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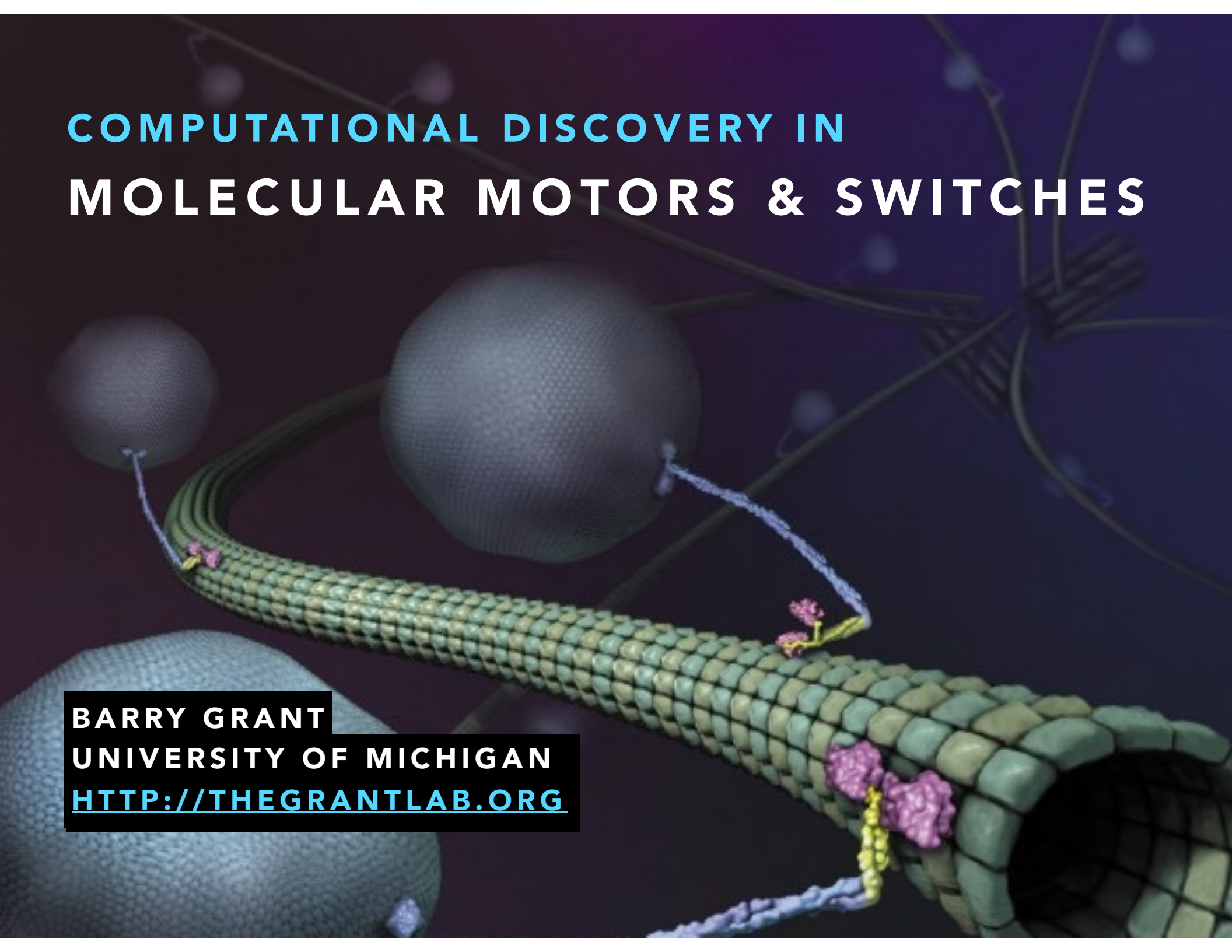


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M.Res. ② Bioinformatics Scientist ⑤ Bioinformatics
Ph.D. ③ Chemistry Faculty ⑥ Bioinformatics



COMPUTATIONAL DISCOVERY IN MOLECULAR MOTORS & SWITCHES

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UNIVERSITY OF MICHIGAN
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COMPUTATIONAL DISCOVERY IN MOLECULAR MOTORS & SWITCHES

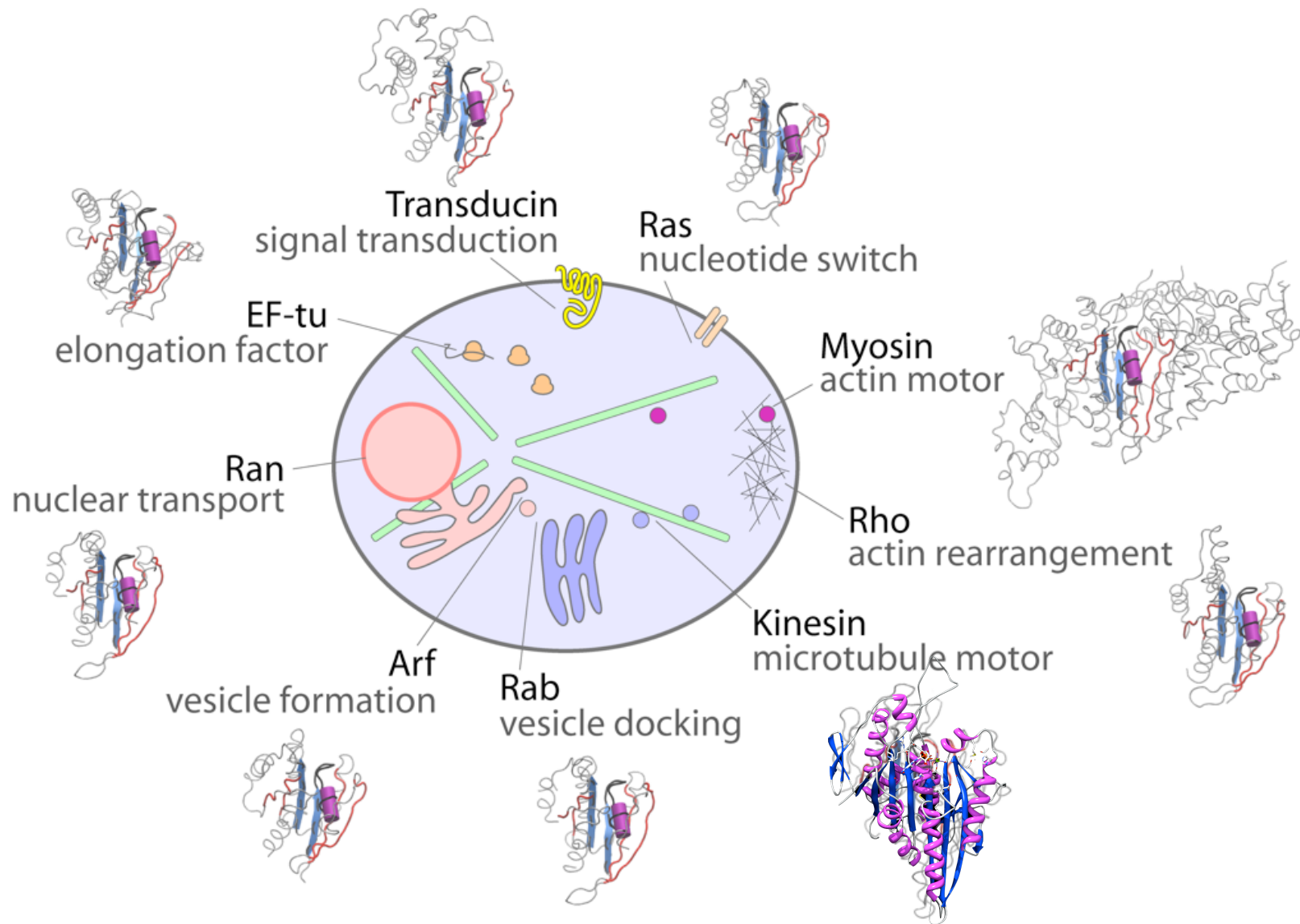
BARRY GRANT
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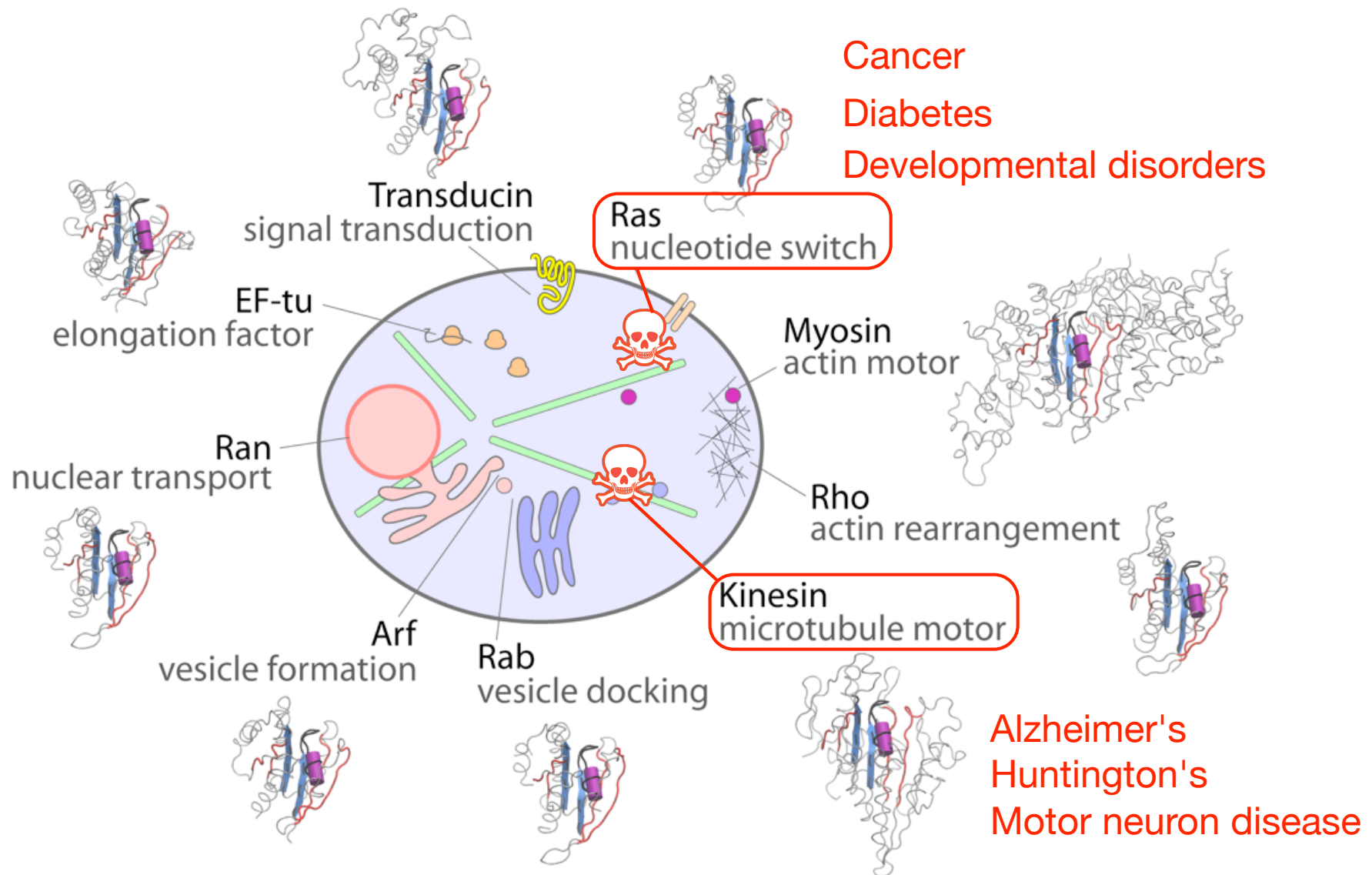
Kinesin Motor



Molecular motors and switches lie at the heart of key biological processes

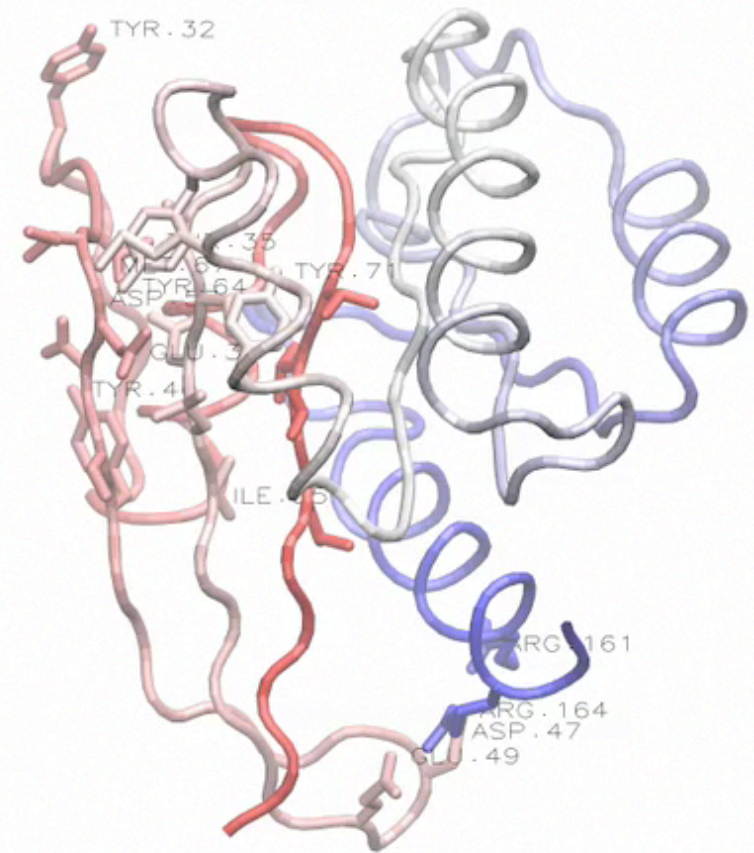
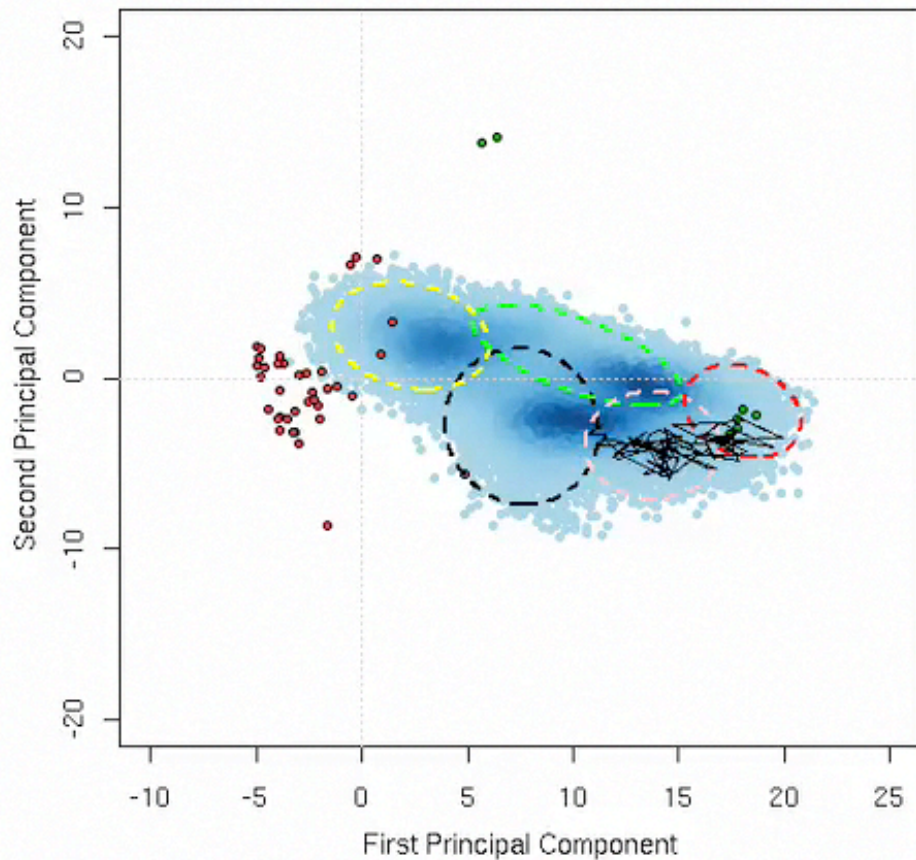


Aberrant function of motors and switches is associated with many **diseases**



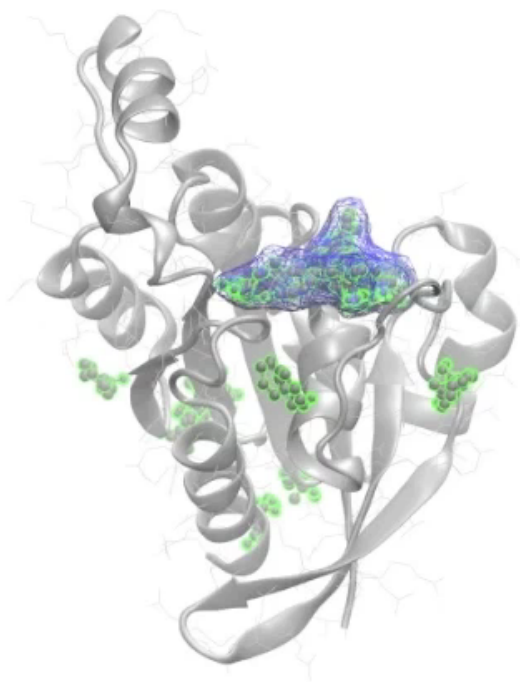
Simulations of conformational activation

Accelerated molecular dynamics simulations reveal the mechanism of Ras molecular switch activation and the perturbing effect of mutations

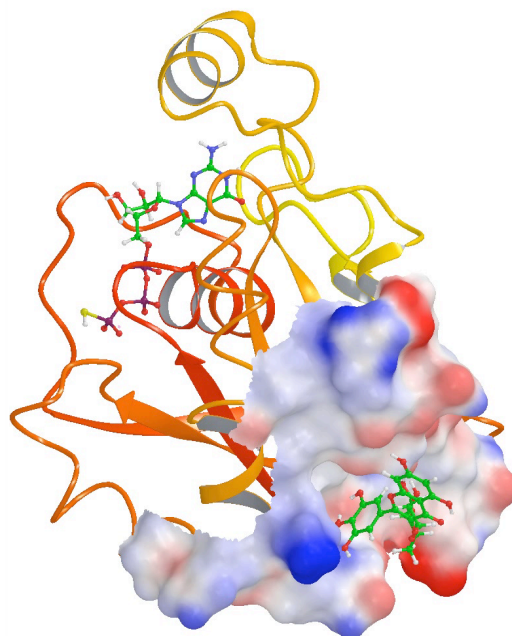


Allosteric inhibitor design & testing

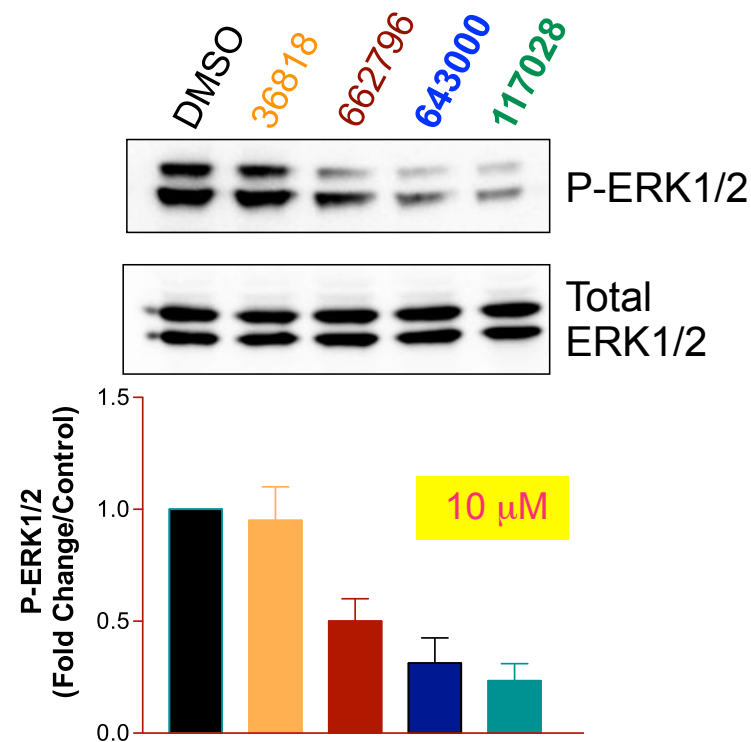
Computational methods can identify novel transient binding pockets & cognate inhibitors that may offer new avenues for future therapeutics



Ensemble binding site mapping



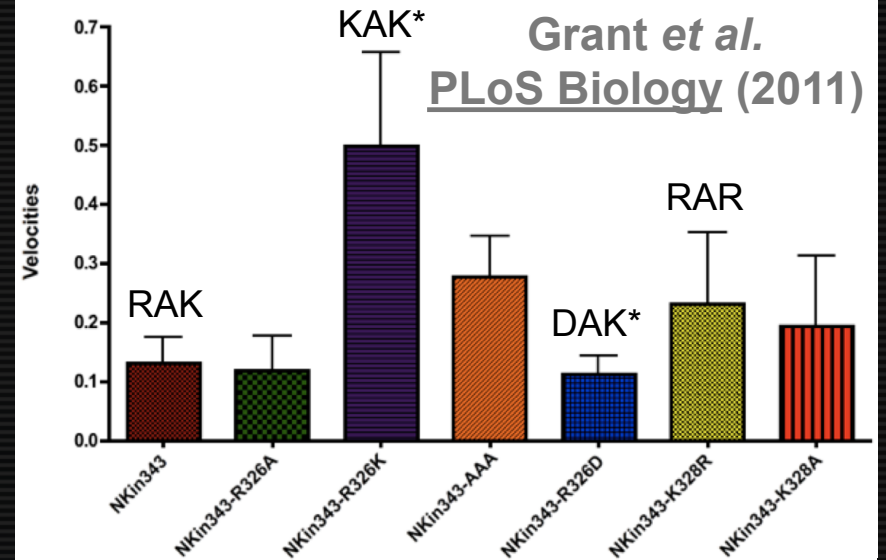
Ensemble small molecule docking



Compound testing in cancer cell lines

MAPPING MOTOR PROCESSIVITY DETERMINANTS

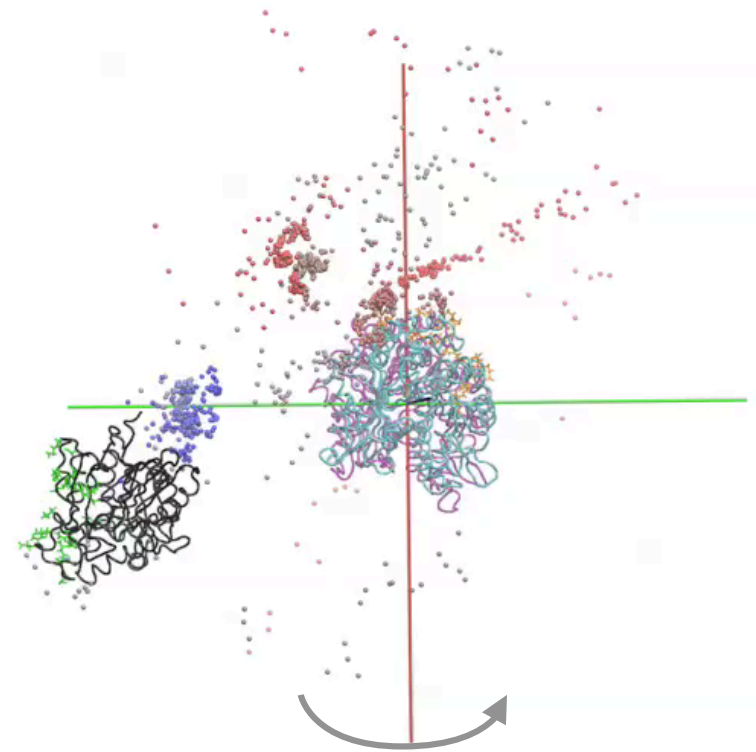
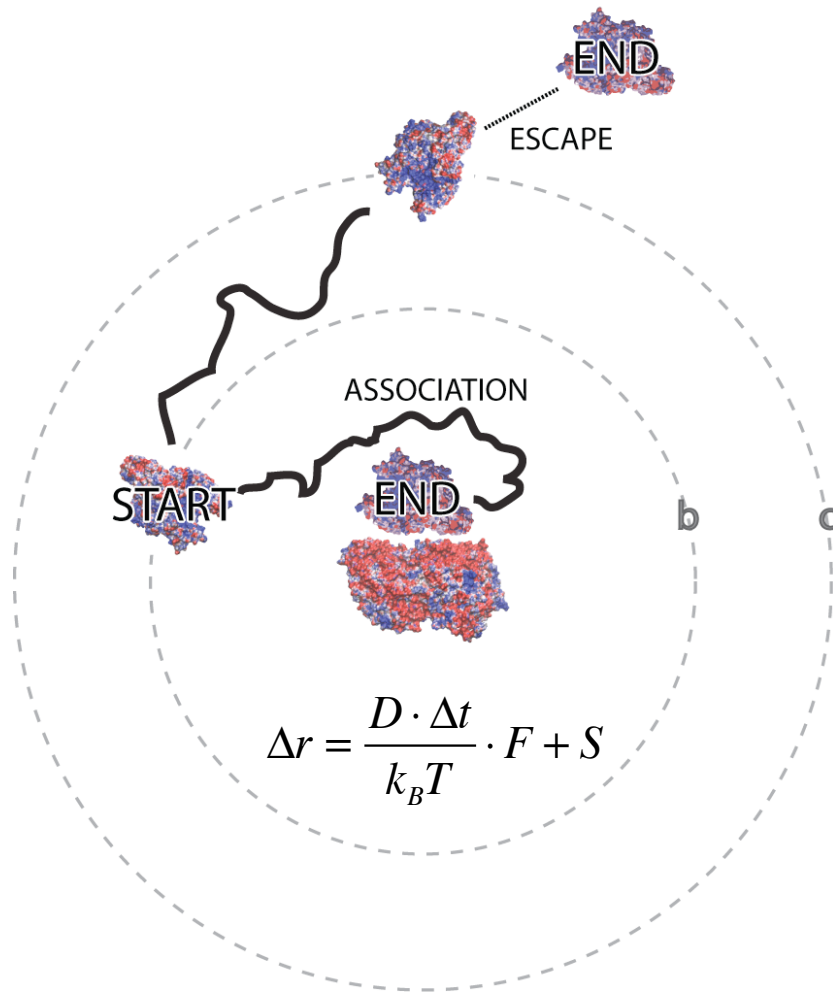
RATIONAL VELOCITY ALTERATION



0.0 sec

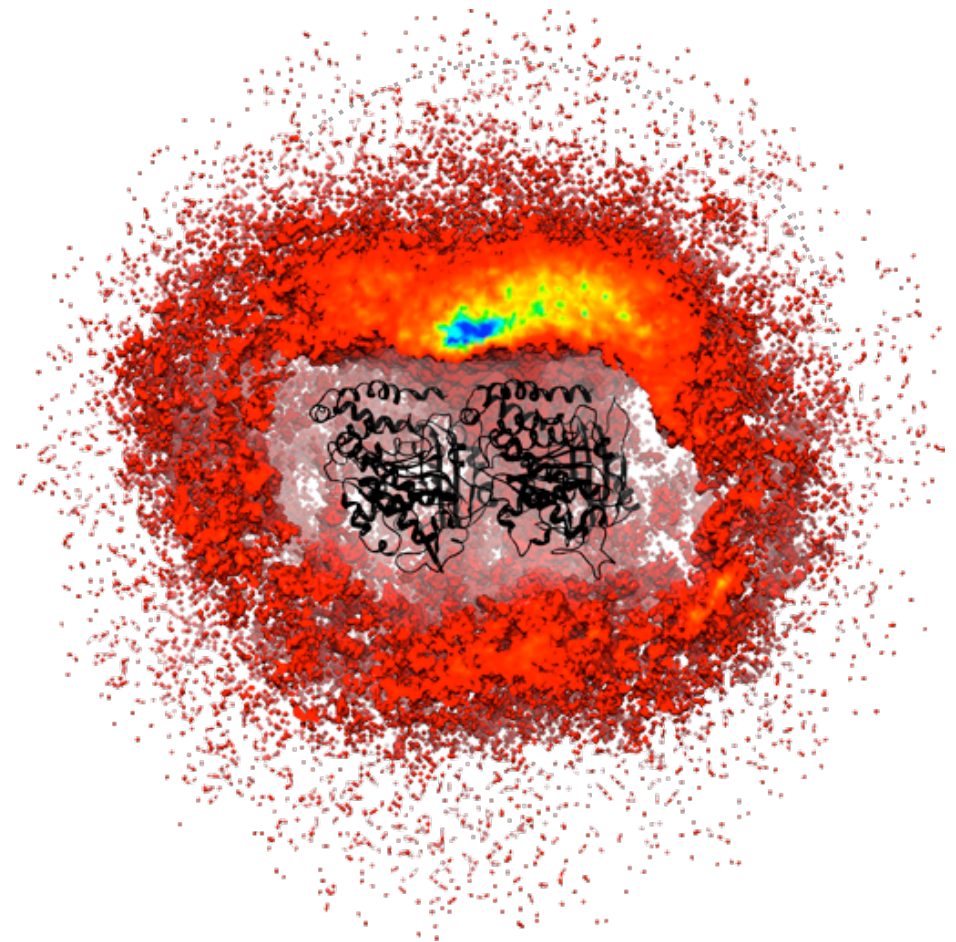
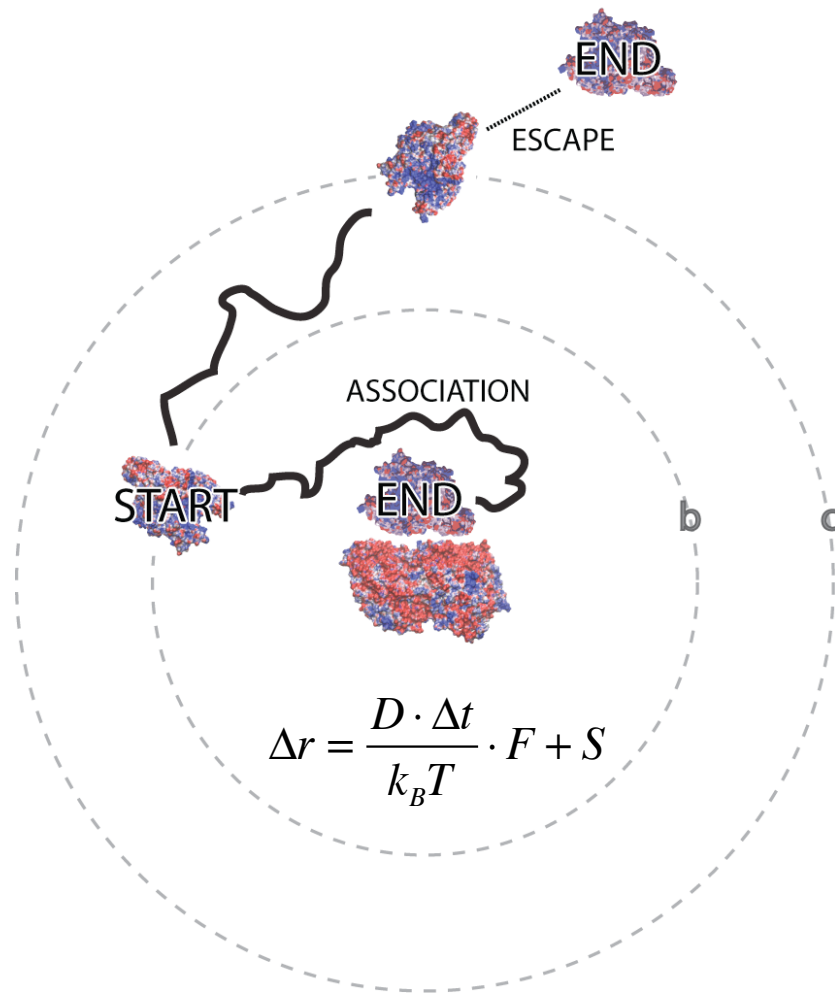
Animation available from: <http://multimedia.mcb.harvard.edu/>

Brownian dynamics model of kinesin-tubulin association



Single Trajectory
PLoS Biology (2011)

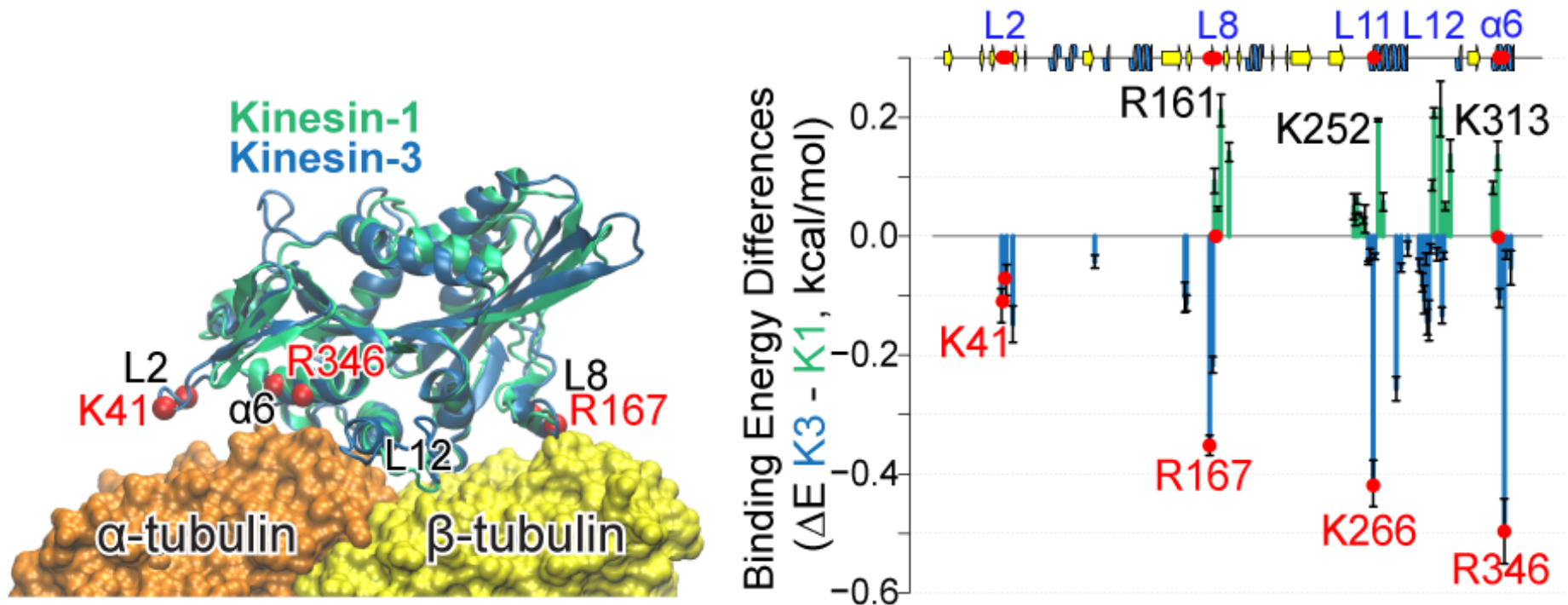
Brownian dynamics model of kinesin-tubulin association



200k Trajectories

Mapping motor processivity determinants

Select family-specific motor-microtubule interactions are predicted to influence complex stability and motor motility



Side Note: Integrating protein structural dynamics and evolutionary analysis with **Bio3D**

The image displays a collage of screenshots related to the Bio3D software and its application in protein structural dynamics and evolutionary analysis.

- Bitbucket Repository:** Shows the Bitbucket interface for the repository `GrantLab/bio3d`, including details like 11 branches, 6 tags, and recent activity.
- Bio3D Website:** Displays the Bio3D website with navigation links (Home, User guide, Demo, Tutorials, Documentation, Download, Grant Lab) and a "Download" button.
- Terminal Window:** Shows R code for dynamic network analysis:

```
library(bio3d)
trj <- read.ncdf("trj.nc")
pdb <- read.pdb("top.pdb")
ca.indxs <- atom.select(pdb, "calpha")
xyz <- fit.xyz(pdb, trj, ca.indxs$xyz)
cij <- dcm(xyz)
net <- cna(cij)
view.cna(net, pdb, launch=TRUE)
par(mfrow=c(1, 2))
plot.cna(net, pdb, full=TRUE, vertex.label=NA)
plot.cna(net, pdb)
```
- Residue Cross Correlation:** A heatmap showing the correlation between residues (Residue No. 50 to 300) with a color scale from -1.0 to 1.0.
- 3D Protein Structure:** A ribbon diagram of a protein structure, colored by domain or region.
- Network Graphs:** Two network graphs showing interactions between residues. The left graph is a large, dense network, and the right graph is a smaller, simplified network with highlighted nodes.

<http://thegrantlab.org/bio3d/>

Skjærven, Yao, ... Grant BMC Bioinf (2014)

Side Note: Integrating protein structural dynamics and evolutionary analysis with **Bio3D**

The image displays a collage of screenshots related to the Bio3D project. At the top, there are screenshots of a Bitbucket repository page for 'GrantLab/bio3d' and a website page for 'thegrantlab.org/bio3d/tutorials'. Below these, the Bio3D web application interface is shown, featuring a navigation menu (SEARCH, ALIGN, FIT, PCA, eNMA, HELP) and a 'Principal Component Visualization' section. A large blue box with the text 'WebApps' is overlaid on the web application interface. To the right, a terminal window shows R code for running the Bio3D package, with a large blue box containing the text 'R Package' overlaid on it. Below the code, there are several plots: a 'Residue Cross Correlation' heatmap, a 'Conformer plot' showing PCA results, and a network graph. The network graph shows nodes representing residues and edges representing interactions, with nodes colored by cluster.

<http://thegrantlab.org/bio3d/>

Skjærven, Yao, ... Grant BMC Bioinf (2014)

ACKNOWLEDGEMENTS

Kristen Verhey (UM, CDB)

Rob Cross (U. of Warwick, UK)

Etsuko Muto (Riken Institute, Japan)

Carolyn Moores (UCL, UK)

Steven Rosenfeld (Cleveland Clinic)

Alemayehu Gorfe (UTMS-H)

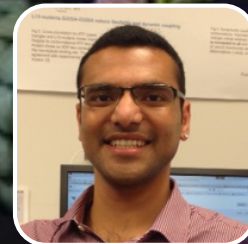
Bjoern Peters (LIAI)

Sivaraj Sivaramakrishnan (UM, CDB)

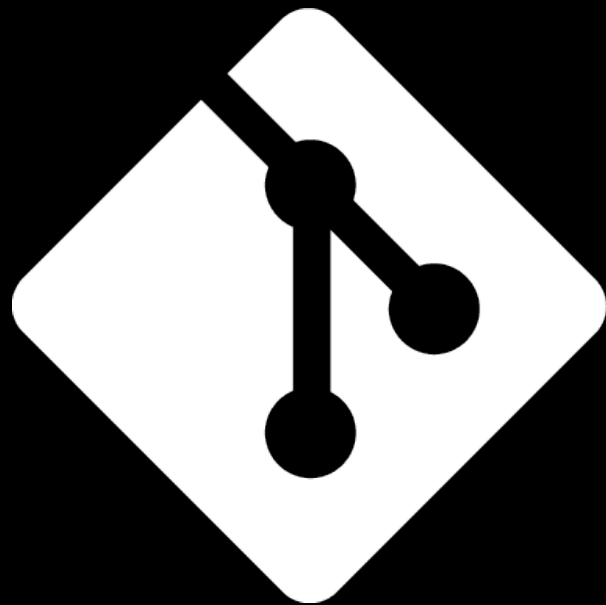
Chao-Yie Yang (UM, Internal Med)

John Traynor (UM, Pharmacology)

Lars Skjærven (U.of Bergen, Norway)



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git

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<http://thegrantlab.org>

What is Git?

(1) An unpleasant or contemptible person. Often incompetent, annoying, senile, elderly or childish in character.



(2) A modern distributed version control system with an emphasis on speed and data integrity.



What is Git?

(1) An unpleasant or contemptible person. Often incompetent, annoying, senile, elderly or childish in character.



(2) A modern distributed version control system with an emphasis on speed and data integrity.



Version Control

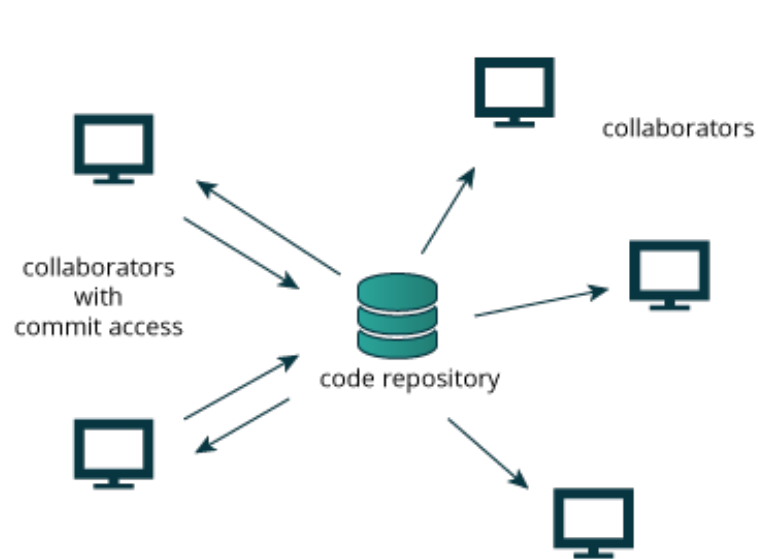
Version control systems (VCS) record changes to a file or set of files over time so that you can recall specific versions later.

Client-server	Free/open-source	CVS (1986, 1990 in C) · CVSNT (1998) · QVCS Enterprise (1998) · Subversion (2000)
	Proprietary	Software Change Manager (1970s) · Panvalet (1970s) · Endeavor (1980s) · Dimensions CM (1980s) · DSEE (1984) · Synergy (1990) · ClearCase (1992) · CMVC (1994) · Visual SourceSafe (1994) · Perforce (1995) · StarTeam (1995) · Integrity (2001) · Surround SCM (2002) · AccuRev SCM (2002) · SourceAnywhere (2003) · Vault (2003) · Team Foundation Server (2005) · Team Concert (2008)
Distributed	Free/open-source	GNU arch (2001) · Darcs (2002) · DCVS (2002) · ArX (2003) · Monotone (2003) · SVK (2003) · Codeville (2005) · Bazaar (2005) · Git (2005) · Mercurial (2005) · Fossil (2007) · Veracity (2010)
	Proprietary	TeamWare (1990s?) · Code Co-op (1997) · BitKeeper (1998) · Plastic SCM (2006)

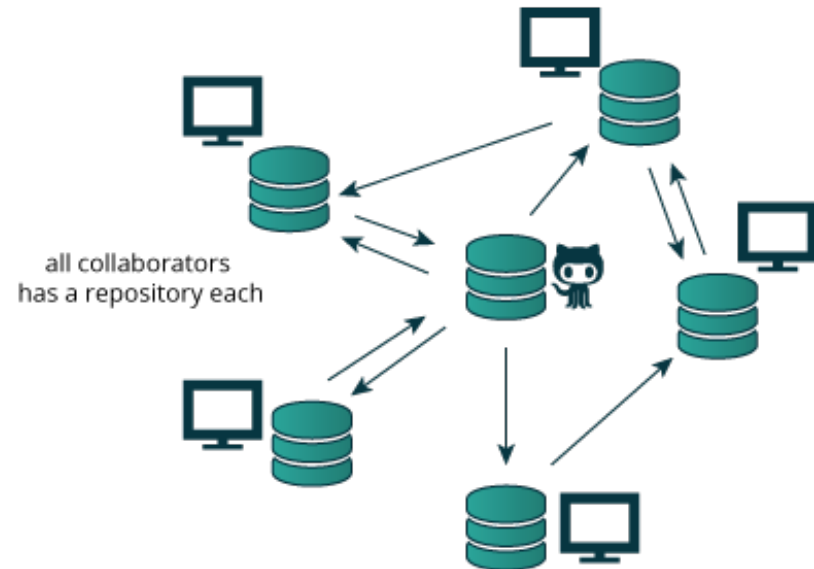
There are many VCS available, see:

https://en.wikipedia.org/wiki/Revision_control

Client-Server vs Distributed VCS



Client-server approach



Distributed approach

Distributed version control systems (DCVS) allows multiple people to work on a given project without requiring them to share a common network.

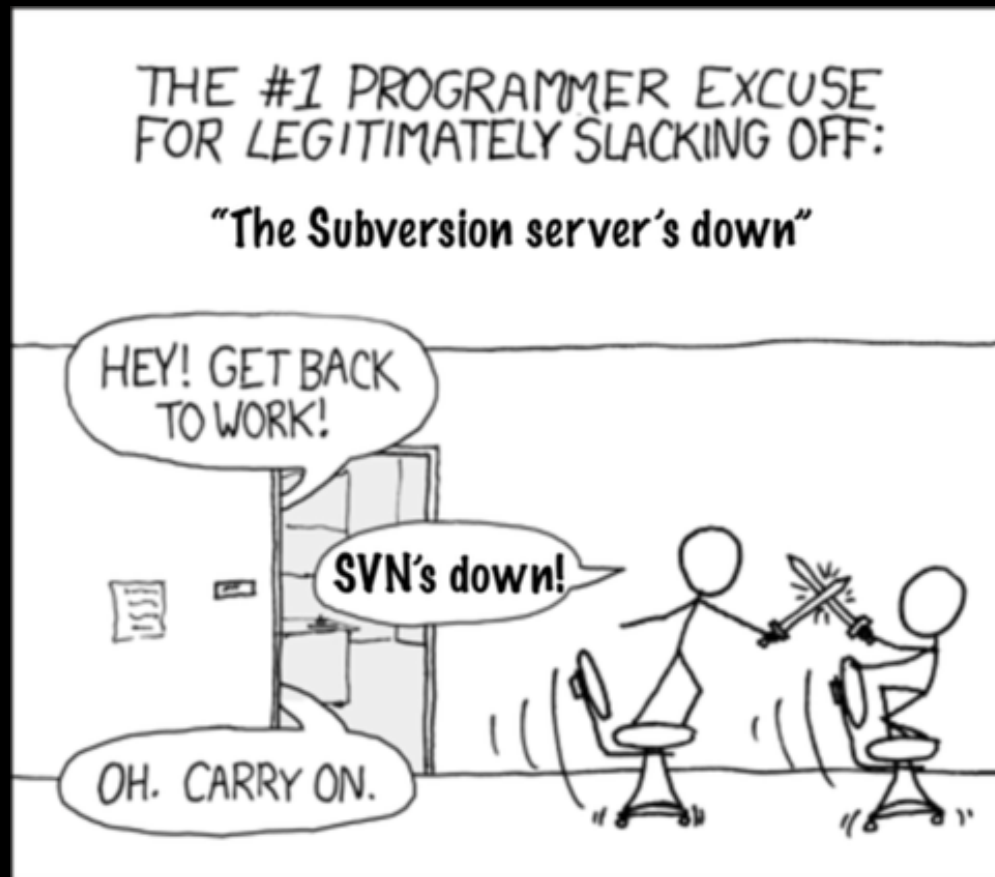
THE #1 PROGRAMMER EXCUSE
FOR LEGITIMATELY SLACKING OFF:

"The Subversion server's down"



<http://tinyurl.com/distributed-advantages>

Git is now the most popular free VCS!



Git offers:

- Speed
- Backups
- Off-line access
- Small footprint
- Simplicity*
- Social coding

<http://tinyurl.com/distributed-advantages>

Why use Git?

Q. Would you write your lab book in pencil, then erase and overwrite it every day with new content?

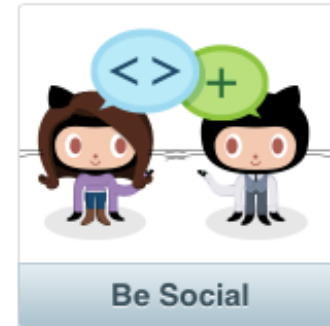
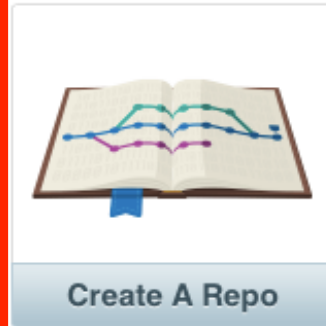
Q. Would you write your lab book in pencil, then erase and overwrite it every day with new content?

Version control is the lab notebook of the digital world: it's what professionals use to keep track of what they've done and to collaborate with others.

Why use Git?

- Provides '**snapshots**' of your project during development and provides a full record of project **history**.
- Allows you to easily **reproduce** and **rollback** to past versions of analysis and compare differences. (N.B. Helps fix software regression bugs!)
- Keeps **track of changes** to code you use from others such as fixed bugs & new features
- Provides a mechanism for sharing, updating and collaborating (like a social network)
- Helps keep your work and software organized and available

Obtaining Git



Sometimes you just need a little help.

How can we help?



<https://help.github.com>

Configuring Git

Do it Yourself!

Configuring Git

(RStudio > Tools > Shell)

First tell Git who you are

```
> git config --global user.name "Barry Grant"  
> git config --global user.email "bjgrant@umich.edu"
```

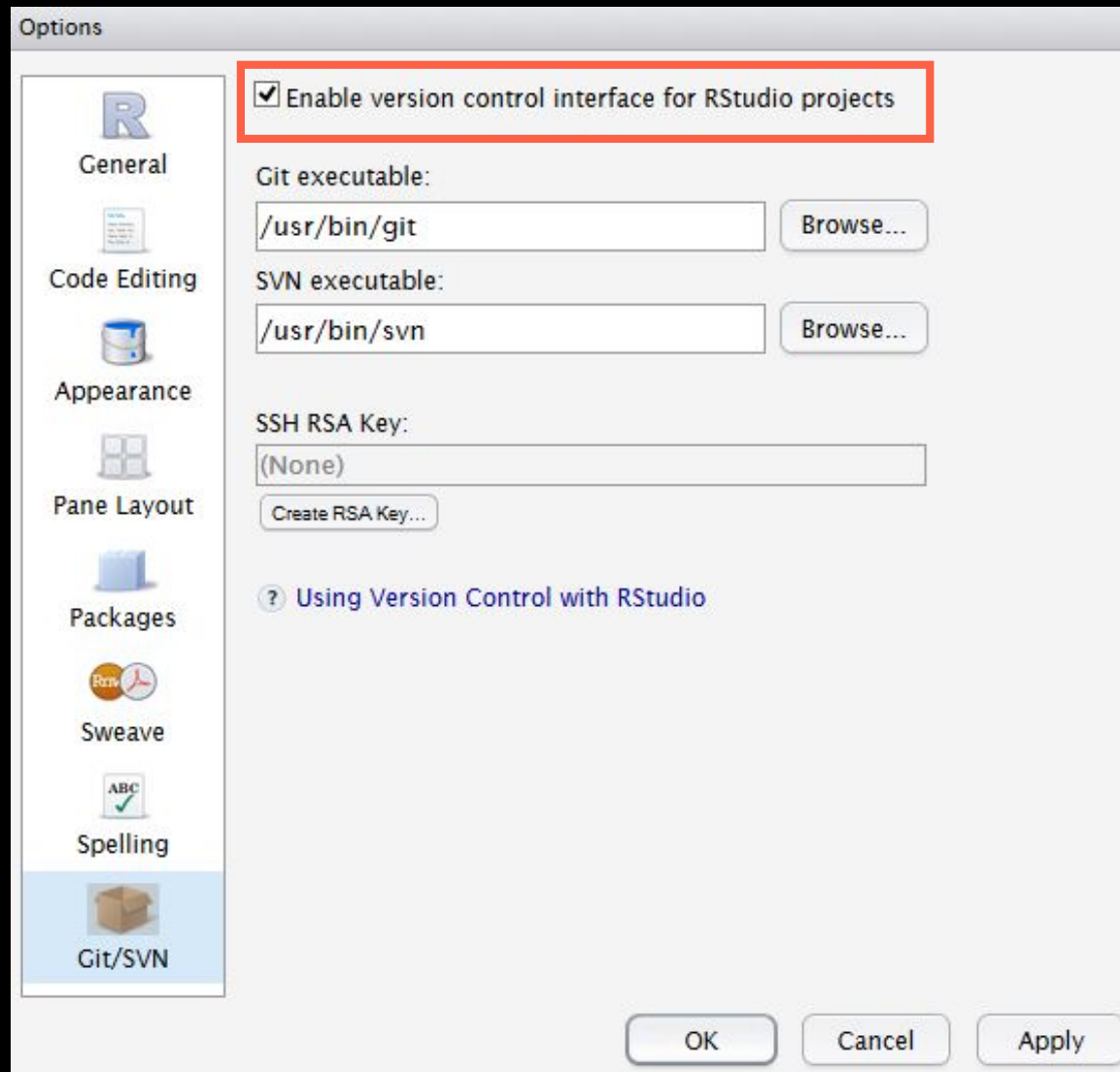

Using Git

Using Git

1. Initiate a Git repository.
2. Edit content (i.e. change some files).
3. Store a 'snapshot' of the current file state.*

Using Git with RStudio

(RStudio > Tools > Global Options > Git/SVN)



Your Turn:

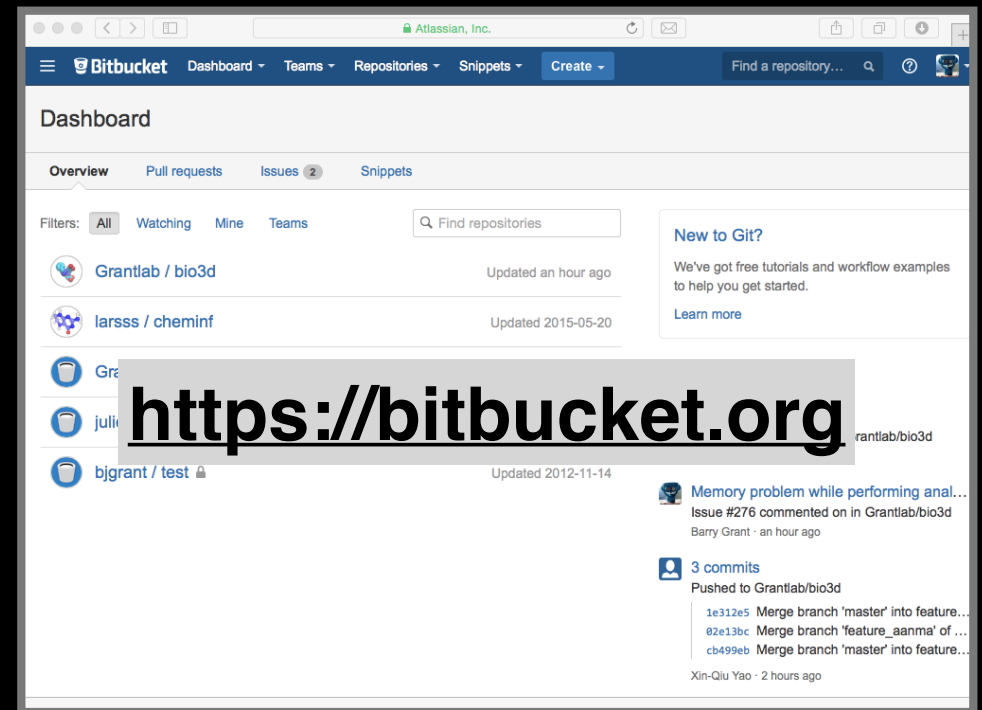
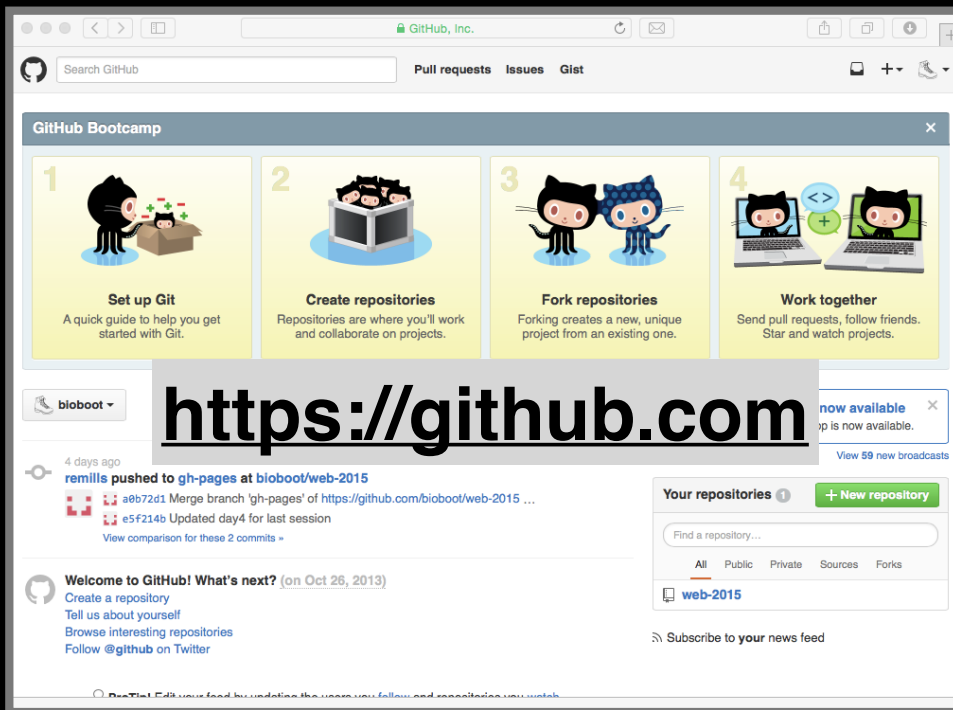
<http://tinyurl.com/rclass-github>

Step 3-4 only please!

(We have already done steps 1 & 2)

GitHub & Bitbucket

GitHub and **Bitbucket** are two popular hosting services for Git repositories. These services allow you to share your projects and collaborate with others using both **'public'** and **'private'** repositories*.



Nikkei
17893.73 0.49%

Hang Seng
21404.96 0.72%

U.S. 10 Yr
-0/32 Yield 2.074%

Crude Oil
39.17 -0.36%

Yen
119.16 0.26%

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TECH

GitHub Raises \$250 Million at \$2 Billion Valuation

Capital raise puts company's total funding at \$350 million



Analytics

How does your organization's talent measure up to its technology?

Read the MIT Sloan report

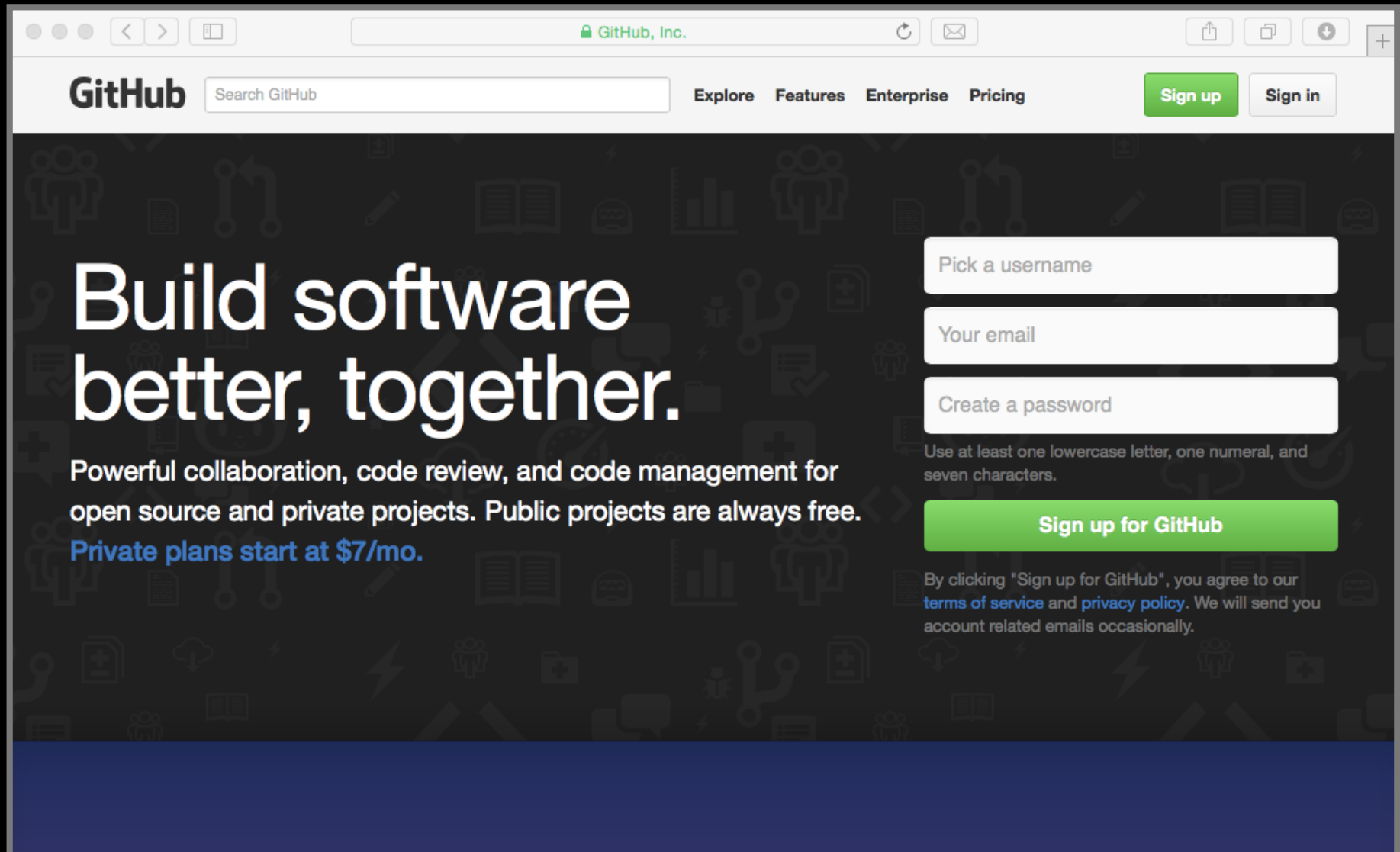


What is the big deal?

- At the simplest level GitHub and Bitbucket offer **backup** of your projects history and a centralized mechanism for **sharing** with others by putting **your Git repo online**.
 - GitHub in particular is often referred to as the “nerds FaceBook and LinkedIn combined”.
- At their core both services **offer a new paradigm for open collaborative project development**, particularly for software.
 - In essence they allow anybody to contribute to any public project and get acknowledgment.

First sign up for a GitHub account

<https://github.com>



The image shows a screenshot of the GitHub website's sign-up page. The browser's address bar displays "GitHub, Inc." and the page title is "GitHub". The navigation bar includes a search box, links for "Explore", "Features", "Enterprise", and "Pricing", and buttons for "Sign up" and "Sign in". The main content area has a dark background with the slogan "Build software better, together." and a description of GitHub's services. On the right, there is a sign-up form with three input fields: "Pick a username", "Your email", and "Create a password". Below the password field is a note about password requirements and a green "Sign up for GitHub" button. At the bottom, there is a disclaimer about terms of service and privacy policy.

GitHub, Inc.

Search GitHub

Explore Features Enterprise Pricing

Sign up Sign in

Build software better, together.

Powerful collaboration, code review, and code management for open source and private projects. Public projects are always free. Private plans start at \$7/mo.

Pick a username

Your email

Create a password

Use at least one lowercase letter, one numeral, and seven characters.

Sign up for GitHub

By clicking "Sign up for GitHub", you agree to our [terms of service](#) and [privacy policy](#). We will send you account related emails occasionally.

Pick the **FREE** plan!

Search GitHub Pull requests Issues Gist

Welcome to GitHub

You've taken your first step into a larger world, **@biobootStudent**.

✓ **Completed**
Set up a personal account

Step 2:
Choose your plan

Step 3:
Go to your dashboard

Choose your personal plan

Plan	Cost	Private repositories	
Large	\$50/month	50	Choose
Medium	\$22/month	20	Choose
Small	\$12/month	10	Choose
Micro	\$7/month	5	Choose
Free	\$0/month	0	Chosen

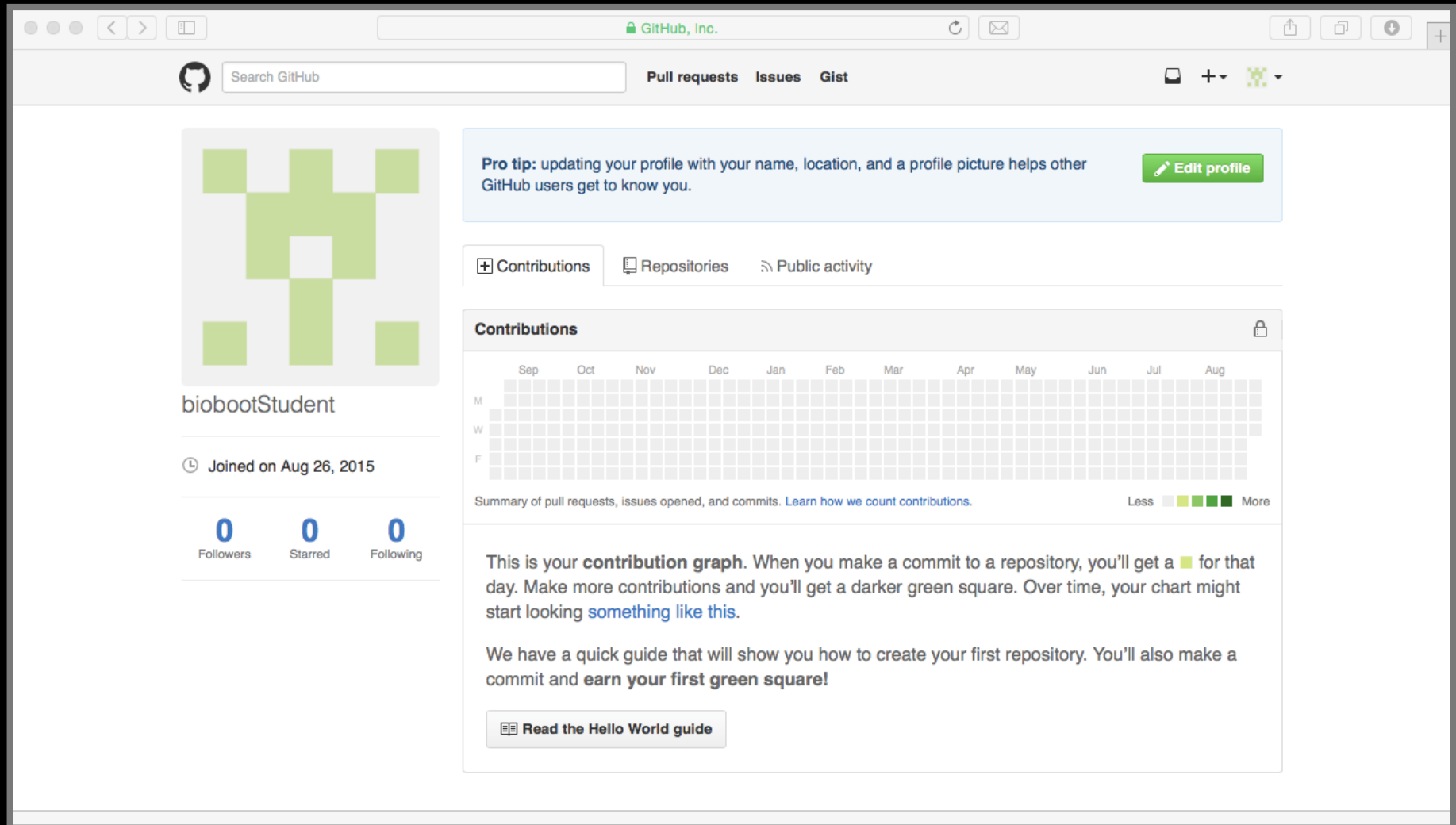
Each plan includes:

- Unlimited collaborators
- Unlimited public repositories
- ✓ Free setup
- ✓ HTTPS Protection
- ✓ Email support
- ✓ Wikis, Issues, Pages, & more

Charges to your account will be made in **US Dollars**. Converted prices are provided as a convenience and are only an *estimate* based on *current* exchange rates. Local prices will change as the exchange rate fluctuates.
Don't worry, you can cancel or upgrade at any time.

Your GitHub homepage

Check your email for verification request



The screenshot shows a web browser window displaying the GitHub profile page for the user 'biobootStudent'. The browser's address bar shows 'GitHub, Inc.' and the page title is 'GitHub, Inc.'. The navigation bar includes a search box, 'Pull requests', 'Issues', and 'Gist' links. The profile section features a green pixelated avatar, the username 'biobootStudent', and a 'Joined on Aug 26, 2015' timestamp. Below this are statistics for 'Followers', 'Starred', and 'Following', all showing a count of 0. A 'Pro tip' banner suggests updating the profile. The main content area has tabs for 'Contributions', 'Repositories', and 'Public activity'. The 'Contributions' tab is active, showing a grid for the months of September through August. The grid is currently empty, with only a few light gray squares visible in the August column. A legend below the grid shows a color scale from light to dark green, with a 'More' button. A text box explains the contribution graph, and a 'Read the Hello World guide' button is at the bottom.

GitHub, Inc.

Search GitHub Pull requests Issues Gist

Pro tip: updating your profile with your name, location, and a profile picture helps other GitHub users get to know you. [Edit profile](#)

Contributions Repositories Public activity

Contributions

Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug

M

W

F

Summary of pull requests, issues opened, and commits. [Learn how we count contributions.](#) Less More

This is your **contribution graph**. When you make a commit to a repository, you'll get a for that day. Make more contributions and you'll get a darker green square. Over time, your chart might start looking [something like this](#).

We have a quick guide that will show you how to create your first repository. You'll also make a commit and **earn your first green square!**

[Read the Hello World guide](#)

Skip the hello-world tutorial

<https://guides.github.com/activities/hello-world/>

The screenshot shows the GitHub homepage for the user 'biobootStudent'. At the top, there is a navigation bar with a search box and links for 'Pull requests', 'Issues', and 'Gist'. A red circle highlights the '+-' button in the top right corner of the navigation bar. Below the navigation bar, a blue notification box states 'Your email was verified.' A large dashed box contains a tutorial card titled 'Learn Git and GitHub without any code!' with the text 'Using the Hello World guide, you'll create a repository, start a branch, write comments, and open a pull request.' and a green 'Let's get started!' button. Below the tutorial card, there is a user profile section for 'biobootStudent' with a dropdown arrow. To the right, there is a 'Your repositories' section with a '+ New repository' button and a message: 'You don't have any repositories yet! Create your first repository or learn more about Git and GitHub.' Below this, there is a 'ProTip!' section with the text: 'ProTip! Feline cephalopod adhesives are great for decorating portable computation devices.' At the bottom, there is a 'ProTip!' section with the text: 'ProTip! Edit your feed by updating the users you follow and repositories you watch.' and a 'Subscribe to your news feed' link.

Name your repo

test

GitHub, Inc.

Home Gmail GCal WolverineAccess 2delicious 2CiteULike 2Papers UMPProxy + Gscholar Plex It! ToRead SCALI Bioinf525_Video Bio3D PCA App Index of /

Search GitHub Pull requests Issues Gist

Owner: biobootStudent

Repository name: demo1_github ✓

Great repository names are short and memorable. Need inspiration? How about **cuddly-octo-broccoli**.

Description (optional): My first github repo

Public: Anyone can see this repository. You choose who can commit.

Private: You choose who can see and commit to this repository.

Initialize this repository with a README: This will let you immediately clone the repository to your computer. Skip this step if you're importing an existing repository.

Add .gitignore: None | Add a license: None ⓘ

Create repository

© 2015 GitHub, Inc. Terms Privacy Security Contact Help

Status API Training Shop Blog About Pricing

Your Turn:

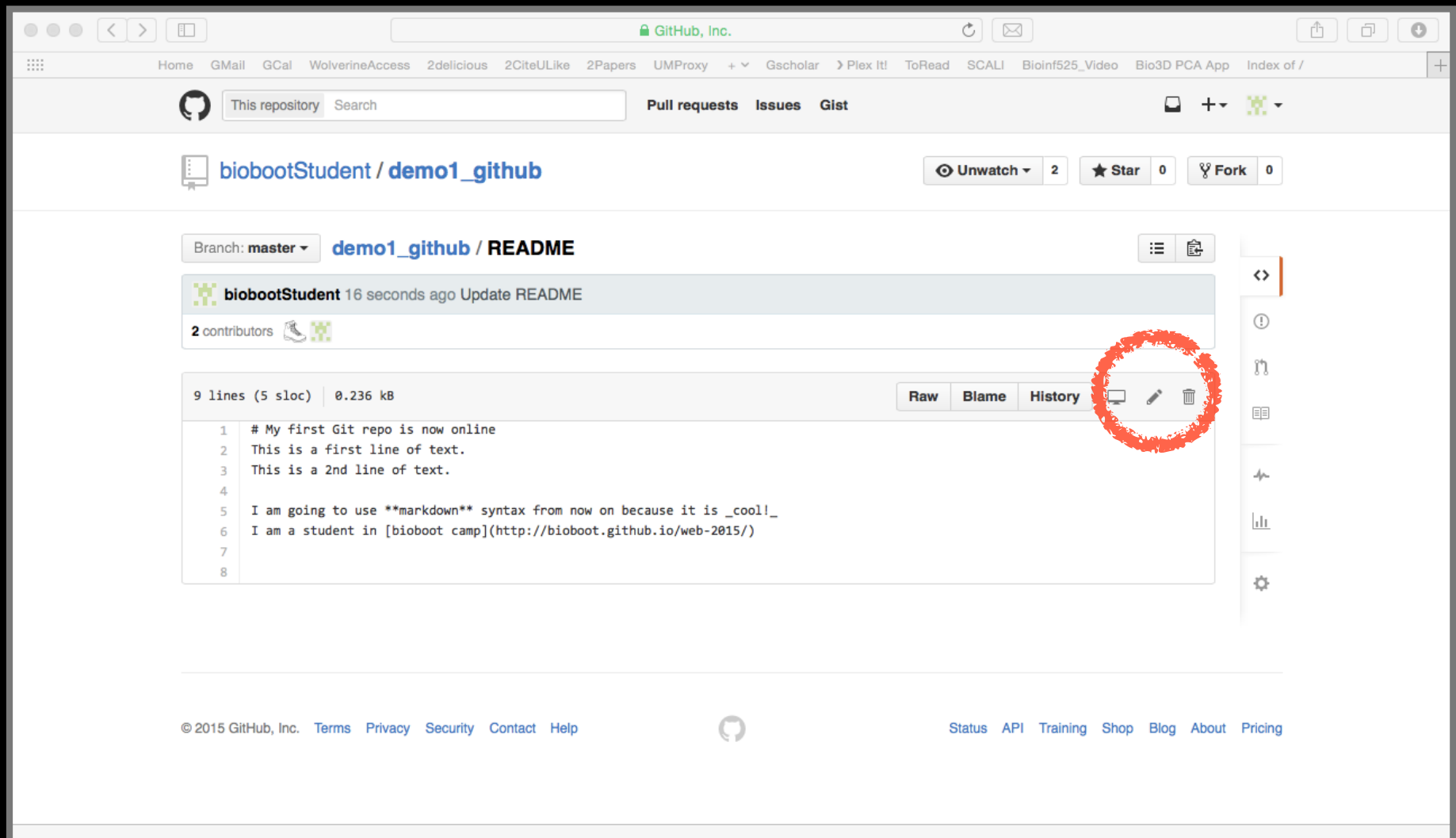
<http://tinyurl.com/rclass-github>

Step 6 only please!

(We have already done steps 1 to 5)

Side-note: How to edit online

Specifically lets add some Markdown content



The screenshot shows a web browser window displaying a GitHub repository page for 'biobootStudent / demo1_github'. The page is on the 'master' branch and shows the 'README' file. The file content is as follows:

```
1 # My first Git repo is now online
2 This is a first line of text.
3 This is a 2nd line of text.
4
5 I am going to use markdown syntax from now on because it is cool!
6 I am a student in [bioboot camp](http://bioboot.github.io/web-2015/)
7
8
```

The 'README' file is 9 lines long (5 sloc) and 0.236 kB in size. The page includes navigation options like 'Raw', 'Blame', and 'History'. A red circle highlights the 'Edit' button (represented by a pencil icon) in the top right corner of the file viewer area. The footer of the page contains copyright information for GitHub, Inc. and various links like 'Terms', 'Privacy', 'Security', 'Contact', 'Help', 'Status', 'API', 'Training', 'Shop', 'Blog', 'About', and 'Pricing'.

Summary

- Git is a popular ‘distributed’ version control system that is lightweight and free
- GitHub and BitBucket are popular hosting services for git repositories that have changed the way people contribute to open source projects
- Introduced basic git and GitHub usage within RStudio and encouraged you to adopt these ‘best practices’ for your future projects.

Learning Resources

- **Set up Git**. If you will be using Git mostly or entirely via **GitHub**, look at these how-tos.
< <https://help.github.com/categories/bootcamp/> >
- **Getting Git Right**. Excellent **Bitbucket** git tutorials
< <https://www.atlassian.com/git/> >
- **Pro Git**. A complete, book-length guide and reference to Git, by Scott Chacon and Ben Straub.
< <http://git-scm.com/book/en/v2> >
- **StackOverflow**. Excellent programming and developer Q&A.
< <http://stackoverflow.com/questions/tagged/git> >

Learning git can be painful!

However in practice it is not nearly as crazy-making as the alternatives:

- Documents as email attachments
- Hair-raising ZIP archives containing file salad
- Am I working with the most recent data?
- Archaeological “digs” on old email threads and uncertainty about how/if certain changes have been made or issues solved

Finally Please remember that **GitHub**
and **BitBucket** are **PUBLIC** and that
you should cultivate your professional
and scholarly profile with intention!