already in the repository with this version. A version bump is required in order to propagate it

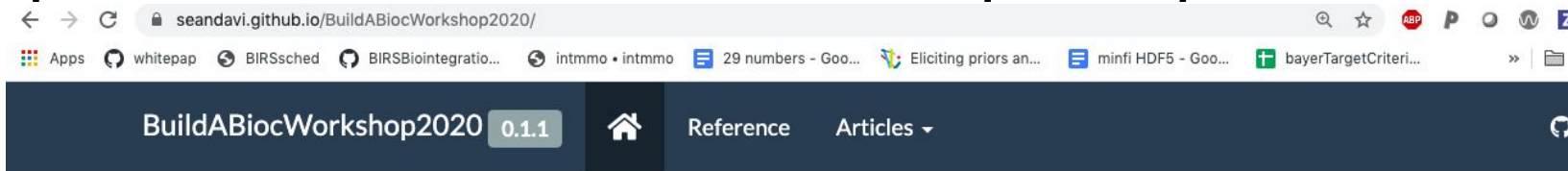
A crossed-out package name indicates the package is [deprecated](#)

SUMMARY	OS / Arch	INSTALL			BUILD			CHECK			BUILD BIN			
<a href="#">malbec1</a>	Linux (Ubuntu 18.04.4 LTS) / x86_64	0	24	1844	1	56	1811	0	51	272	1488			
<a href="#">tokay1</a>	Windows Server 2012 R2 Standard / x64	0	27	1814	1	66	1774	8	65	404	1297	0	2	1772
<a href="#">merida1</a>	macOS 10.14.6 Mojave / x86_64	0	38	1822	1	85	1774	0	55	272	1447	0	0	1774

# Opportunities for build system/ecosystem/users

- Containerization of builder infrastructure
- Binary package repositories for container users
- Continuous integration/delivery via github actions
- Data services
- Analysis services: GA4GH Tool Registry Service, and Workflow Execution Service are standards to watch for large genomic workflows

# Example from Sean Davis: workshop components



BuildABiocWorkshop2020 0.1.1

Reference Articles

## BuildABiocWorkshop2020

This package is a template for building a Bioconductor 2020 workshop. The package includes Github actions to:

1. Set up bioconductor/bioconductor\_docker:devel on Github resources
2. Install package dependencies for your package (based on the DESCRIPTION file)
3. Run `rcmdcheck::rcmdcheck`
4. Build a pkgdown website and push it to github pages
5. Build a docker image with the installed package and dependencies

## Responsibilities

This year, package authors will be primarily responsible for:

1. Creating a landing site of their choosing for their workshops (a website). This website should be listed in the DESCRIPTION file as the URL .
2. Creating a docker image that will contain workshop materials and the installed packages necessary to run those materials. The name of the resulting docker image, including “tag” if desired, should be listed in a non-standard tag, `DockerImage:` in the DESCRIPTION file.

## Links

Browse source code at

<https://github.com/seandavi/BuildABiocWorkshop2020/>

Report a bug at

<https://github.com/seandavi/BuildABiocWorkshop2020/issues/new/choose>

## License

[Full license](#)

MIT + file LICENSE

## Developers

Sean Davis

Author, maintainer 

# "workshop" concept deployed in support of this talk

The screenshot shows the GitHub interface for the repository `vjcitn/intmmo`. The repository is described as "Software for integrative multi-modal (pkgdown at <https://vjcitn.github.io/intmmo>)". It has 37 commits, 2 branches, 0 packages, 0 releases, 1 environment, and 1 contributor. The current branch is `gh-pages`. The commit history table below shows several recent commits, including deployments to `gh-pages` and updates to workflow files and images.

Repository: `vjcitn / intmmo` (Unwatch 1, Star 0, Fork 0)

Code | Issues 0 | Pull requests 0 | ZenHub | Actions | Projects 0 | Wiki | Security 0 | Insights | Settings

Software for integrative multi-modal (pkgdown at <https://vjcitn.github.io/intmmo>) Edit

Manage topics

37 commits | 2 branches | 0 packages | 0 releases | 1 environment | 1 contributor

Branch: `gh-pages` | [New pull request](#) | [Create new file](#) | [Upload files](#) | [Find file](#) | [Clone or download](#)

Commit	Message	Time
<code>vjcitn</code>	Deploying to gh-pages from @ 144774f 🚀	Latest commit <code>ddcab7c</code> yesterday
<code>.github/workflows</code>	first attempt	11 days ago
<code>articles</code>	Deploying to gh-pages from @ 144774f 🚀	yesterday
<code>inst/images</code>	first attempt	11 days ago
<code>reference</code>	Deploying to gh-pages from @ 144774f 🚀	yesterday
<code>vignettes</code>	minor changes, new figure	yesterday
<code>404.html</code>	Deploying to gh-pages from @ 144774f 🚀	yesterday
<code>DESCRIPTION</code>	minor changes, new figure	yesterday

Branch: gh-pages [intmimo / .github / workflows / basic\\_checks.yaml](#) Find file Copy path

vjcitn first attempt 1e60b37 11 days ago  
1 contributor

69 lines (60 sloc) 2.26 KB Raw Blame History

```
1 on: [push]
2 jobs:
3   job1:
4     runs-on: ubuntu-latest
5     container: bioconductor/bioconductor_docker:devel
6     steps:
7       - uses: actions/checkout@v1
8
9       - name: Query dependencies
10        run: |
11          install.packages('remotes')
12          saveRDS(remotes::dev_package_deps(dependencies = TRUE), ".github/depends.Rds", version = 2)
13        shell: Rscript {0}
14
15       - name: Cache R packages
16        if: runner.os != 'Windows'
17        uses: actions/cache@v1
18        with:
19          path: /usr/local/lib/R/site-library
20          key: ${{ runner.os }}-r-1-${{ hashFiles('.github/depends.Rds') }}
21          restore-keys: ${{ runner.os }}-r-1-
```

# github actions builds a formatted site



## intmmo – software considerations for integrative analysis of multimodal omics experiments

Support for a talk by Vince Carey at Banff 2020 multiomics workshop

### Links

Browse source code at

<https://github.com/vjcitr/intmmo/>

Report a bug at

<https://github.com/vjcitr/intmmo/issues/new/choose>

### License

[Full license](#)

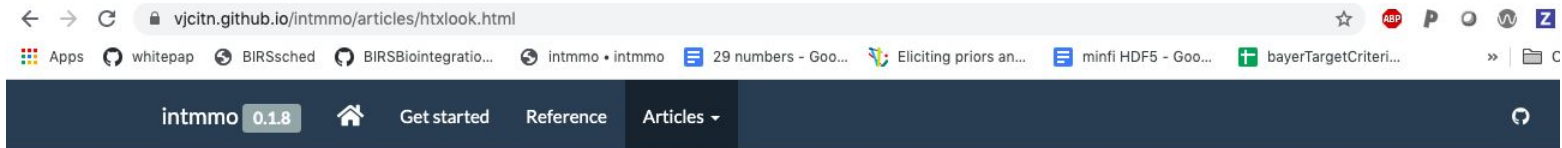
[MIT](#) + file [LICENSE](#)

### Developers

Vincent Carey

Author, maintainer 

# The "article" illustrates use of HSDS/restfulSE



## A look at a cloud-resident data service: HSDS (HDF Scalable Data Service)

### Contents

Taking a look at  
HumanTranscriptomeCompendium

Vince Carey<sup>1</sup>

Source: `vignettes/htxlook.Rmd`

## Taking a look at HumanTranscriptomeCompendium

```
suppressPackageStartupMessages({  
  library(BiocStyle)  
})
```

Following on Sean Davis' BigRNA project, in which 181000+ RNA-seq studies in NCBI SRA are processed by a salmon-based workflow, we transformed the gene-level quantifications to HDF5 and loaded them into the HDF Scalable Data Service (HSDS).

The `restfulSE` package uses `rhdf5client` to implement a `DelayedArray/SummarizedExperiment` interface to this collection of transcriptomes.

```
suppressPackageStartupMessages({  
  library(HumanTranscriptomeCompendium)  
  library(SummarizedExperiment)  
})  
htx = htx_load()  
#> Loading required namespace: BiocFileCache  
#> using temporary cache /tmp/RtmpiZ3hcG/BiocFileCache
```

```
library(HumanTranscriptomeCompendium)
library(SummarizedExperiment)
})
htx = htx_load()
#> Loading required namespace: BiocFileCache
#> using temporary cache /tmp/RtmpiZ3hcG/BiocFileCache
#> adding RDS to local cache, future invocations will use local image
#> adding rname 'https://s3.amazonaws.com/bcfound-bigrna/rangedHtxGeneSE.rds'
htx
#> class: RangedSummarizedExperiment
#> dim: 58288 181134
#> metadata(1): rangeSource
#> assays(1): counts
#> rownames(58288): ENSG00000000003.14 ENSG00000000005.5 ...
#> ENSG00000284747.1 ENSG00000284748.1
#> rowData names(0):
#> colnames(181134): DRX001125 DRX001126 ... SRX999990 SRX999991
#> colData names(4): experiment_accession experiment_platform
#> study_accession study_title
system.time(lka <- assay(htx))
#> Loading required package: rhdf5client
#> user system elapsed
#> 0.178 0.000 0.178
lka
#> <58288 x 181134> matrix of class DelayedMatrix and type "double":
#>
#> ENSG00000000003.14 DRX001125 DRX001126 DRX001127 ... SRX999990
#> ENSG00000000005.5 40.001250 1322.844547 1528.257578 . 1149.0341
#> ENSG000000000005.5 0.000000 9.999964 6.000006 . 0.0000
#> ENSG000000000419.12 64.000031 1456.004418 2038.996875 . 1485.0003
#> ENSG000000000457.13 31.814591 1583.504257 1715.041308 . 631.7751
#> ENSG000000000460.16 12.430602 439.321234 529.280324 . 945.6903
#> ... . . . .
#> ENSG00000284744.1 1.05614505 24.81388079 32.29261298 . 7.316061
#> ENSG00000284745.1 0.99999879 15.99996994 16.99999743 . 0.000000
#> ENSG00000284746.1 0.00000000 0.00379458 0.00000000 . 0.000000
#> ENSG00000284747.1 7.77564984 270.83296409 239.88056843 . 108.011633
#> ENSG00000284748.1 1.00000768 22.23010514 37.73881938 . 11.278980
```

## Contents

Taking a look at  
HumanTranscriptomeCompendium



# Conclusions

- Rapid evolution in biotech and information technology lead to unstable software development situations
- Team coordination is crucial to avoid needless redundancy and gain mileage on all components
- Pain points for developers should be eased with continuous integration enhancements
  - Github actions should play a useful role
- GA4GH standards (TRS, WES) should be revisited frequently