Setup and usage of an e-BioScience infrastructure for high throughput DNA sequence analysis

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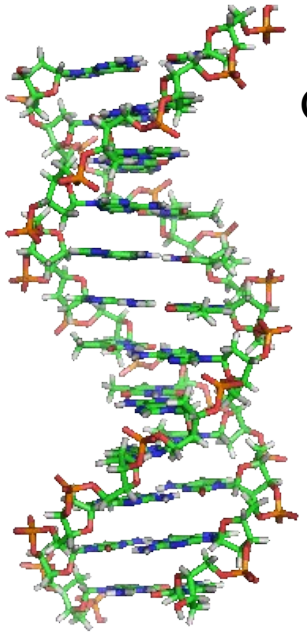
Co-authors: Michel de Vries, Katja Ritz, Frank Baas, Antoine van Kampen



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Traditional sequencing

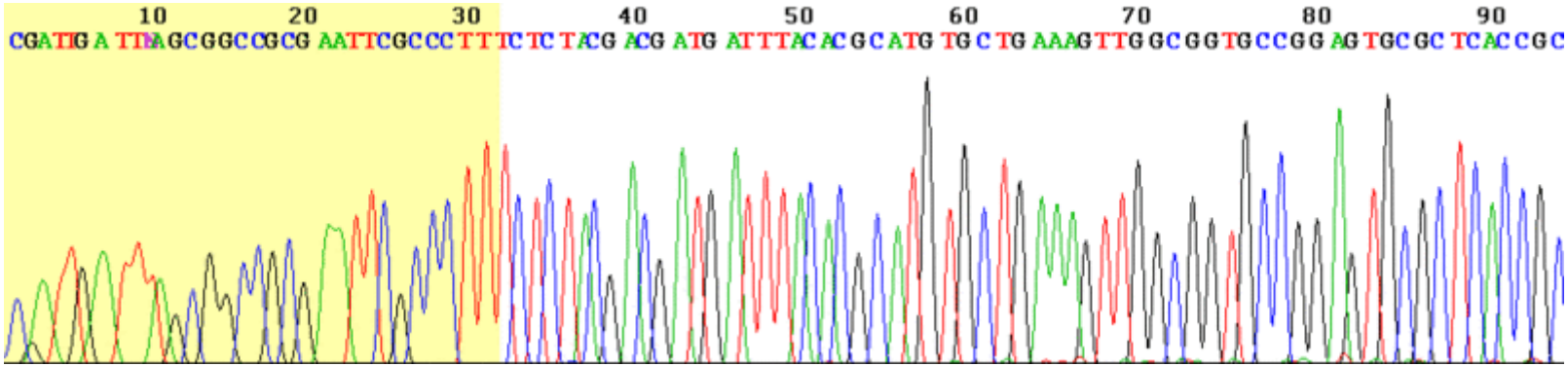
Since 1963

Gel or capillary sequencing

One sequence at the time

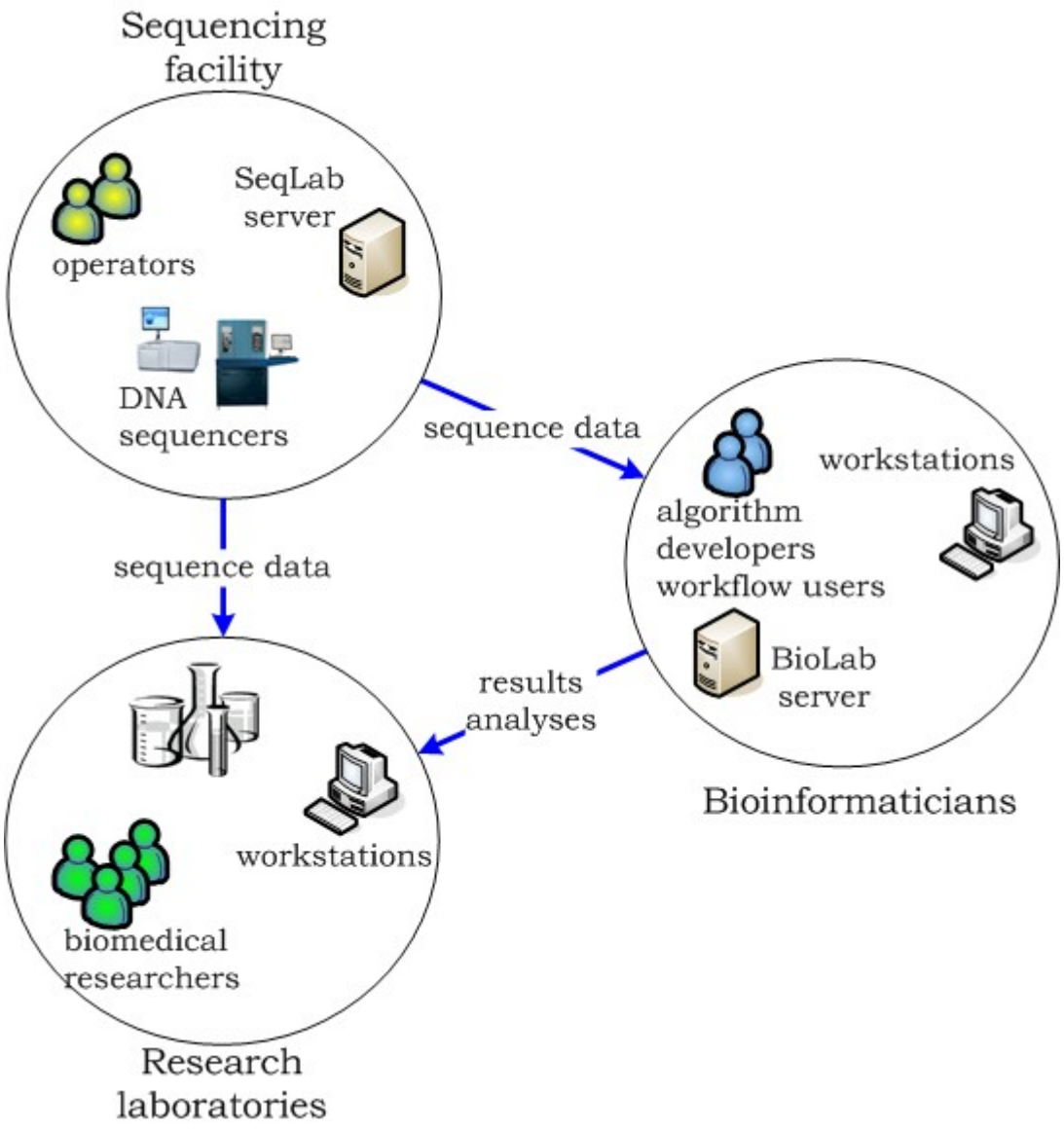
Robots: up to 384 samples in one run

http://whitehead.mit.edu/



http://en.wikipedia.org/wiki/DNA_sequencing

Resources


Sequencing facility
SeqLab server
operators
DNA sequencers
sequence data
sequence data
workstations
algorithm developers
workflow users
BioLab server
Bioinformaticians
results analyses
workstations
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High throughput DNA sequencing

Aka: Second generation, next generation or massively parallel sequencing

Since 2005

Characteristics:

Immobilize DNA fragments on a bead or plate

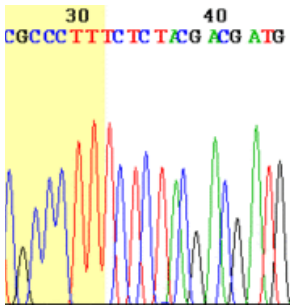
Multiply DNA fragments in parallel

Flow of labelled nucleotides over plate
(and make pictures)

Process images to determine nucleotide sequence

```
>GCJ743F01C2VYF length=227 xy=1145_3765 region=1 run=R_2010_02_19_06_54_29_
TGCGTTTTTACTTTCTTCAGGGATACCATTTAACCTGTAGTCTGCTGTTGGGGTAATCTG
AGTCTGATGTGGCAAGTTCTGCTGCGTTTGCATCAATGGCATGTTTGTGCTATCATAGTT
GTCTGTGTGTAAACGGAGGTATGATTTACCCCGAGTCACAGGGGTTTGGAACCACAGGTA
ACGCGTTTAGACCAGGGGTTCCATGCTAATCTCTCTATCTTGGACCA
>GCJ743F01C3XSO length=219 xy=1157_3654 region=1 run=R_2010_02_19_06_54_29_
TGTAGTTTTCTTTCTTCAGGGATACCATTTACCTGTAGTCTGCTGTTGGGGTAATCTGAG
TCTGATGTGGCAAGTTCTGCTGCGTTTGCATCAATGGCATGTTTGTGCTATCATAGTTGT
CTGTGTGTAAACGGAGGTATGATTTCCCCGAGTCACAGGGTTGGAACCACAGGTAAGCGT
```

Traditional versus high throughput DNA sequencing



http://en.wikipedia.org/

http://www.454.com/

http://solid.appliedbiosystems.com/

Sanger, one run:

? hours (human genome took 15 years)

1-384 sequences

300-1000 nt per sequence

1 KB - 384 KB data

= 1,000-384,000 bases

Year: 1963 – now

Roche 454, one run:

7.5 hours

1,000,000 sequences

500 nt per sequence

35 GB data (including images)

500 MB data (excluding images)

= 500,000,000 bases

Year: 2005 – now

ABI SoLiD, one run:

3-5 days

150,000,000 sequences

50-100 nt per sequence

2-4 TB data (raw data)

= 15,000,000,000 bases

Year: 2005 – now

Applications

T and B cell variation

Bacterial genomes

Gene expression

Re-sequencing

Alternative splicing

Virus discovery

Use case: virus discovery

Laboratory

Blood sample: extract viral DNA and RNA

Viruses in small concentrations

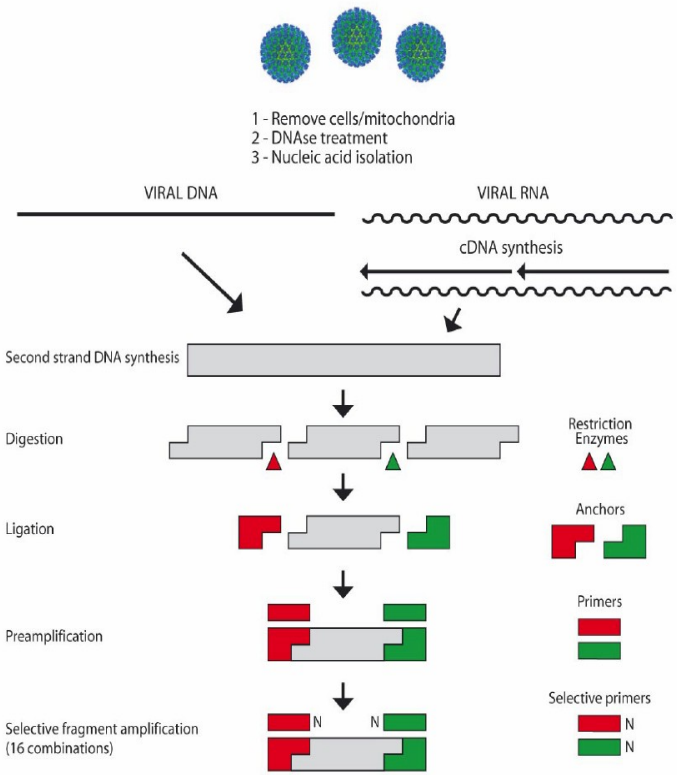
Sample also contains human material

Bioinformatics

Identify all sequences (sequence alignment)

Filter out human material

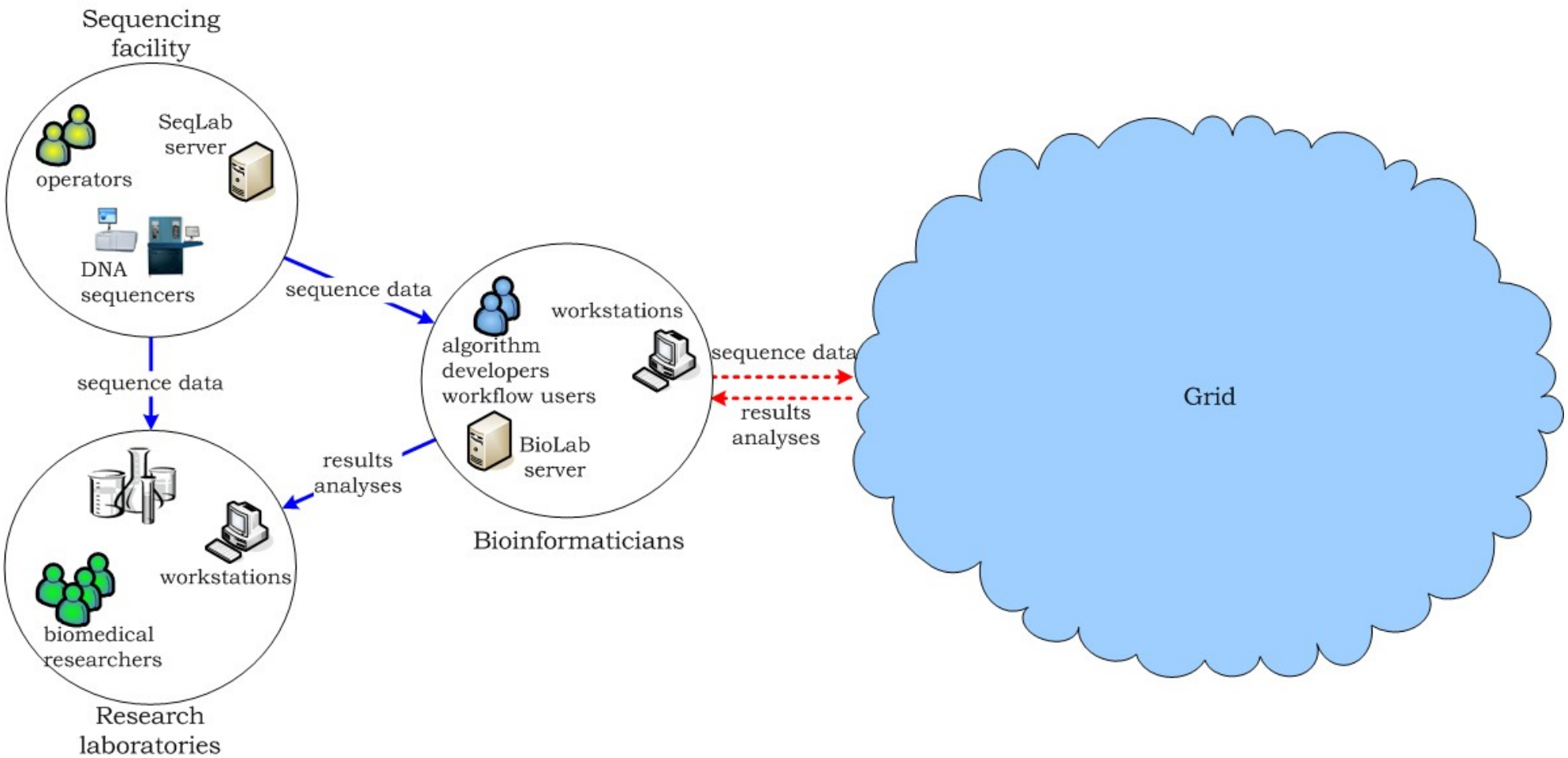
Report viral and bacterial DNA/RNA in sample



Michel de Vries

11 experiments
6,000,000 sequences
Repeat after database updates

Resources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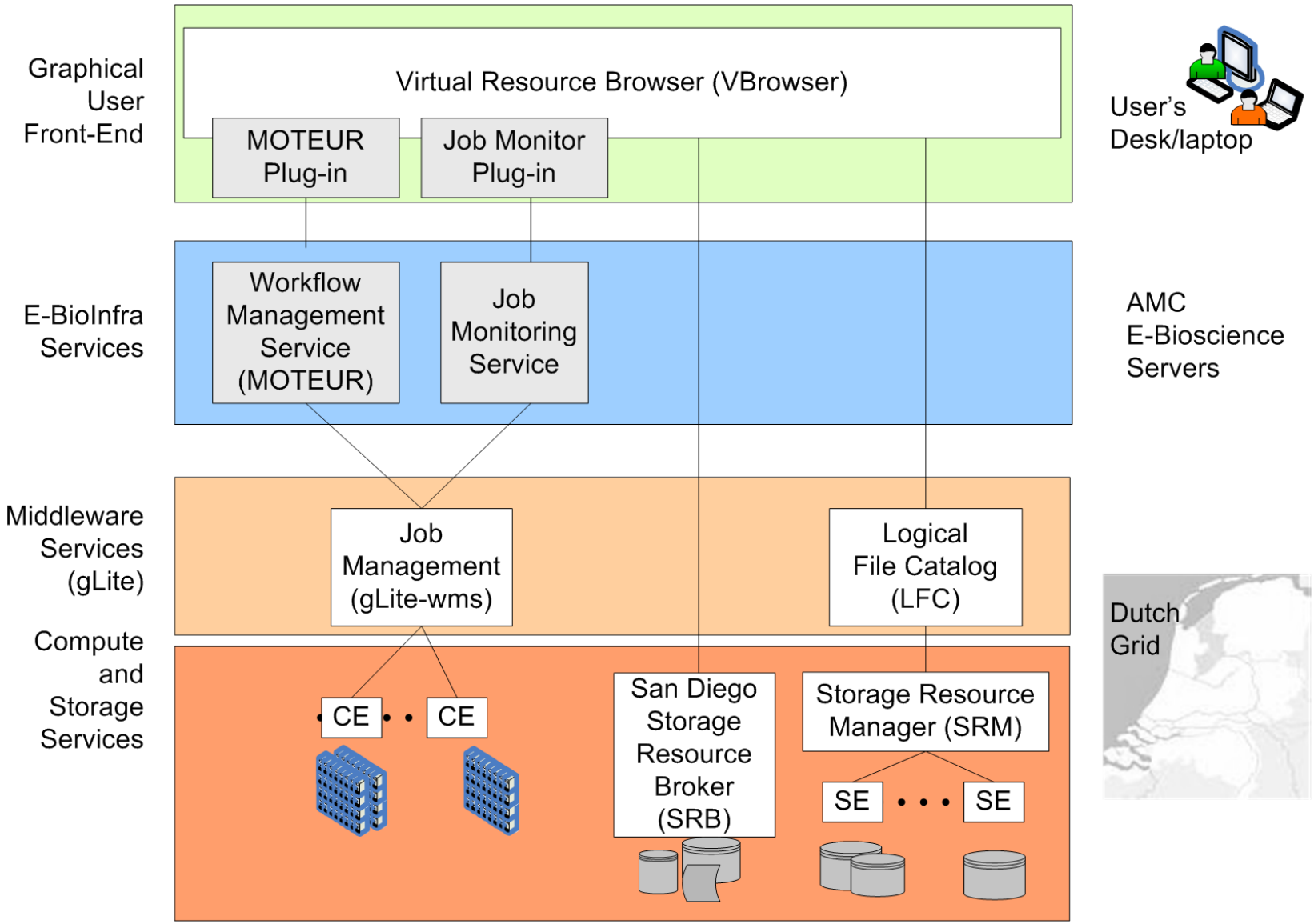
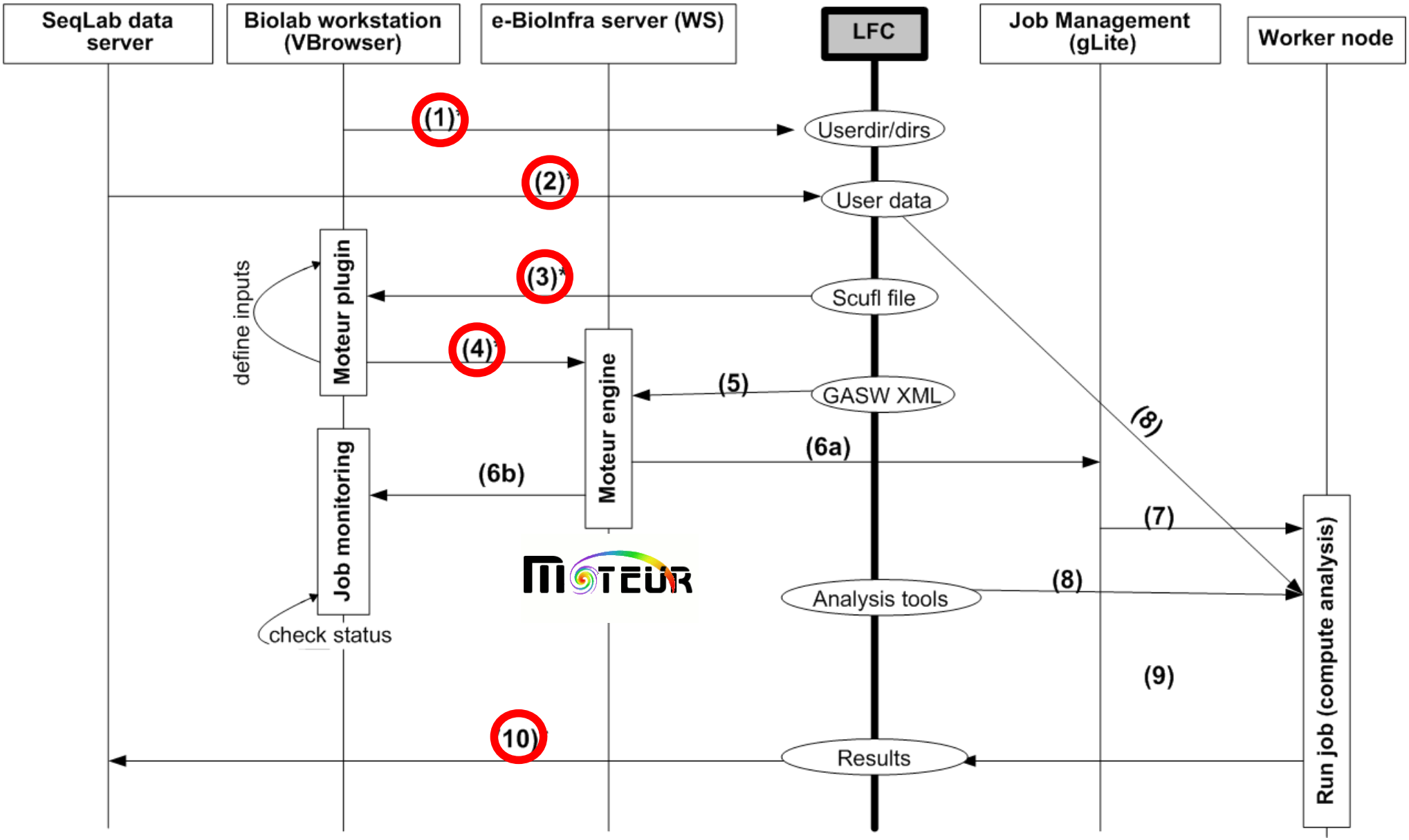
eBioScience infrastructure



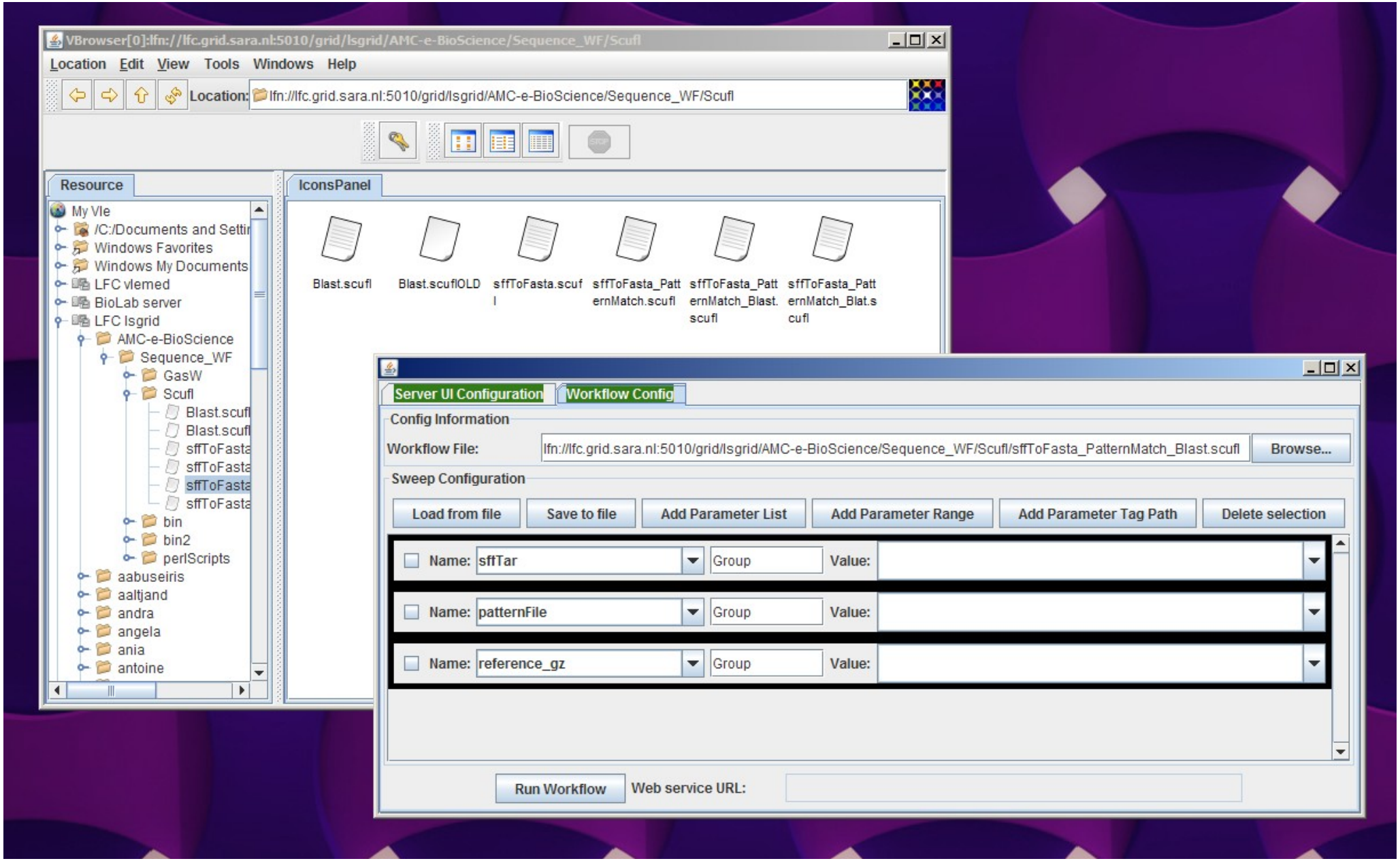
Olabarriaga SD, Glatard T, de Boer PT: A Virtual Laboratory for Medical Image Analysis. IEEE Transactions on Information Technology In Biomedicine, in press

http://www.vl-e.nl/vlemed
http://www.bioinformaticslaboratory.nl/

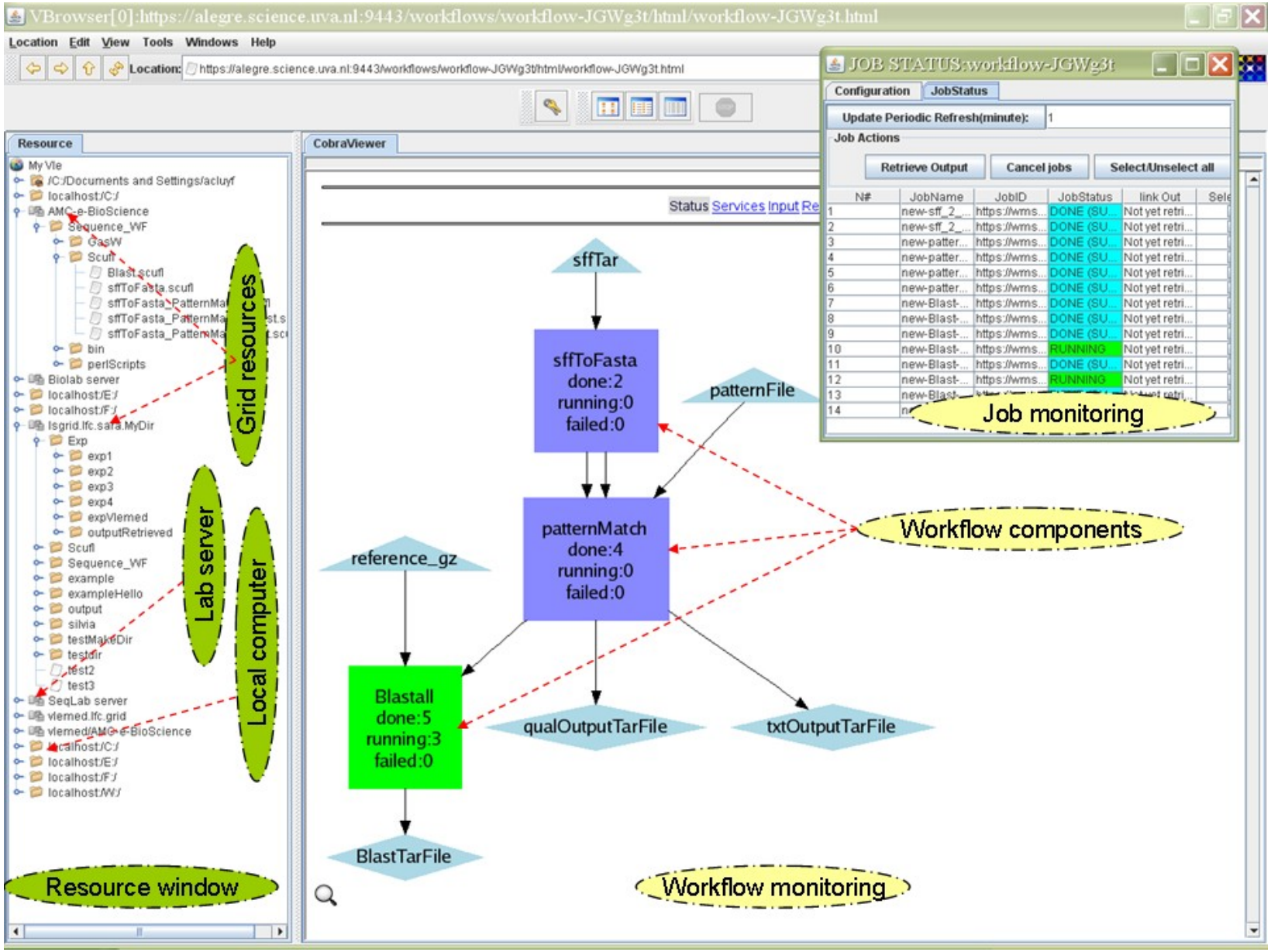
User actions and automated actions



In practice – workflow submission



In practice – workflow monitoring



Collaborators monitor progress via web browser

Bioinformatics Laboratory

Jump | Search

Sequencing

Hello Barbera Van Schaik
Log Out

Create personal sidebar

- **Sequencing Web**
- Create New Topic
- Index
- Search
- Changes
- Preferences

TWiki > Sequencing Web > SPneumoniae (2010-04-02, BarberaVanSchaik)

Edit | Attach

Streptococcus pneumoniae

Contact: JurgenPiet

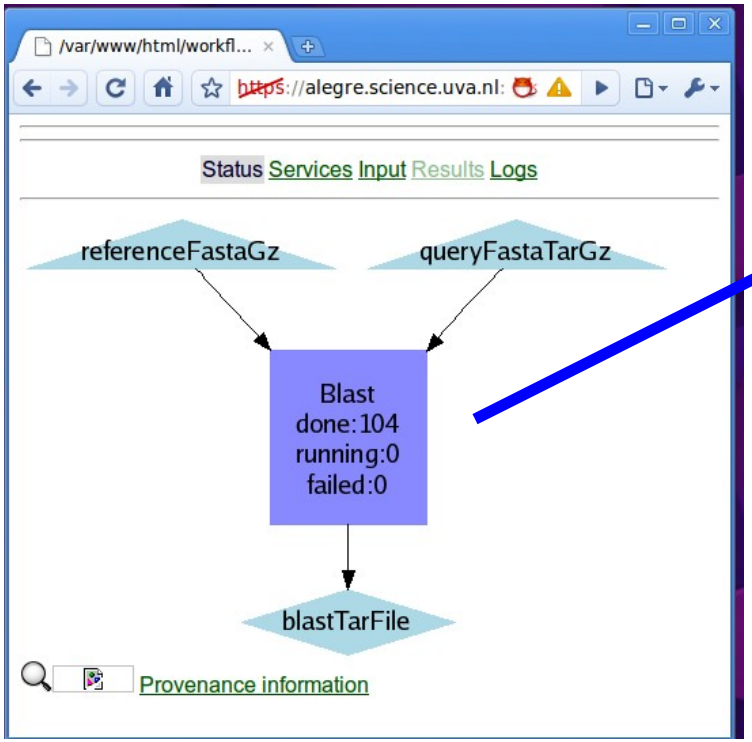
Contact biolab: BarberaVanSchaik

- Streptococcus pneumoniae
  - Description
  - Sequence runs
  - Methods

April 2010

- 2-4-2010: Submitting grid jobs in batch (bacteria section in chunks)
  - Test: https://alegre.science.uva.nl:9443/workflows/workflow-B1XLq8/html/workflow-B1XLq8.html
  - Real: https://alegre.science.uva.nl:9443/workflows/workflow-MOGk4Y/html/workflow-MOGk4Y.html

Collaborators monitor progress via web browser



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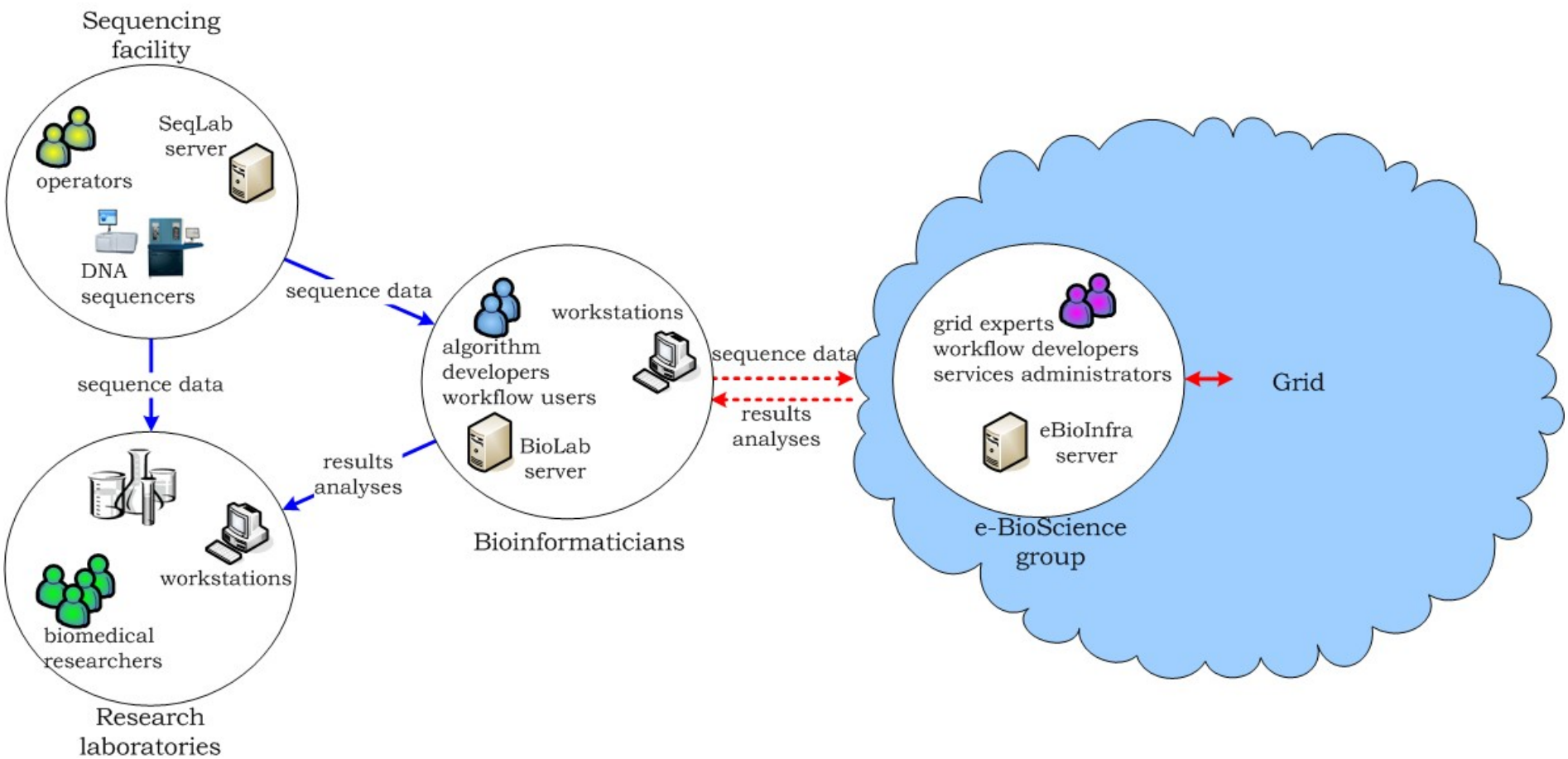
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Troubleshooting

What if jobs fail?

Examine workflow.out and workflow.err (via vbrowser or web browser)

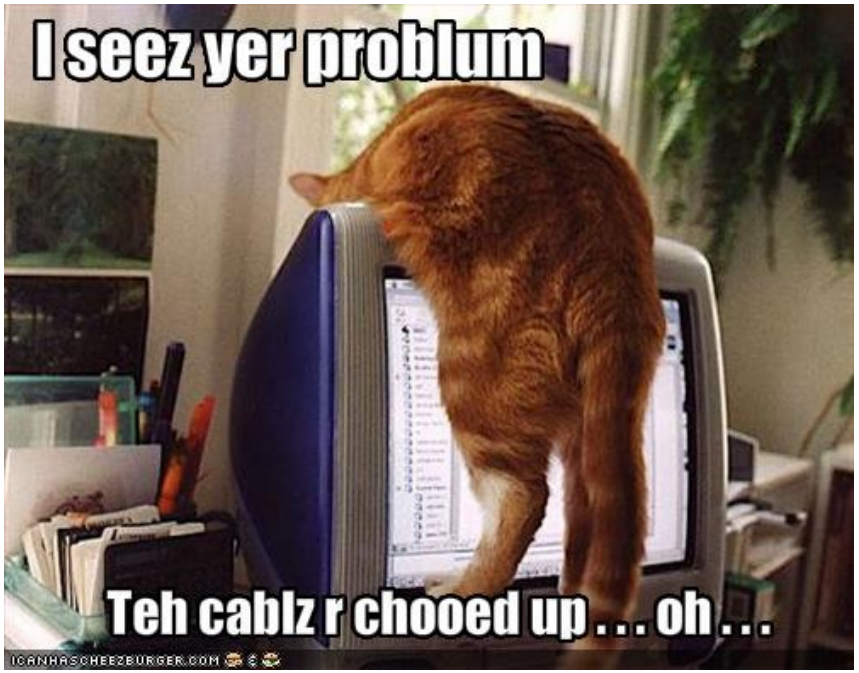
Retrieval of std.out and std.err (job monitoring plug-in)

Check health of servers and services

Check e-mail notifications
e.g. scheduled downtimes

Check if data and programs are replicated

Ask the expert



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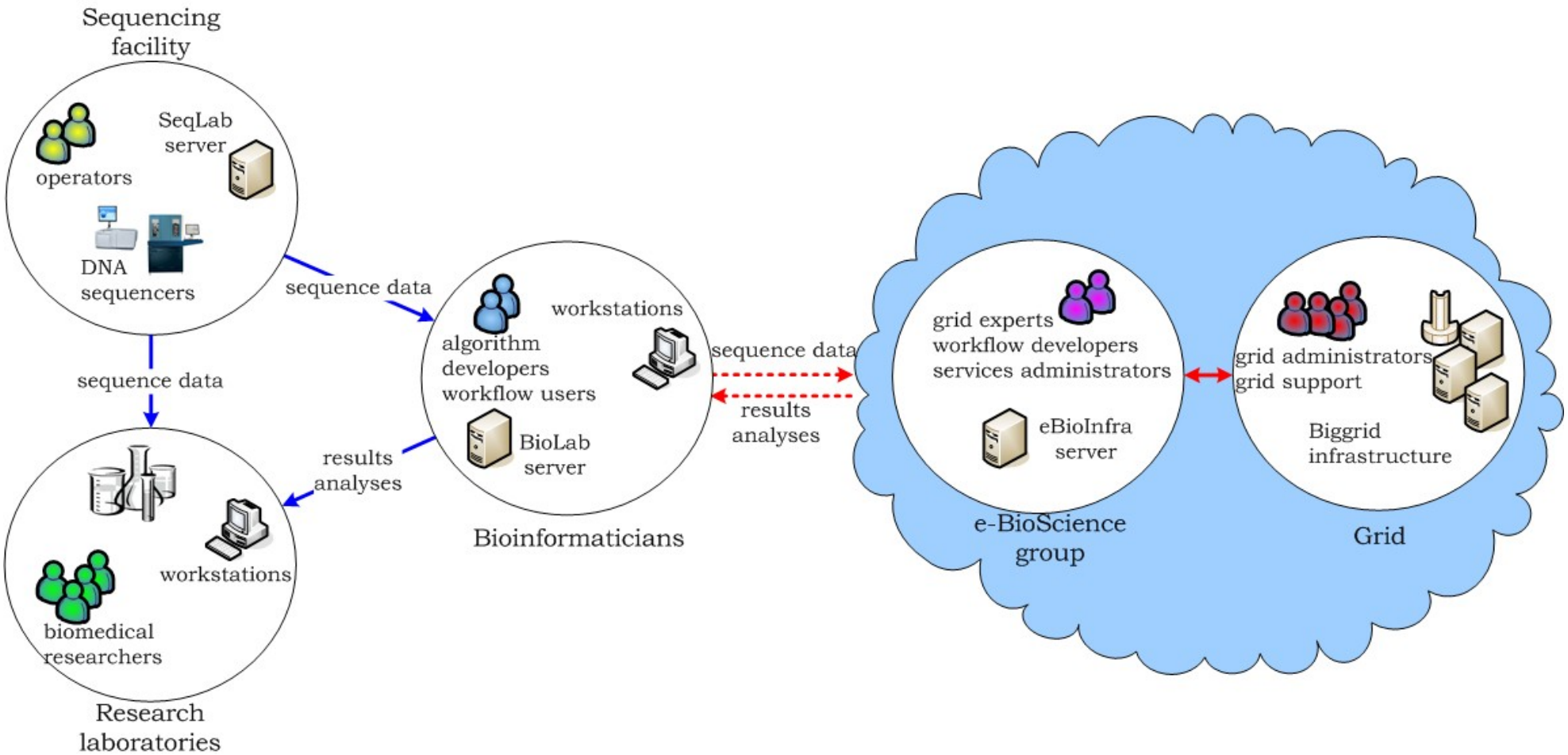
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Important issues

Data security
especially for analysis of patient samples

Maintenance of reference databases/software
e.g. GenBank database updates

User friendliness of interface(s)

Documentation

Support

Positive experiences from the pilot study

Faster: DNA sequence data analyzed more quickly

Easier: Workflows are easier to use than using grid directly

Automation: Parameter sweep (iteration operators)

Collaboration: Grid admins, e-bioscientists, bioinformaticians, the lab

Acknowledgements

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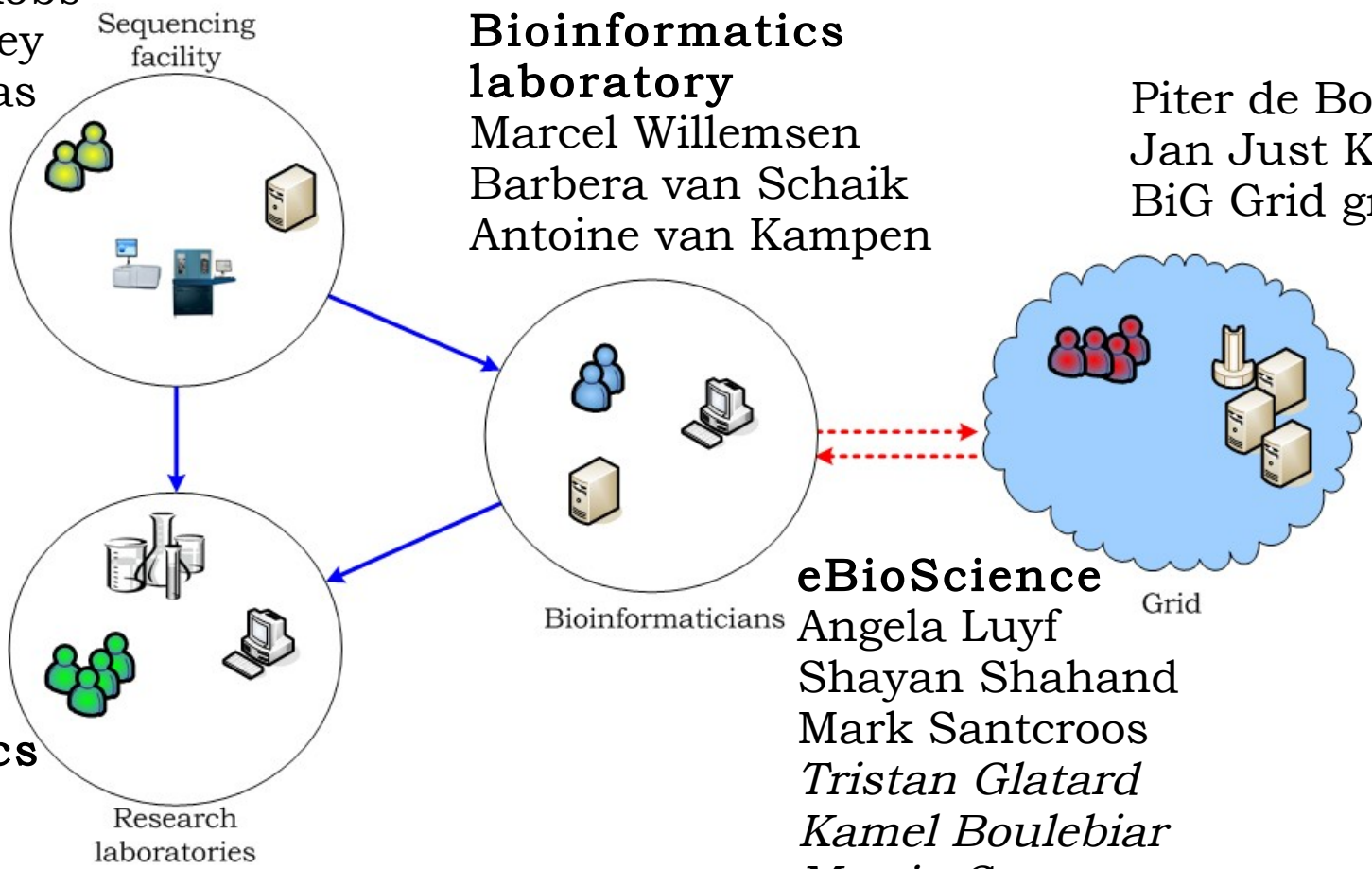

eBioScience
Angela Luyf
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Tristan Glatard
Kamel Boulebiar
Martin Stam
Silvia Olabarriaga
Antoine van Kampen

Neurogenetics
Katja Ritz
Frank Baas

Virus discovery unit
Michel de Vries
Martin Deijs
Lia van der Hoek