Genome informatics for translation to clinical diagnostics

"user-friendly web-based tools bring sequence data to the clinic"

NHMRC New Investigator Grant - Pitch

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Motivation

NGS technology shows great promise for understanding genetic basis of disease and personalised medicine

.....but.....

identification of known or novel pathogenic variants

- found among a host of common and rare polymorphisms
- identification of clinically relevant variants is time consuming
  - large potential for analysis induced false negatives
- larger datasets (WES/WGS) contain **thousands** to **millions** of variants
- aggravated by complex conditions/disorders
  - multitudes of genes / mutations responsible for symptoms or important for treatment

current tools are limited and specialised

making data available (interpretable) to end user ie. clinician/patient

visualisation and interactivity incredibly powerful tools ('big data')

I'm an emerging researcher (3.5 years out from PhD)

Major drivers for change

paywalls

- nearly all software suites are licensed == '$$$'
- might not be an issue for institutes, harder for non-research

'blackbox' software

- mysterious to users
- difficult/impossible to modified (closed-source)
  - those not closed source are tailored to specific lab/job (i.e. CPIPE)
- can be hard to use / require specific skills
  - not everyone is a bioinformatician

NO software readily accessible and user-friendly for end users 'on the ground'

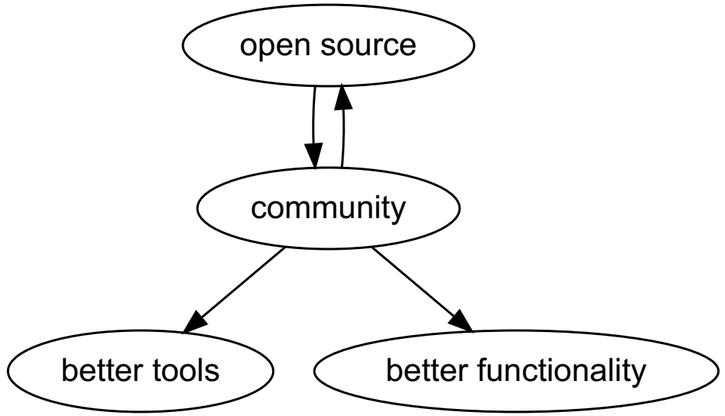
Significance

current methods fall into either:

pay to use **free but tricky**

open-source software is the backbone of bioinformatics

Accessible, flexible, powerful, and ... free



wide benefit: research | diagnostic | clinical | public

Aims

address shortfall in current methods

- free and simple

Shiny integration

- the power of R/RStudio
- visualisation/interactivity front and center

ease of use

- want it to work in the hands of all end users
  - clinic
  - research
  - public?

modularity (full extensible and upgradable)

cloud integration and deployment options

VCF files are powerful but clumsy*

[*] *if you are not familiar with the commandline*

To 95% of people these are just really large complex text files

- no easy interaction
- no ready visualisation

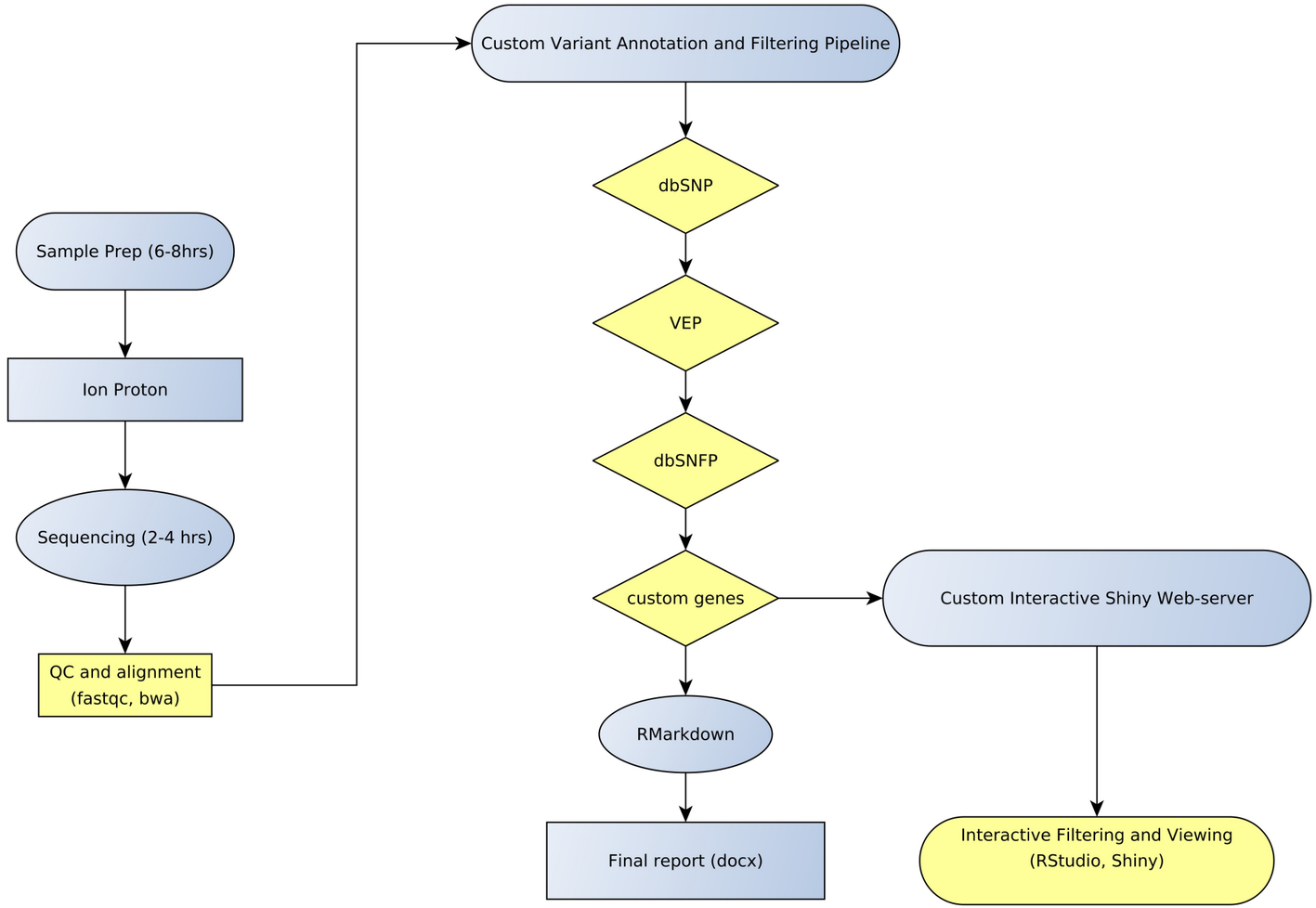
variant filtering process is complicated**

[**] *even if you are familiar with the commandline*

A large number of people still do this manually...
...this is what computers are for!

Progress to date

WESTARC - live demonstration



Research Design

Develop a series of modules, each achieving a specific task:

- initial QC and sequence alignment
  + including functionality for structural variation (routinely overlooked)
- VCF annotation and manipulation
  + currently only accessible to 'advanced' users
- simple interactive 'base' fontend (i.e. WESTARC)
  + include database interfacing
- Additional analysis interface
  + phenotype, case/control, sample comparison ...

Provide to clinical end users:

- have access to several engaged clinical geneticists (testing group?)

Distribute:

- GitHub, docker, & online cloud server (Amazon S3)

Expected outcomes

> *simple, scalable and robust method for the annotating and categorising genetic variants enabling more rapid and effective analysis of potentially pathogenic variants*

A fully operational suite of software 'modules':

- integrate into an easy-to-use workflow
- can handle all forms of sequence data
- open-source / free to use and develop

Deployment of an user friendly app version / suite of apps:

- integration with existing databases
- cloud deployment
- docker integration

Direct to consumer:

- putting the **'power'** back in the hands of those that matter

Team members on this submission

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