Supporting DNA sequencing at scale with OpenStack

Dave Holland
What I’ll talk about

● The Sanger Institute’s work
● Motivations for using OpenStack
● Our journey
● Our projects that are using OpenStack
● Next steps
DNA sequencing (the 30-second summary)
Then...

capillary sequencer
~2Mb / day
...and now

Illumina NovaSeq 6000
~3Tb per sequencer / day
(2-day cycle)
Oxford Nanopore
MinION and SmidgION
up to 20Gb / 48 hours
Total amount of DNA read by the Wellcome Sanger Institute

Cumulative total of Petabases of DNA sequenced by the Wellcome Sanger Institute
Whole genome sequencing will ‘transform the research landscape for a wide range of diseases’

UK Biobank enters exciting new phase of genetics research

News article 6 Apr 2018

UK Biobank is working with the Wellcome Sanger Institute to sequence the full genomes of 50,000 UK Biobank volunteer participants

50,000 whole-genome sequences over 18 months
25 Genomes Project

25 previously unsequenced UK organisms:
- giant hogweed
- red squirrel
- golden eagle
- European robin
- ...

[Image of butterflies and other organisms]
Darwin Tree of Life Project (UK)
A MOONSHOT FOR BIOLOGY

Sequence the DNA of all life on Earth in 10 years
Motivations for using OpenStack
The Sanger Institute
Traditional HPC Environment

LSF 9
~10,000 cores in main compute farm
~10,000 cores across smaller project-specific farms
~15PB Lustre high-performance storage

**Limited security** - “isolation” is only POSIX file permissions

**Limited flexibility** - no root access, incompatible software dependencies

Pipelines and stacks are complex - scientific reproducibility is hard
HPC and cloud computing are complementary

**Traditional HPC**
- Highest possible performance
- A mature and centrally managed compute platform
- High-performance Lustre filesystems for data intensive analysis

**Cloud compute**
- Full segregation of projects ensures data security
- Developers no longer tied to a single stack
- Reproducibility through containers / images and infrastructure-as-code
But there’s a catch or two...

● Large number of traditional/legacy pipelines
  ○ They require a performant shared POSIX filesystem, while cloud workloads support object stores
● We do not always have the source code or expertise to migrate
● We need multi-gigabyte per second performance
● The tenant will have root
  ○ and could impersonate any user, but Lustre trusts the client’s identity assertions, just like NFSv3
● The solution must be simple for the tenant and administrator
Our journey
Step by step

2015: sysadmin training and experiments
2016: trial system offered to scientists (Kilo)
2017: production Flexible Compute Environment (Liberty)
2018: move to Pike; added hypervisors and storage
2019: move to Queens; Ceph upgrade
Production hardware

- 107 compute nodes (Supermicro) each with:
  - 512GB RAM, 2x 25GbE, 2x Intel E52690v4 (14 cores @ 2.6GHz)

- 6 control nodes (Supermicro)
  - 256GB RAM, 2x 100GbE, NVMe

- Total 53 TB RAM, 2996 cores, 5992 with hyperthreading

- 9 Ceph nodes running “Jewel”
  - 60x 6TB SATA, 2x 2TB NVMe, 2x 100GbE

- 1PB usable, 3-way replicated

- Arista 7060CX switches, spine/leaf
Challenges
Liberty (RHOSP8) - “Delta”

- default file descriptor limits for Glance, Cinder, RabbitMQ etc way too low
- NIC hardware acceleration works fine with the correct kernel/driver (thanks to Mellanox)
- races when scheduling many instances; mitigate by directing nova_osapi to a “primary” server
- faulty fibres caused NIC flaps and RabbitMQ problems
RabbitMQ

Andy Riley’s “Bunny Suicides”
Liberty (RHOSP8) - “Delta”

- not enough hypervisor memory reserved, neutron-openvswitch-agent fails to allocate memory
- various package upgrades (Glance, Neutron, Dnsmasq etc) for particular bugs encountered or security fixes
- work with Arista on portchannel/LACP instability
Ceph

- standalone Ceph to support multiple OpenStack deployments
- generally robust in the face of spontaneous machine hangs and rack failures
- OSD start-up race due to single shared lock
- niggles with ceph-ansible
Ansible for customisation

- scheduler tweaks (stack not spread, CPU/RAM overcommit)
- hypervisor tweaks (instance root disk on Ceph or hypervisor)
- enable SSL for Horizon and API
- change syslog destination
- add “MOTD” to Horizon login page
- change session timeouts
- register systems with Red Hat
- and more…

- but deployer’s Puppet overwrites some of these
Monitoring

- evolved from “bare minimum” to customer and engineer views, scorecard, availability report
- custom Nagios scripts, active and passive checks
- Grafana for metrics
- rsyslog and ELK for logging
<table>
<thead>
<tr>
<th>HPC Services</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>farm3 LSF</td>
<td>scratch114</td>
<td>Zeta VM creation</td>
<td>Zeta controllers</td>
<td></td>
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<td>farm4 LSF</td>
<td>scratch115</td>
<td>S3 interface</td>
<td>Zeta compute</td>
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<td>cgp LSF</td>
<td>scratch116</td>
<td>Cinder (volume)</td>
<td>Ceph nodes</td>
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<td>pcs5 LSF</td>
<td>scratch117</td>
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<td>CloudForms VMs</td>
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<td>scratch118</td>
<td>Neutron (network)</td>
<td>Zeta undercloud</td>
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<td>vr LSF</td>
<td>scratch119</td>
<td>Horizon (web UI)</td>
<td>CVX servers</td>
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<td>CloudForms</td>
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<td>Eta networkers</td>
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<td>ELK stack</td>
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<td>Eta VM creation</td>
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<td>UKB seq-stor</td>
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<td>Eta controllers</td>
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<td>Eta compute</td>
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<td>Eta web UI</td>
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<td>Eta undercloud</td>
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</tr>
</tbody>
</table>

- **OK**
- **Warning Threshold Breached**
- **Critical Threshold Breached**
- **Acknowledged/Maintenance**
- **No Data Available**
<table>
<thead>
<tr>
<th>Host</th>
<th>Service</th>
<th>Status</th>
<th>Duration</th>
<th>Attempt</th>
<th>Last Check</th>
<th>Status Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>zeta.internal.sanger.ac.uk</td>
<td>Cinder API Health</td>
<td>Ok</td>
<td>3d 15h 48m 50s</td>
<td>1.5</td>
<td>09/11/2018 12:21:55</td>
<td>HTTP OK: Status line output matched &quot;200&quot; - 754 bytes in 0.166 second response time</td>
</tr>
<tr>
<td></td>
<td>Glance-API and Glance-Registry API Health</td>
<td>Ok</td>
<td>3d 15h 49m 30s</td>
<td>1.5</td>
<td>09/11/2018 12:22:47</td>
<td>HTTP OK: Status line output matched &quot;200&quot; - 22609 bytes in 0.244 second response time</td>
</tr>
<tr>
<td></td>
<td>Heat API Health</td>
<td>Ok</td>
<td>3d 15h 50m 26s</td>
<td>1.5</td>
<td>09/11/2018 12:24:11</td>
<td>HTTP OK: Status line output matched &quot;200&quot; - 223 bytes in 0.274 second response time</td>
</tr>
<tr>
<td></td>
<td>Horizon Web GUI Health</td>
<td>Ok</td>
<td>3d 15h 50m 35s</td>
<td>1.5</td>
<td>09/11/2018 12:21:55</td>
<td>HTTP OK: HTTP/1.1 200 OK - 9690 bytes in 0.036 second response time</td>
</tr>
<tr>
<td></td>
<td>Insdance Creation</td>
<td>Ok</td>
<td>3d 3h 3m 58s</td>
<td>1/1</td>
<td>09/11/2018 12:20:43</td>
<td>OK success - test duration 40.253437288 seconds</td>
</tr>
<tr>
<td></td>
<td>Keystone Public-SSL API Health</td>
<td>Ok</td>
<td>3d 15h 52m 3s</td>
<td>1.5</td>
<td>09/11/2018 12:21:23</td>
<td>HTTP OK: Status line output matched &quot;200&quot; - 513 bytes in 0.010 second response time</td>
</tr>
<tr>
<td></td>
<td>Neutron agent status</td>
<td>Ok</td>
<td>3d 15h 50m 36s</td>
<td>1/1</td>
<td>09/11/2018 12:25:03</td>
<td>HTTP OK: Status line output matched &quot;200&quot; - 265 bytes in 0.008 second response time</td>
</tr>
<tr>
<td></td>
<td>Neutron API Health</td>
<td>Ok</td>
<td>3d 15h 48m 7s</td>
<td>1.5</td>
<td>09/11/2018 12:24:09</td>
<td>HTTP OK: Status line output matched &quot;200&quot; - 265 bytes in 0.008 second response time</td>
</tr>
<tr>
<td></td>
<td>Nova service status</td>
<td>Ok</td>
<td>3d 15h 50m 36s</td>
<td>1/1</td>
<td>09/11/2018 12:25:03</td>
<td>HTTP OK: Status line output matched &quot;200&quot; - 265 bytes in 0.008 second response time</td>
</tr>
<tr>
<td></td>
<td>OpenStack database backup status</td>
<td>Ok</td>
<td>10d 2h 52m 12s</td>
<td>1.5</td>
<td>09/11/2018 12:24:35</td>
<td>OK latest backup overcloud_db_zeta-ctrl0_20181106_010001.tarb2 is 11 hours old</td>
</tr>
<tr>
<td></td>
<td>Ping</td>
<td>Ok</td>
<td>3d 15h 52m 46s</td>
<td>1.5</td>
<td>09/11/2018 12:24:54</td>
<td>PING OK - Packet loss = 0%. RTA = 0.16 ms</td>
</tr>
<tr>
<td></td>
<td>SSH</td>
<td>Ok</td>
<td>3d 15h 54m 27s</td>
<td>1.5</td>
<td>09/11/2018 12:21:16</td>
<td>SSH OK - OpenSSH_7.4 (protocol 2.0)</td>
</tr>
<tr>
<td></td>
<td>SSL Certificate</td>
<td>Ok</td>
<td>3d 15h 52m 53s</td>
<td>1.5</td>
<td>09/11/2018 12:24:32</td>
<td>OK - Certificate *.Internal.sanger.ac.uk will expire on Sat 18 Jan 2020 11:11:00 GMT.</td>
</tr>
</tbody>
</table>
Metrics

● collectd + libvirtd + Python graphitesend
● custom scripts to aggregate CPU use for efficiency “score”
● need to scale up number of carbon-cache processes
● Grafana dashboards
Viewing 4 metrics for 1 interface

Ethernet17/1 on leaf-3-1

- Bitrate Out: 143.2 Mbps
- Unicast Packets Out: 27.5 kpps
- Multicast Packets Out: 0 kpps
- Broadcast Out: 6 kpps
Upgrades and expansions
OpenStack growth

- entire system physically relocated in July 2018 due to power requirements
- 99 compute nodes added during Q4 2018
- newer hardware generation
  - different CPU/RAM ratio $\Rightarrow$ new flavours
  - AVX512
Queens (RHOSP13) - “Eta”

- current production system
- many of our original customisations and fixes no longer necessary
- sideways-upgrade was time-consuming but gave reassurances of stability and known process
Queens (RHOSP13) - “Eta”

- Containerised overcloud services mean different ways of managing/customising services.
- Composable roles - RabbitMQ cluster separate from tenant network routers.
- Tenant networks can be VLAN via Arista ml2 plugin (but still VXLAN by default).
- Enabled CPU overcommit, 8x, “o” flavours.
- Enabled jumbo frames.
Ceph growth

- expansion: 1PB $\rightarrow$ 4.5PB usable
  - 9 servers $\rightarrow$ 51 servers
  - 540 OSDs $\rightarrow$ 3060 OSDs
- current use: 1.8PB as S3 objects, 200TB as Cinder volumes
Ceph upgrades

- in-place and automated (after extensive testing)
- version 10 (Jewel) to 12 (Luminous)
  - for bug fixes and features
  - completed
- storage format change: FileStore to BlueStore
  - for performance
  - underway
Enhancements
Ceph

- automated radosgw/S3 public bucket scan

From: ssg-lsg@sanger.ac.uk
Date: Sun, 1 Apr 2018 00:01:26 +0100
To: dh3@sanger.ac.uk
Subject: S3 public-readable bucket warning

Hello dh3,

A recent review showed that you have public-readable rgw/S3 bucket(s):

  frobnitz public

This means that the contents are accessible by anyone on the Internet, without authentication. If this is not your intention, please address this URGENTLY, e.g. with both these commands:

  s3cmd setacl s3://bucketname --acl-private
  s3cmd setacl s3://bucketname --acl-private -r
Provider networks

- “Secure Lustre” - strong tenant isolation for a POSIX filesystem
- scientific instruments
- next iteration of LSF compute clusters
- niggles with security groups
- “a hammer for all screws”? e.g. faster S3 access
“But what’s it all for?”
Services and applications implemented on OpenStack

- Mutational Signatures
- HGI Arvados and Spark/Hail
- widespread test, dev, CI (Gitlab runners)
- dynamic expansion of LSF clusters
- Mattermost
- CellphoneDB - receptor/ligand database
- CloudForms
- ...
Services currently on OpenStack:

- Mutational Signatures
- HGI Arvados
- Gitlab CI runners
- farm4 - extending LSF into OpenStack
- Mattermost
- CellphoneDB
- CloudForms
- ...

Sample

- TUMOUR
- NORMAL
- MSK0.4_NORMAL
- MSK0.4_TUMOUR

Sample has no substitutions.
Aker - orchestration of scientific operations
jupyter-config.yaml

---
proxy:
  secretToken:
    c65b857a6ba98ee5562f4ea7d78f949d3539
auth:
  admin:
    users:
      - ak27
      - vk6
      - svd
  type: ldap
  ldap:
    server:
      address: ldap-ro.internal.sanger.ac.uk
      dn:
        templates:
          - 'uid={username},ou=people,dc=sanger,dc=ac,dc=uk'
  ingress:
    enabled: false
    hosts:
      - jupyter.cellgeni.sanger.ac.uk
      - jupyter.cellgeni.internal.sanger.ac.uk
  singleuser:
    defaultUrl: "/lab"
    memory:
      limit: 20G
      guarantee: 16G
    cpu:
      limit: 4
      guarantee: 2
    image:
      name: quay.io/cellgeni/cellgeni-jupyter
      tag: v0.2.8
    lifecycleHooks:
      postStart:
        exec:
          command: ["bash", "/poststart.sh"]
UK Biobank - Vanguard

- 50,000 whole genome sequences in 18 months
- £30M MRC funding
- 4.5PB of sequence
- started August 2018; 50% done
- completion expected in October 2019
Compare and contrast

First draft of the human genome (Nature, 15 February 2001)

- took 10 years
- cost $2.7 billion
Best Use of HPC in the Cloud

Readers’ Choice: The Wellcome Sanger Institute using a private OpenStack cloud enhances IT environment necessary to sequence and assemble 100 complete human genomes per day.
Why use OpenStack?

In our developers’ words:

“We pursued the VMware route [but found that] the level of access we would have on the VMware machines is too burdensome”

“Quick turnaround”

“Scaling”
Education and training

- Hashicorp products
- Ceph (for sysadmins)
- bespoke end-user training (OCF)
OpenStack


This is a collection of end-user documentation for the Sanger OpenStack systems, a.k.a. the Flexible Compute Environment.

New to OpenStack? Start here...

- Mile-high overview: How do I get started with Flexible Compute
- If you want to use the web interface: read Welcome to OpenStack
- For information on the command-line: Using the Openstack CLI
- Requesting a new project group or an account on the flexible compute platform

Flexible Compute Capacity Management
- OpenStack object store (S3-alike) quickstart
- Work-In-Progress: Internal Cloud Best Practice Advice
- How can I tell if should I be running my application or software on the FCE?
- But what tools are available to me?
- How can I request a new feature?

Having trouble?
Try this: Commonly encountered errors

More advanced topics
- Tracking your resource use
- Customising your instances
- Sending email from OpenStack instances
- Using affinity and anti-affinity groups
- Loadbalancer as a service
- Distributed applications: links and resources
- Guidance for running Docker within flexible compute environments
The Sanger community

- user engagement
- Slack
- coffee mornings
The wider community

- OpenStack Summits
- OpenStack Days
- Scientific SIG
- openstack-discuss mailing list
The future
Upgrades

- planning to follow Red Hat LTS releases: Train/RHOSP16
- serious consideration of in-place “fast forward” upgrade
- sideways-upgrade is painful for users
Desirable features

Driven by user demand

- Manila - filesystem-as-a-service (on CephFS?)
- Sahara - Spark
- Ironic - bare-metal instances
- Murano - application catalogue
- Reaper - pre-emptible instances
- GPUs?
Containers

- Docker, Singularity, Kubernetes already in use
  - users need lots of sysadmin help
- high demand for managed service
- currently planning an evaluation
Offsite DR/BCP

- small OpenStack and Ceph clusters at JSDC
- currently investigating global load-balancing options
- open questions about user federation/identity management
- need to investigate Ceph replication
Data flow model
Evolution and federation

Global Alliance
GA4GH APIs

Public clouds

Private clouds

EBI Embassy Cloud
Sanger Flexible Compute

OICR Collaboratory
GDC Cloud (Genomic Data Commons)
Standardised pipelines

ICGC/TCGA Project
- Analyse 2,800 WGS Cancers
- 3 Analysis Pipelines
- (Broad, Sanger & DKFZ)
- Need to use multiple Data Centres

Problem: analysis pipelines NOT portable

Software Go To Data:
Analysis Pipeline available in multiple Data Centres

IT Advancements

Science Advancements
Large Collaborative Projects

happy scientists
Future science
Conclusion
“It is difficult to predict the further outcome of DNA research, but we may reasonably hope for further unexpected and exciting discoveries - some of which will help in the conquest of diseases.” - Fred Sanger, Lasker Award acceptance in 1979
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https://hpc-news.sanger.ac.uk/

https://sangerinstitute.blog/