

# Cloud BioLinux: Pre-configured and On-demand Bioinformatics Computing for the Genomics Community

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<http://www.jcvl.org/cms/about/bios/kkrampis/>

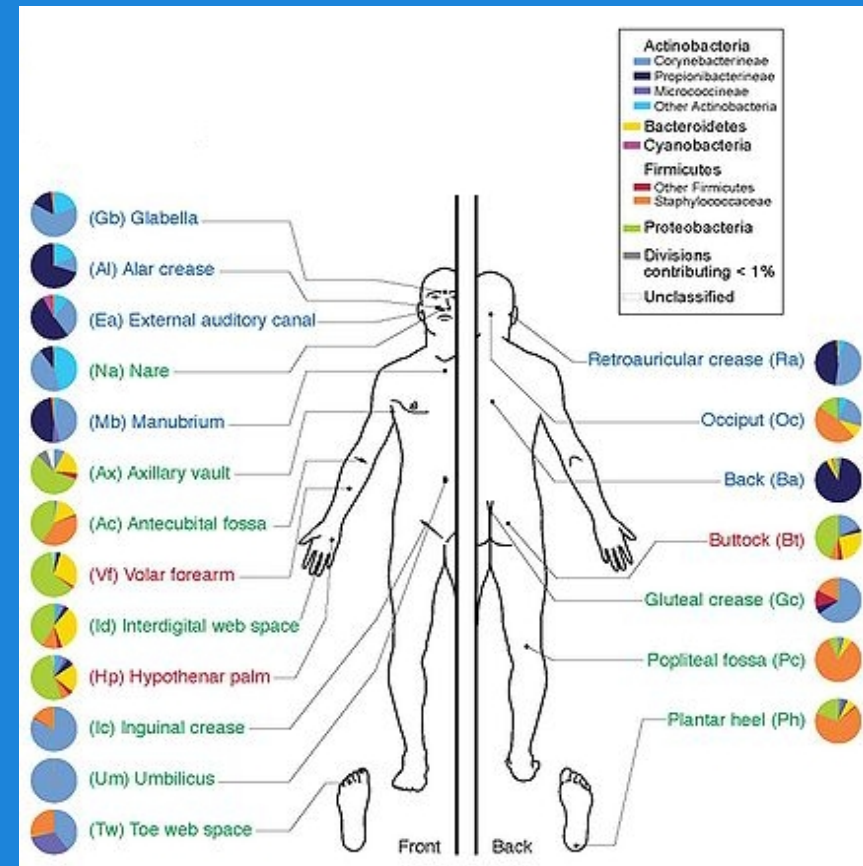
# J. Craig Venter Institute (JCVI)

## Large-scale genome sequencing and bioinformatics computing

- Human Microbiome Project (HMP): sequencing and assembly of 1000 reference microbe genomes from the human body
- Global Ocean Sampling (GOS) survey: metagenomic sequencing of microbes sampled from oceans around the world



— 2003 – 2008 Routes — 2009 – 2010 Route



# JCVI: sequencing and computing infrastructure

sequencing laboratory: 454, Solexa, HiSeq, and IonTorrent on the way

Vendor:	Roche			Illumina			ABI		
Technology:	454			Solexa GA			SOLiD		
Platform:	GS20	FLX	Ti	I	II	IIx	1	2	3
Images: (TB)		0.01	0.03	1	2.2	5.6	3.6	5	3.8
PA Disk: (GB)		3	15	350	500	550	600	1500	2400
PA CPU: (hr)		140	220	160	120	NA	NA	NA	NA
SRA: (GB)		1	4	60	100	3.5	200	280	1200

# JCVI: sequencing and computing infrastructure

- large-scale sequencing needs large-scale informatics
- workhorse : ~1000 node Sun Grid Engine (SGE) cluster
- research in data processing and software development model with Hadoop / MapReduce and a small private cloud
- bioinformatics department (57 bioinformaticians + software developers)



# A new paradigm: Low-cost, bench-top sequencers

- small-scale sequencers available: GS Junior by 454, MiSeq by Illumina
- complete sequencing of bacterial, viral, small fungal genomes
- RNAseq (gene expression), ChiPseq (protein interactions), gene variant discovery
- sequencing as a standard technique in basic genetics research - like PCR ?

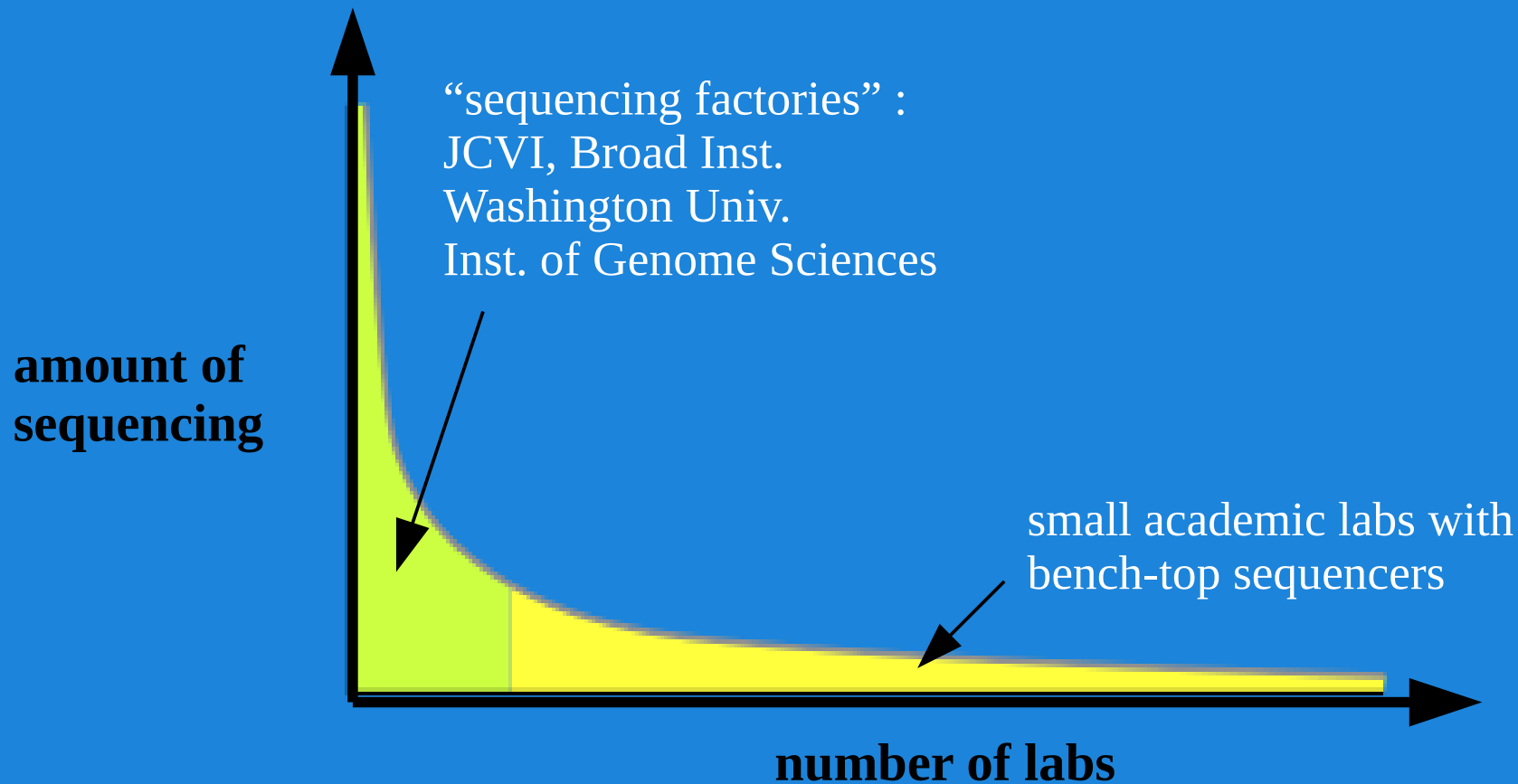


<http://www.gsjunior.com/>



<http://www.illumina.com/systems/miseq.ilmn>

Will small academic labs lead by individual PIs  
become the long tail of sequencing ?



# Sequencers shipped with minimal computational capacity

- Problem 1: sequence analysis requires plenty of computational capacity

For example: genome assembly, BLAST and genome annotation

- Problem 2: bioinformatics tools need expertise with unix/linux operating systems, software libraries, compiling source code etc.

Difficult to install and use for biologists



# Each lab with a sequencer building an informatics infrastructure ?

- difficult for individual PIs to get additional funds to build clusters
- funds for personnel to maintain the clusters and software
- duplication of effort across labs
- sub-optimal utilization of the hardware
- few sequencing runs per year





## Solution ? Large sequencing centers offering bioinformatics services

- Bioinformatic Resource Centers (BRCs) by NIAID
- bioinformatic services usually coupled with sequencing of a genome
- provide data access and on-line tools
- cannot provide bioinformatic support for every PI in a lab acquiring a sequencing instrument
- need end-to-end solutions, users submit sequence data and get final annotation



# Solving Problem 1: sequence analysis requires computational capacity

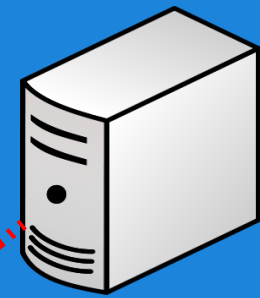
- computational capacity on-demand without investment on hardware
- Amazon Elastic Compute Cloud (EC2), pay-by-the-hour computing
- cloud servers cost \$0.085 - \$2 per hour
- max capacity per server 64GB RAM / 8 CPU (but a PI can run thousands of servers)
- access to computing resources without institutional, economic or national boundaries



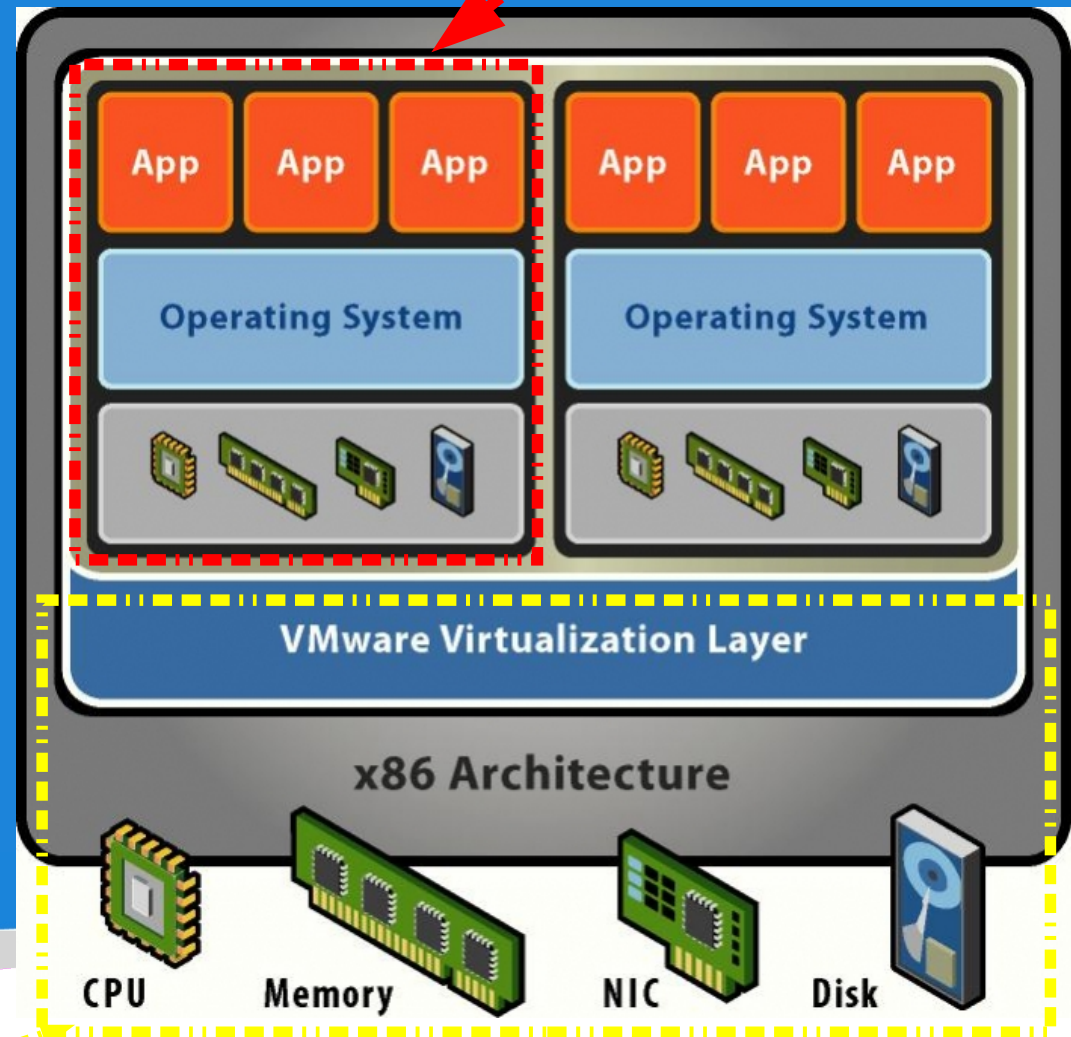
750 hours free for new users:  
<http://aws.amazon.com/free/>



# Cloud Computing and Virtualization



- operating system, bioinformatics software and data, are pre-installed on a Virtual Machine (VM)
- a VM is a full-featured unix/linux server, in the form of a single, executable binary file
- the cloud provides the physical computational resources and virtualization layer to run the VM

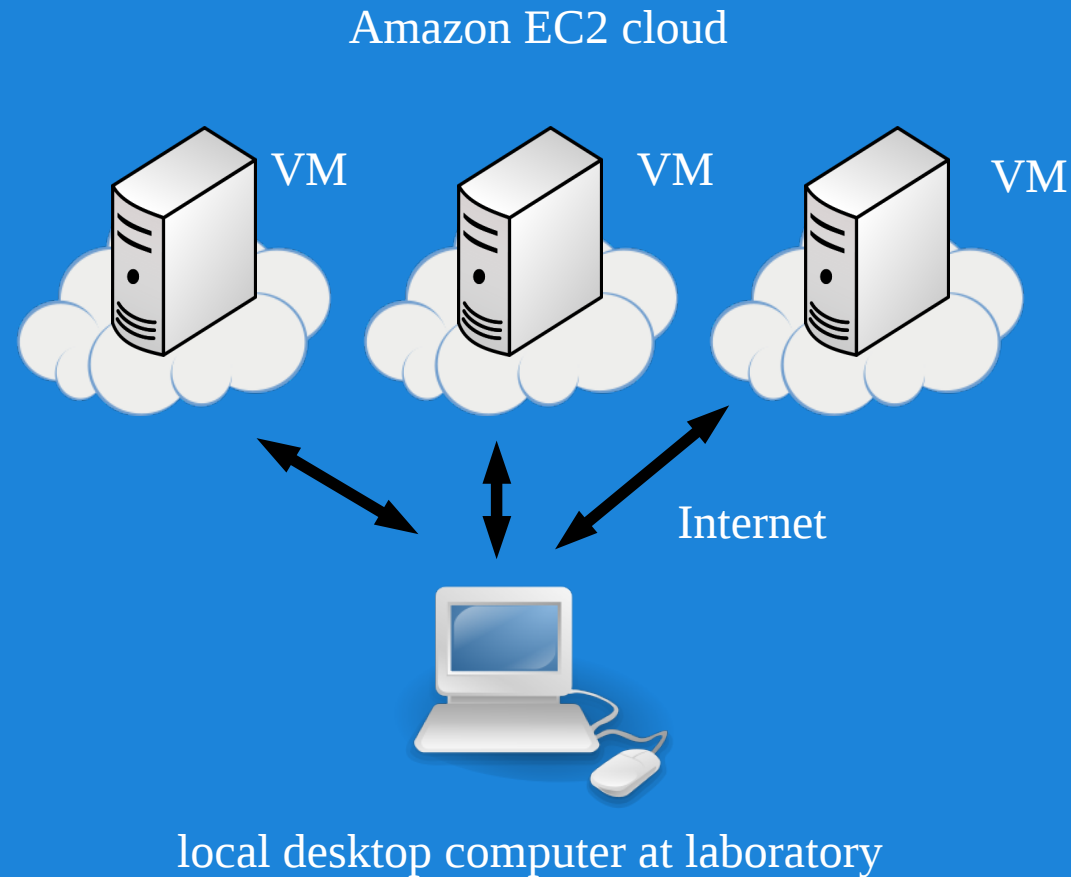


Credit: VMware Inc.

J. Craig Venter™  
INSTITUTE

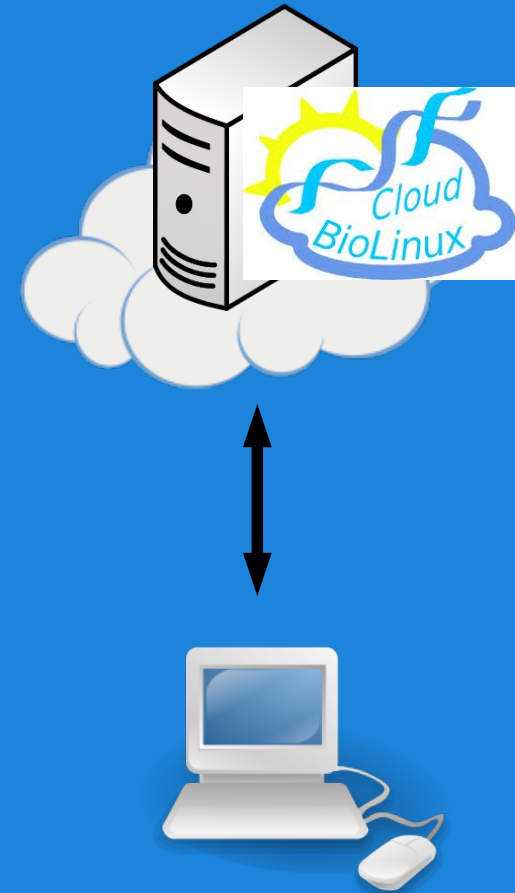
## Solving Problem 2: bioinformatics tools need software engineering expertise

- a VM with pre-installed bioinformatics software publicly accessible on the cloud
- no need to compile source code, set-up configuration files, or other software dependencies
- PIs rent computational capacity to run the VM
- bioinformatics software can be accessed from anywhere in the world via a local computer with Internet access
- no need for sequencing informatics infrastructure at each laboratory



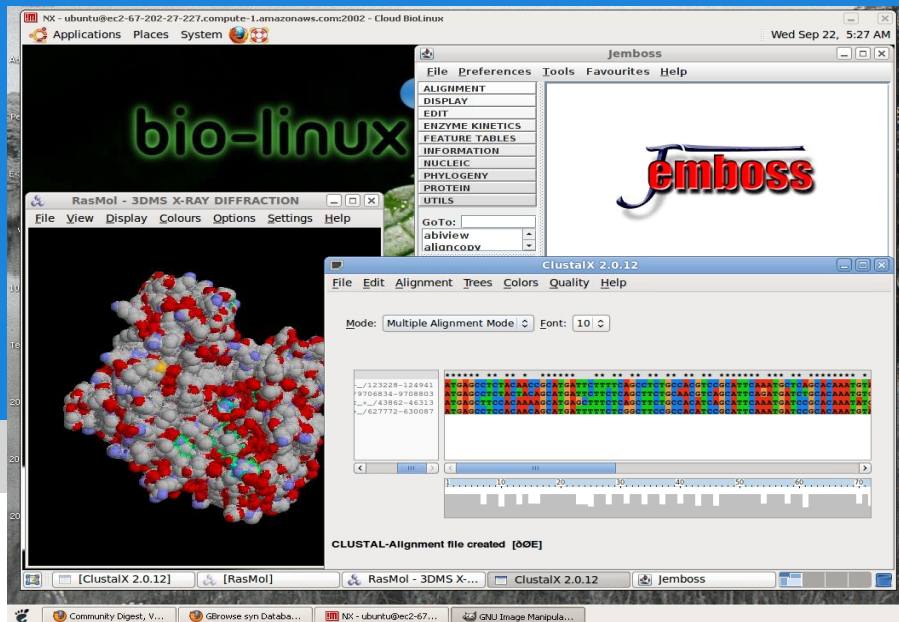
# Solving Problems 1 & 2: the Cloud BioLinux project

- Cloud BioLinux: a publicly accessible Virtual Machine (VM) on the Amazon EC2 cloud
- 100+ pre-installed bioinformatics tools on the VM with a graphical interface for non-technical users
- sequence analysis, genome assembly, annotation, phylogeny, molecular modeling, gene expression
- a researcher can initiate a practically unlimited number of Cloud BioLinux VMs for large-scale data analysis



# Cloud BioLinux for Bioinformatics

- how the Cloud BioLinux project came to be, what it can offer to small labs for genome sequence analysis
- where and how do I run Cloud BioLinux, especially if I am not a computer expert
- besides end-users, how bioinformatics developers are provided a framework for modifying and sharing VM configurations and data



<http://www.cloudbiolinux.org>

<http://tinyurl.com/BioLinux-NEBC>

# The making of Cloud Biolinux



[tinyurl.com/BioLinux-NEBC](http://tinyurl.com/BioLinux-NEBC)

+



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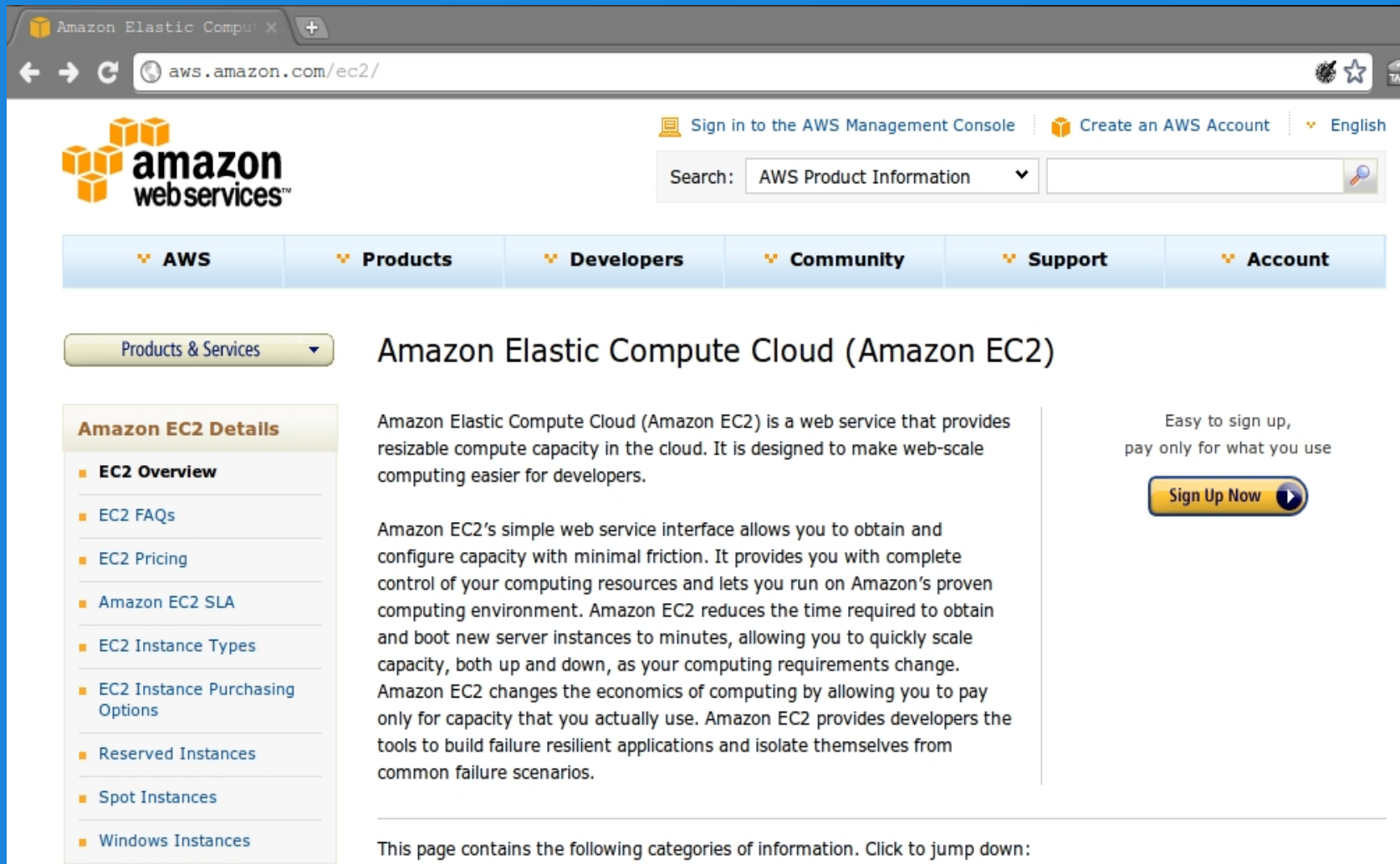


<http://www.cloudbiolinux.org>

- JCVI bioinformatics cloud computing research
- NEBC BioLinux software repository
- community effort at BOSC 2009 – 11
- initially: a VM on Amazon EC2 with the tools copied and installed from the NEBC repository
- now: developer's framework for creating a customized cloud VM for bioinformatics
- main contributors:



# Accessing Cloud BioLinux



The screenshot shows the Amazon Elastic Compute Cloud (Amazon EC2) product page. The browser address bar displays [aws.amazon.com/ec2/](http://aws.amazon.com/ec2/). The page features the Amazon Web Services logo, navigation links for AWS, Products, Developers, Community, Support, and Account, and a search bar. The main content area is titled "Amazon Elastic Compute Cloud (Amazon EC2)" and includes a "Sign Up Now" button. A sidebar on the left lists "Amazon EC2 Details" with links to EC2 Overview, EC2 FAQs, EC2 Pricing, Amazon EC2 SLA, EC2 Instance Types, EC2 Instance Purchasing Options, Reserved Instances, Spot Instances, and Windows Instances.

Amazon Elastic Compute Cloud (Amazon EC2) is a web service that provides resizable compute capacity in the cloud. It is designed to make web-scale computing easier for developers.

Amazon EC2's simple web service interface allows you to obtain and configure capacity with minimal friction. It provides you with complete control of your computing resources and lets you run on Amazon's proven computing environment. Amazon EC2 reduces the time required to obtain and boot new server instances to minutes, allowing you to quickly scale capacity, both up and down, as your computing requirements change. Amazon EC2 changes the economics of computing by allowing you to pay only for capacity that you actually use. Amazon EC2 provides developers the tools to build failure resilient applications and isolate themselves from common failure scenarios.

Easy to sign up, pay only for what you use

[Sign Up Now](#)

This page contains the following categories of information. Click to jump down:

- EC2 Overview
- EC2 FAQs
- EC2 Pricing
- Amazon EC2 SLA
- EC2 Instance Types
- EC2 Instance Purchasing Options
- Reserved Instances
- Spot Instances
- Windows Instances

Account on the Amazon EC2 cloud <http://aws.amazon.com/ec2>



# Launch Cloud BioLinux through the EC2 cloud console

The screenshot shows the AWS Management Console in Mozilla Firefox. The browser address bar displays <https://console.aws.amazon.com/ec2>. The console header includes the AWS logo, navigation links (Products, Developers, Community, Support, Account), and a welcome message for J. Craig Venter Institute. The main content area is the Amazon EC2 Console Dashboard, which is divided into several sections:

- Navigation:** A sidebar on the left with a region dropdown set to "US East". It lists various EC2-related services such as EC2 Dashboard, Instances, Spot Requests, AMIs, Bundle Tasks, Volumes, Snapshots, Elastic IPs, Security Groups, Placement Groups, Load Balancers, and Key Pairs.
- Getting Started:** A yellow box with the text "To start using Amazon EC2 you will want to launch a virtual server, known as an Amazon EC2 instance." Below this text is a "Launch Instance" button, which is circled with a dashed black line. A note below the button states: "Note: Your instances will launch in the US East (Virginia) region."
- Service Health:** A section showing the current status of Amazon EC2 in the US East - N. Virginia region. The status is "OK" (indicated by a green checkmark). The details section shows "[RESOLVED] Increased tagging error rates" with a link to "View complete service health details".
- My Resources:** A section displaying the number of EC2 resources in the US East (Virginia) region. The resources listed are: 2 Running Instances, 0 Elastic IPs, 2 EBS Volumes, 4 EBS Snapshots, 3 Key Pairs, 5 Security Groups, 0 Load Balancers, and 0 Placement Groups. A "Refresh" button is located to the right of the resource list.
- Related Links:** A section with links to Documentation, All EC2 Resources, Forums, Feedback, and Report an Issue.

At the bottom of the screenshot, the URL <http://tinyurl.com/cloud-biolinux-tutorial> is displayed.

# Cloud BioLinux and VM launch wizard

Request Instances Wizard

CHOOSE AN AMI | INSTANCE DETAILS | CREATE KEY PAIR | CONFIGURE FIREWALL | REVIEW

Choose an Amazon Machine Image (AMI) from one of the tabbed lists below by clicking its **Select** button.

Quick Start | My AMIs | **Community AMIs**

Viewing: All Images |  | 1 to 1 of 1 Items

AMI ID	Root Device	Manifest	Platform	
ami-6011e409	ebs	767506454313/Cloud Biolinux with FreeNX 09_2010	Other Linux	Select

Community AMIs,  
search for Cloud  
BioLinux VM  
identifier  
(most recent update:  
cloudbiolinux.org)

Request Instances Wizard

CHOOSE AN AMI | **INSTANCE DETAILS** | CREATE KEY PAIR | CONFIGURE FIREWALL | REVIEW

Provide the details for your instance(s). You may also decide whether you want to launch your instances as "on-demand" or "spot" instances.

Number of Instances:  Availability Zone:

Instance Type:

Type	CPU Units	CPU Cores	Memory
Micro (t1.micro)	Up to 2 ECUs	1 Core	613 MB
<b>Large (m1.large)</b>	4 ECUs	2 Cores	7.5 GB
Extra Large (m1.xlarge)	8 ECUs	4 Cores	15 GB
High-Memory Extra Large (m2.xlarge)	6.5 ECUs	2 Cores	17.1 GB
High-Memory Double Extra Large (m2.2xlarge)	13 ECUs	4 Cores	34.2 GB
High-Memory Quadruple Extra Large (m2.4xlarge)	26 ECUs	8 Cores	68.4 GB
High-CPU Extra Large (c1.xlarge)	20 ECUs	8 Cores	7 GB

Launch Instance | EC2 Instances let you... costs into much smaller | Request Spot Instance | Launch Instance

select computational  
capacity for the VM

File Edit View History Bookmarks Tools Help

Stop Back Forward Home Shareaholic <https://console.aws.amazon.com/ec2> amazon.com x executable Print

aws.amazon.com AWS Products Developers Community Support Account Welcome, J. Craig Venter Institute Settings Sign Out

Amazon S3 **Amazon EC2** Amazon VPC Amazon Elastic MapReduce Amazon CloudFront Amazon RDS

Navigation  
Region: US East

EC2 Dashboard

INSTANCES  
Instances  
Spot Requests

IMAGES  
AMIs  
Bundle Tasks

ELASTIC BLOCK STORE

My Instances  
Launch Instance Instance Actions Reserved Instances Show/Hide Refresh Help

Viewing: All Instances All Instance Types 1 to 4 of 4 Instances

Instance	AMI ID	Root Dev	Type	Status	Lifecycle	Public D	Security	Key Pair	Moni
i-49201823	ami-6011e409	ebs	m1.large	pending	normal		default	jcvi_key	disab
<input checked="" type="checkbox"/> i-f7340c9d	ami-6011e409	ebs	m1.large	running	normal	ec2-184-	default	jcvi_key	disab
<input type="checkbox"/> i-795b6313	ami-6816e301	ebs	m1.large	terminated	normal		default	jcvi_key	disab
<input type="checkbox"/> i-f9330b93	ami-6011e409	ebs	m1.large	terminated	normal		default	jcvi_key	disab

1 EC2 Instance selected

Root Device: /dev/sda1 Root Device Type: ebs

Block Devices: /dev/sda1=vol-68cce401:attached:2010-09-22T22:57:42.000Z

Lifecycle: normal

Public DNS: ec2-184-73-27-151.compute-1.amazonaws.com

Private DNS: ip-10-245-207-16.ec2.internal

Private IP Address: 10.245.207.16

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NX - Cloud Biolinux

**NOMACHINE**

General Advanced Services Environment

Server

Host: ec2-184-73-27-151.comput Port: 22

Remember my password Key...

Desktop

Unix GNOME Settings...

MODEM ISDN ADSL WAN LAN

Display

1024x768 W 800 H 600

Use custom settings Settings...

Delete Save Ok Cancel

- remote desktop connection client
- free and open-source : <http://nomachine.com>

# Cloud BioLinux with remote desktop connection

The screenshot displays a remote desktop session titled "NX - ubuntu@ec2-67-202-27-227.compute-1.amazonaws.com:2002 - Cloud BioLinux". The desktop environment includes the following windows and elements:

- Jemboss:** A menu-driven interface with options: ALIGNMENT, DISPLAY, EDIT, ENZYME KINETICS, FEATURE TABLES, INFORMATION, NUCLEIC, PHYLOGENY, PROTEIN, UTILS. The "GoTo:" field contains "abiview" and "aliancopy".
- RasMol - 3DMS X-RAY DIFFRACTION:** A window showing a 3D molecular model of a protein structure, rendered in red, white, and blue spheres.
- ClustalX 2.0.12:** A window displaying a sequence alignment. The alignment shows four sequences with gaps (indicated by asterisks) and a scale bar at the bottom. The text "CLUSTAL-Alignment file created [øØE]" is visible at the bottom of the window.

The desktop background features the "bio-linux" logo in green and black. The taskbar at the bottom includes icons for [ClustalX 2.0.12], [RasMol], RasMol - 3DMS X..., ClustalX 2.0.12, and Jemboss. The system tray shows the date and time: "Wed Sep 22, 5:27 AM".

- Applications
- Places
- System
- Accessories
- Bioinformatics
- Graphics
- Internet
- Programming
- Science
- Sound & Video
- System Tools
- Ubuntu Software Center
- CLC Sequence Viewer
- clustalw
- clustalx
- Cn3D
- dendroscope
- entrez
- Exchanger
- fastDNAMl
- Forester ATV
- gap4
- jalview
- Jemboss
- maxdLoad2
- mesquite
- Mr Bayes Multi
- oligoarray
- omegamap
- pfaat
- pregap4
- sequin
- sqint
- taverna
- TaxInspector
- tetra
- treeview
- trev

Jemboss

File Preferences Tools Favourites Help

ALIGNMENT  
DISPLAY  
EDIT  
ENZYME KINETICS  
FEATURE TABLES  
INFORMATION  
NUCLEIC  
PHYLOGENY  
PROTEIN  
UTILS

GoTo:

- abiview
- aligncopy
- aligncopypair
- allversusall
- antigenic
- backtranambig
- backtranseq
- banana
- bioesd
- btwisted
- cai
- cathparse
- chaos
- charge
- checktrans
- chips
- cirdna
- codcmp
- codcopy
- coderet
- compseq
- consambig

Keyword Search  GO

AND  OR

(No Current Jobs)



# Cloud BioLinux:

## sharing data & results with VM snapshots

- access rights to the “snapshot” VM: public or for specific user
- other researchers access the VM with all the software, data, analysis results directly on the cloud
- storage cost: 0.10\$ / GB / month

### Set AMI Permissions

This image is currently Private

Public  Private

**Add Launch Permission:**  
AWS Account Number 1:  add additional users

**Remove Launch Permission:**  
No user permissions



aws.amazon.com | AWS | Products | Developers | Community | Support | Account

Amazon S3 | **Amazon EC2** | Amazon VPC | Amazon Elastic MapReduce | Amazon CloudFront | Amazon RDS

### Navigation

Region: US East

- > EC2 Dashboard
- INSTANCES
  - > Instances
  - > Spot Requests
- IMAGES
  - > AMIs
  - > Bundle Tasks

### My Instances

Launch Instance | Instance Actions | Reserved Instances

Viewing: All Instances

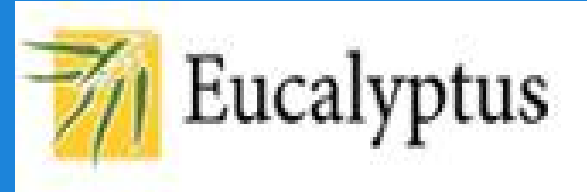
Instance Management

- Connect
- Get System Log
- Get Windows Admin Password
- Create Image (EBS AMI)**
- Add/Edit Tags
- Bundle Instance (S3 AMI)
- Launch More Like This
- Disassociate IP Address

Root Dev	Type	Status	Lifecycle	Public D	Security	Key Pair	Moni
efs	m1.large	● running	normal	ec2-67-2	default	jcv_i_key	disab
efs	m1.large	● running	normal	ec2-184-	default	jcv_i_key	disab
efs	m1.large	● terminated	normal		default	jcv_i_key	disab
efs	m1.large	● terminated	normal		default	jcv_i_key	disab

# Research at JCVI with Cloud BioLinux

- bioinformatics data analysis pipelines are complex
- approach: pre-install pipelines and all their dependencies within a VM
- make VM available on Amazon EC2
- we use private clouds, Eucalyptus & OpenStack
- open-source cloud platforms, fully compatible with Amazon EC2 (identical API)
- easy to set up on a local computer cluster, comes with Ubuntu Linux server edition
- also can run on your laptop with VirtualBox



instructions and VM at <http://www.cloudbiolinux.org>

**All reads**

**Search for all barcodes**

Discard: reads w/o barcode and reads with more than one barcode.

**Set of uni-barcoded reads**

***de novo  
assembly***

**tBLASTX against reference  
sequence**

1. Trim SISPA barcode and n-mer
2. Discard chimeric/non-flu reads
3. Assemble by segment (CLCbio)

**Set of 8 best consensus sequences for  
each sample**

**(8 segments for each sample)**

JCVI's Viral Genome  
Sequencing Pipelines

Phase I-a  
Sequencing & Assembly



**8 best consensus for each sample**  
(8 segments for each sample)

**For each segment:**

1. BLASTN against a DB of full length segments
2. Select best reference for each segment

**Set of 8 best GenBank references**

1. CLC mapping for each technology
2. Update references with variations identified by multiple technologies
4. CLC mapping using updated references and all reads

**Assembled genomes**

**mapping  
assembly**

JCVI's Viral Genome  
Sequencing Pipelines

Phase I-b  
Sequencing & Assembly

# JCVI's Viral Genome Sequencing Pipelines

## Phase II Annotation

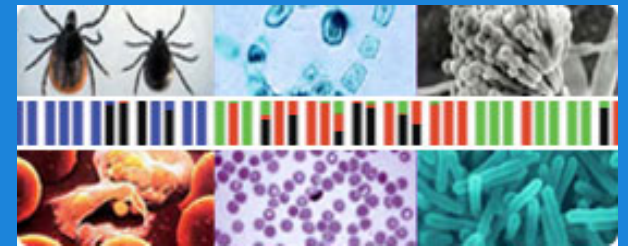
- Assembled genomes as input to Viral Genome ORF Reader (VIGOR)  
Wang et al. BMC Bioinformatics 2010, 11:451
- detect coding regions, frame shifts, overlapping and embedded genes
- successfully used for annotating the influenza virus, rotavirus, rhinovirus, coronavirus and subtypes

## Phase III Annotation Visualization & Editing



# Research at JCVI with Cloud BioLinux

- Funded by NIAID until 2013, focus on Viral, end-to-end, sequencing-to-annotation pipelines
- approach: pre-install pipelines and all their software dependencies in a VM
- export VM on Amazon EC2: pipelines ready to execute, no need to purchase hardware
- users simply need a web browser
- benefits small laboratories that lack resources or expertise
- if you own a cluster: download and run VM on your private Eucalyptus or Openstack cloud



JCVI - GSC



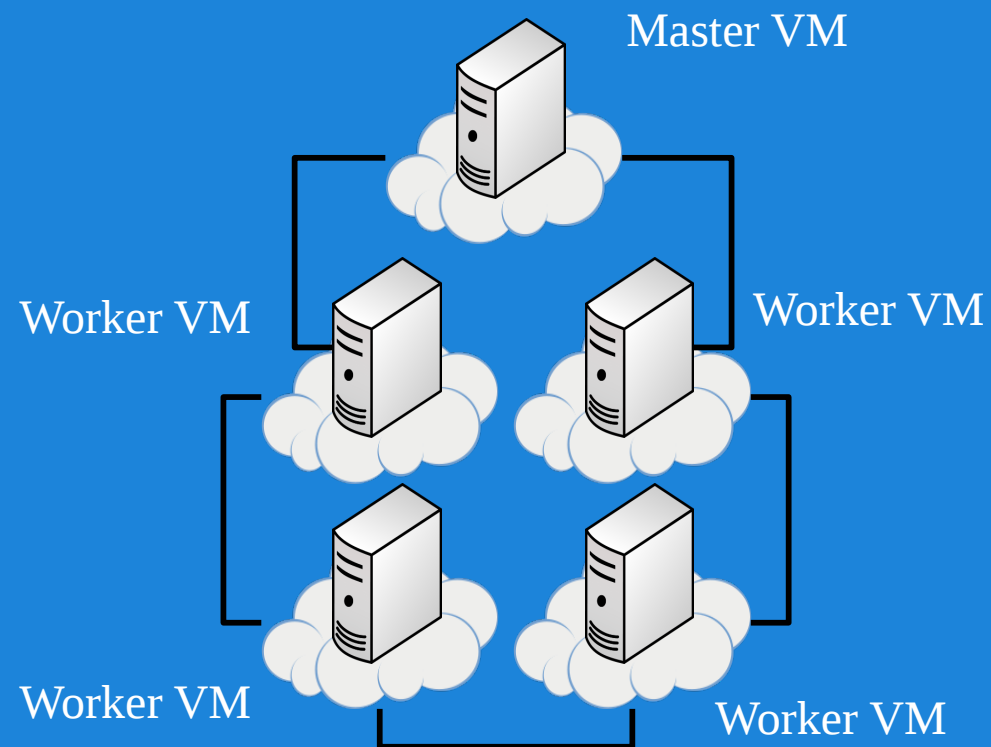
National Institute of Allergy and Infectious Diseases

Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases.

J. Craig Venter™  
I N S T I T U T E

# Scalable Data Analysis with Cloud BioLinux

- Sun / Oracle Grid Engine (GE) cluster: computational task scheduling
- Cloud BioLinux VM, dual role: Master or Worker
- Master VM coordinates distribution of computational tasks, Workers runs the computes
- The Master VM contains all code needed to start Workers and assemble a virtual cluster on the cloud
- Currently works on Amazon EC2



# Scalable Data Analysis with Cloud BioLinux

**Galaxy** There is a new version of CloudMan: [What's New](#) | [Update CloudMan](#) Info: [report bugs](#) | [wiki](#) | [screencasts](#)

## Galaxy CloudMan Console

Welcome to the Galaxy Cloud Manager. This application will allow you to manage this cloud and the services provided within. If this is your first time running this cluster, you will need to select an initial data volume size. Once the data store is configured, default services will start and you will be add and remove additional services as well as 'worker' nodes on which jobs are run.

[Terminate cluster](#) [Add instances](#) [Remove instances](#) [Access Galaxy](#)

### Status

Cluster name: local test

Disk status: 0 / 0 (0%)

Worker status: Idle: 0 Available: 0 Requested: 0

Service status: Applications Data

**Master Node**  
Node231xQ  
Alive: 8m 6s  
Type: d1.xtreme

Cluster status log

- Galaxy Cloudman: users can control size of cluster, storage through a web-browser accessible interface
- Currently in the process of porting to Eucalyptus
- Users can download a VM which can bootstrap GE clusters on their private cloud
- Elastic capacity, size of virtual cluster

Afgan et al. BMC Bioinformatics 2010 11(Suppl 12):S4



# Cloud BioLinux for Software Developers

- Issue 1: for researchers with sensitive data a public cloud might not be an option moving VMs across clouds is not trivial, need low level operations
- Issue 2: bioinformatic specializations (ex. sequencing, phylogeny, protein structure) over-sized VM with too much software for all specializations
- Cloud BioLinux VM deployment framework

# Framework for Cloud Software Developers

- open-source framework to customize cloud Virtual Machines
- python Fabric automated deployment tool ( DevOps )
- software installed in the VM listed in simple text configuration files
- Fabric scripts automatically pull and install software from repositories
- available from: <https://github.com/chapmanb/cloudbiolinux>



100644 | 39 lines (38 sloc) | 0.668 kb

```
1 ---
2 # Top level configuration file that specifies w
3 # should be installed. New sections that are ad
4 # files should go here. Comment out any groups
5 # installed.
6 packages:
7   - desktop
8   - programming
9   - distributed
10  - amazon
11  - python
12  - r
13  - ruby
14  - perl
15  - java
16  - erlang
17  - haskell
18  - databases
19  - math
20  - viz
21  - web
22  - bio_general
23  - bio_search
24  - bio_alignment
25  - bio_nextgen
26  - bio_sequencing
27  - bio_annotation
28  - bio_microarray
29  - bio_visualization
30  - bio_utils
31  - phylogeny
```

## software domains in Cloud BioLinux:

Genome sequencing, *de novo* assembly, annotation, phylogeny, molecular structures, gene expression analysis

high-level configuration describing software groups for each group individual bioinformatics tools

```
516 - apache2
517 bio_general:
518   - emboss
519   - emboss-data
520   - emboss-lib
521   - primer3
522   - readseq
523   - bio-linux-taverna
524   - bio-linux-xcut
525 bio_search:
526   - blast2
527   - hmmer
528   - ncbi-tools-bin
529   - bio-linux-blast+
```

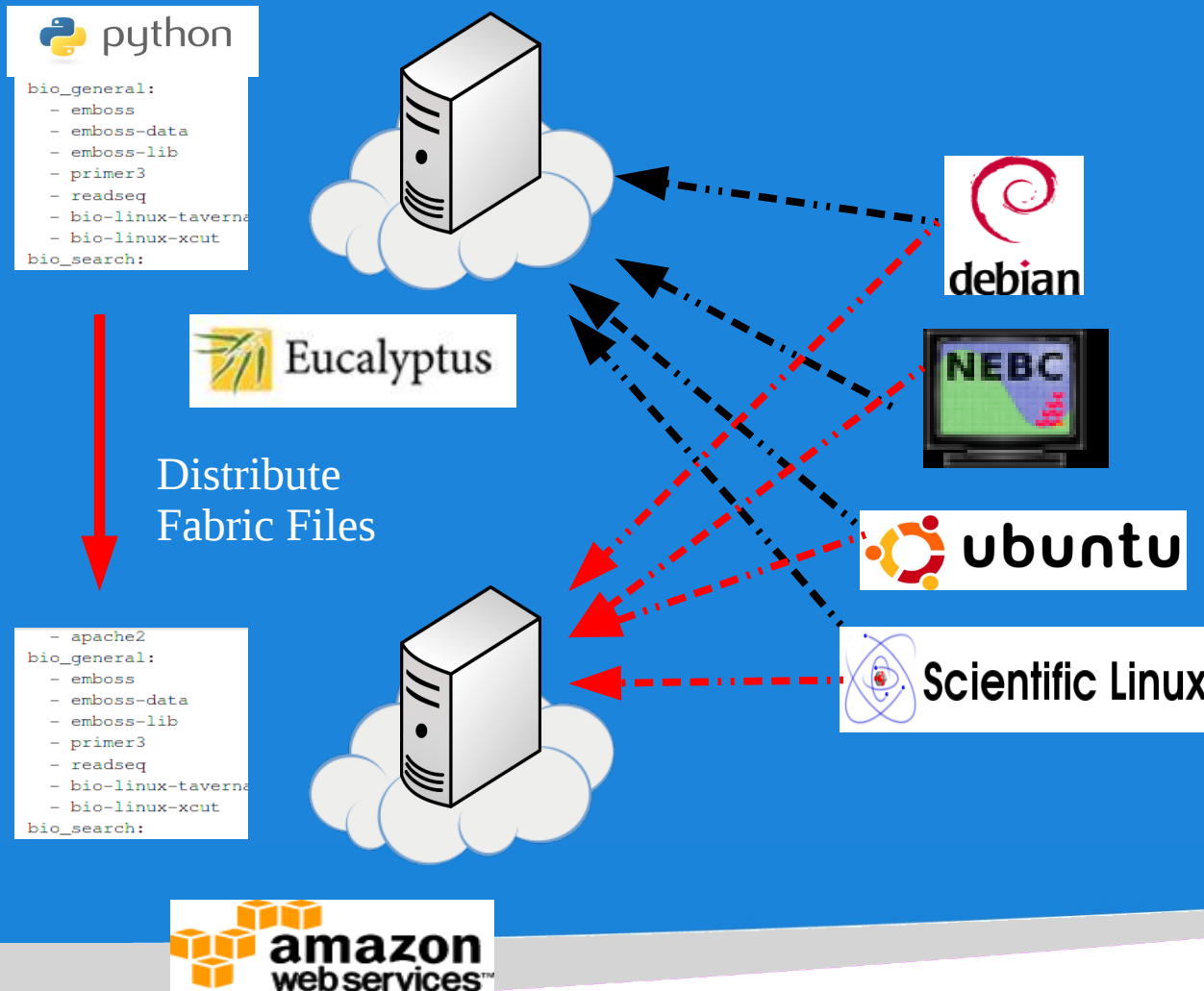




# Framework for Cloud Software Developers

Customize  
Fabric Files

Custom VM



- start a fresh VM on Amazon or private cloud
- edit Fabric files to mix and match software from repositories – customized VM
- use source code repository to share configuration files
- share configuration of VM as source code

# Acknowledgments & Credits

*Brad Chapman* - development of the Fabric scripts, website

*Tim Booth, Mesude Bicak, Dawn Field* – BioLinux 6.0 development

*Enis Afgan* – Cloudman and Cloud BioLinux integration

*Members of the Cloud Biolinux community* - <http://groups.google.com/group/cloudbiolinux>

*Alex Richter* – porting Cloudman to Eucalyptus open-source cloud

JCVI IT dept. - technology support

*Maria Giovanni, Punam Mathur* - NIAID / GSC funding

*Karen Nelson* – JCVI support for Cloud BioLinux

NIAID / OCICB – Bioinformatics Festival

*Thank you !*

*kkrampis@jcv.org*  
*<http://www.cloudbiolinux.org>*  
*<http://www.slideshare.com/agbiotec>*

**J. Craig Venter™**  
I N S T I T U T E