SPHN: Building an interoperable environment for biomedical research in Switzerland

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SPHN/BioMedIT node head, SIB - Swiss Institute of Bioinformatics and University of Basel

on behalf of, and with contributions from:
SPHN Data Coordination Center
BioMedIT nodes (University of Basel, ETH-Z, SIB)

e-IRG Workshop, CERN
21 May 2019
Bridging the gap between data science and health
Homo sapiens is now the best characterized model organism for biomedical research
• More data collected in hospitals than in any biomedical research project
• Healthy citizen data increasingly collected with smart mobile technologies

Large, complex datasets require advanced data science techniques
• Computing infrastructures and methodologies

How to leverage these data ethically, legally and efficiently for the benefit of patients, citizens and the society?

* [https://understandingpatientdata.org.uk/]
Swiss Personalized Health Network SPHN

- A national initiative to promote research in Personalized Health
- Proposed in 2014, started in 2017
- Partners: university hospitals, schools of higher education, research institutes, and other organizations
- Mandated by the SERI (SBFI), co-mandated by the FOPH (BAG)
BioMedIT

Create secure environment to work with human data in Swiss academic institutions

BioMedIT network
coordinated by SPHN DCC (mandate to SIB)

IT infrastructure and project support
• Core-IT (SIB, Lausanne)
• sciCORE (University Basel)
• SIS (ETHZ)

Data infrastructure
• HES-SO (Geneva)

Project support
• S3IT (University Zurich)

Aligned with SPHN
SPHN, BioMedIT, PHRT

SPHN: a SAMW/SIB project with the aim to promote the development of personalized medicine/health in Switzerland

BioMedIT: an SIB project with the aim to create an IT environment for research with biomedical data in academia

PHRT: an ETH project with the aim to develop new technologies in support of personalized health
BioMedIT focus: infrastructure
SPHN/BioMedIT – integrating hospital data for research
To develop and implement the required infrastructure, SPHN funds the following project types:

<table>
<thead>
<tr>
<th>Project type</th>
<th>Description</th>
<th>Funding scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrastructure implementation projects</td>
<td>Projects that are devoted to build a progressive shareable data system enabling nationwide interoperability of molecular and clinical patient data.</td>
<td>Collaboration agreements</td>
</tr>
<tr>
<td>Infrastructure development projects</td>
<td>Projects that thrive to develop and test new technologies, methods and infrastructures for personalized health related research in connection with infrastructure implementation.</td>
<td>Call for proposals*</td>
</tr>
<tr>
<td>Driver projects</td>
<td>These projects are based in a concrete research field (e.g. cancer research/oncology) and will push the development of clinical data management systems in all University Hospitals by testing data interoperability &amp; data sharing principles within the whole network.</td>
<td>Call for proposals*</td>
</tr>
</tbody>
</table>

*Coordinated call for proposals with ETH- Domain SFA-PHRT: Joint proposals between ETH researchers and non ETH researchers can be submitted for both type of projects.
### Driver projects (call 2017)

<table>
<thead>
<tr>
<th>Project</th>
<th>Leader(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swiss Frailty Network and Repository</td>
<td>Heike Bischoff-Ferrari</td>
</tr>
<tr>
<td>Population-wide screens of the human immune repertoire: a reverse personalized-medicine approach (CCIP)</td>
<td>Adriano Aguzzi</td>
</tr>
<tr>
<td>Swiss Molecular Pathology Breakthrough Platform (SOCIBP)</td>
<td>Mark Rubin</td>
</tr>
<tr>
<td>Swiss Personalized Oncology (SPO)</td>
<td>Olivier Michiélin and Mohamed Bentires-Alj</td>
</tr>
<tr>
<td>PRECISE: Identification of biomarkers and therapeutic targets in inflammatory disease immunotherapy by high-dimensional single cell analysis and cluster proteomics</td>
<td>Manfred Claassen</td>
</tr>
<tr>
<td>PSSS: Personalized Swiss Sepsis Study: Detection and modelling of sepsis using machine learning to analyse continuous ICU monitoring, laboratory, microbiology, and -omics data for personalized sepsis management</td>
<td>Adrian Egli</td>
</tr>
</tbody>
</table>

+ 8 infrastructure development projects  
Domains: patient-data governance, e-consent management, data de-identification, NLP processing of patient records, variants database (oncology)
## Driver projects (call 2018)

<table>
<thead>
<tr>
<th>Project</th>
<th>Description</th>
<th>Responsible</th>
</tr>
</thead>
<tbody>
<tr>
<td>SACR: The Swiss Ageing Citizen Reference</td>
<td>Clinical Research from multi-modality big data sources without proprietary interfaces in a multicenter approach</td>
<td>Nicole Probst</td>
</tr>
<tr>
<td>CREATE PRIMA: Clinical Research from multi-modality big data sources without proprietary interfaces in a multicenter approach</td>
<td>Joerg Leuppi</td>
<td></td>
</tr>
<tr>
<td>IMAGINE: Radiomics for comprehensive patient and disease phenotyping in personalized health</td>
<td>Matthias Guckenberger</td>
<td></td>
</tr>
<tr>
<td>SOIN: Swiss Ophthalmic Imaging Network</td>
<td>Thomas Wolffensberger</td>
<td></td>
</tr>
<tr>
<td>SHFN: SWISSHEART Failure Network</td>
<td>Christian Matter, Johachim Buhmann</td>
<td></td>
</tr>
</tbody>
</table>

+ 5 infrastructure development projects

Domains: variants database (non-oncology), reference datasets, QC metrics in radiology, secure distributed computing algorithms
Technical mandates in a nutshell

Hospitals (and supporting platforms)
- Make patient data discoverable (aggregated queries, semantics)
- Use harmonized processes (contracts) for data exchange

Research organizations
- Establish IT infrastructure adhering to common security standards
- Establish interoperable services (data management and compute) in support of biomedical research
- Make IT infrastructure available for any research project in Switzerland

Researchers (with SPHN funding)
- Help building the infrastructure:
  - by providing real-life research use cases
  - by committing to use the infrastructure
BioMedIT project organization

- SPHN National Steering Board (NSB)
  - Data Coordination Center (DCC) & BioMedIT Board
  - Scientific Expert Board (SEB)
  - Ethical Legal Social Issues (ELSIag)

Working Groups:
- Hospital IT
- Semantic Interoperability
- Project Metadata & Techn. Interoperability
- Bioinformatics & Data Analytics
- IT Security

Driver Projects
Infrastructure Development Projects
Platforms
IT security consensus
Biomedical data are sensitive

Subject to data protection laws and strong ethical requirements
Consensus required between healthcare providers and research organizations
Regulations applicable to biomedical research

**Switzerland:**
- Federal Act on Data Protection (SR 235.1)
- Federal Data Protection Ordinance (SR 235.11)
- Human Research Act (SR 810.30)
- Human Research Ordinance (SR 810.301)
- Swiss Penal Code (SR 311.0)

**State:**
- Data access conditions
- Scope of usage context (*informed consent*)
- General processes of data management
- Consequences in case of misconduct

**European Union:**
- General Data Protection Regulation (Regulation (EU) 2016/679)

Impact on Swiss regulations anticipated
SPHN information security framework

Initial workshop
12-13 December 2017

Stakeholders:
• Hospitals IT security officers
• Industry consultants
• Academic research IT

Published: 23 August 2018

Swiss regulations
• Federal Act on Data Protection (SR 235.1)
• Federal Data Protection Ordinance (SR 235.11)
• Freedom of Information Act (SR 152.3)
• Human Research Act (SR 810.30)
• Human Research Ordinance (SR 810.301)
• Swiss Penal Code (notably Art. 321bis, SR 311.0)
• SPHN Ethical Framework

IT security management standards
• NIST Cybersecurity Framework

EU regulations
• General Data Protection Regulation (Regulation (EU) 2016/679)
  (or the Directive 95/46/EC until May 24, 2018)
Security framework (highlights)

SPHN Information Security Policy

Secure authentication
- Reference researcher identity provider with institutional control (e.g. Swiss EDU-ID)
- Two-factor authentication

Secure data transfers
- Encryption specifications

Secure storage
- Unix group-based access control
- Physical infrastructure access control
- Encryption of inactive data (e.g. backups)

Auditable processes and incident reporting
- Data and infrastructure access logging
- Mandatory reporting of incidents (processes)

User awareness
- Data Use Agreement
- Training
Data classification

**Public**: information shared and available outside of SPHN.

**Internal**: information that may be shared within SPHN. This information is not intended to be shared outside SPHN and respective projects/initiatives. The impact of the information leaking outside of SPHN would be minor.

**Confidential**: the access to this information must be restricted only to those parties within SPHN that have a legitimate need to have access to it. **All personal data (either identifying data or pseudonymized) are confidential.** The impact of leaking this information to parties with no legitimate use or to the public may cause major harm to the person from whom the data originate, to the original Data Provider (Controller), to the research organization, or to SPHN.
IT infrastructures for biomedical research
BioMedIT infrastructures goals

**Regulations**
- Legal
- Ethical
- Best Practices
- CH, USA, EU

**High Performance**
- Fast Network
- GPUs
- Parallel Filesystems

**Easy to use**
- As on the notebook
- No security hassles
- Free access to the Net
- Interactive

**Flexible**
- Fast changes
- Cutting edge software
- State full nodes
- DB servers

Slide credit: Christian Bolliger, SIS ETHZ
Leonhard Med > Security + Usability

Switch WAN
Internet

Demilitarized Zone

- Jump Hosts
- Proxy Hosts
- RD Gateway
- Web-File Transfer

Login Node

Compute nodes some with GPUs
Bare Metal

Remote Desktops

Project specific virtual servers
(DB, WebServices)

System & Home storage
(NFS)

Big Data Storage
(Lustre)

Secure Zone

OpenNebula

Slide credit: Christian Bolliger, SIS ETHZ
sciCORE Med - BioMedIT architecture

SPHN Information Security compliant framework

Interactive nodes

Multi-tenancy management

Virtualized services

Bare-metal compute

Logs and security

Management Dashboard

openstack

dermatology

Compute

Networking

Storage

Software stack

docker

Storage

University of Basel
Core-IT BioMedIT Architecture

Physical layout

Logical layout

Project A

Project B

Project C

OpenStack

Slade credit: Roberto Fabbretti, Vital-IT
Network interoperability challenge

2017-2020
5 University hospitals
3 Research IT infrastructures
2 ETH platforms
10+ additional partners
(cohorts, regional hospitals, …)

Data transfers
• Channel encryption
• Project-specific encryption
Semantic challenge: Hospital data heterogeneity

Type of data: (low degree of data quality, high numbers, large heterogeneity)

- **Minimal patient dataset**: ELECTRONIC HEALTH RECORD FOR CLINICAL RESEARCH
- Quality identifiers (availability and quality of clinical, imaging and biobanking data)
- Biobanking material (tissue, liquid, images, functional data)
Data semantics

Core terms defined through SPHN Driver projects
Call 2017
• Oncology
• Sepsis (intensive care)
• Immune repertoire
• Ageing

SPHN semantic interoperability WG coordinates:
• Across hospitals
• Across domains

Core vocabularies
• SNOMED CT
• ICD-10, ICD-O
• LOINC
Hospitals data discoverability

- Data-warehouse
  - Common formats and standards (semantics)

- Hospitals and Institutions
  - USB Basel
  - HUG Geneva
  - Insel Bern
  - ETHZ Zürich

- Distributed federated query system

- Searching patients Meta-Data
  - Encoded data transferred after patient has given general consent
Workflow interoperability

• Supporting reproducible research
  • Repeatable data analysis (same data)
  • Reusable in different context (different data)

• Workflows executable everywhere
  • Work with local data
Virtualization technologies

Key for
- Dependencies encapsulation (long-term reproducibility)
- Portability

Source: Greg Kurtzer, Singularity Containers for Science
Container types

Docker

- Widely used
- Security issues (commonly unsupported in HPC environments)
- Federation and orchestration tools (Kubernetes, Swarm)
- Docker Hub repository
- Built-in support from cloud providers

Singularity

- More secure to run than Docker in multi-user environment
- Out of the box support for GPU’s and other hardware
- Can pull Docker images and convert to Singularity
- Singularity Hub repository
- Convenient default data mounts

Slide credit: Kevin Sayers, SPHN DCC
Workflow strategies

Workflow

• Samtools
• Bowtie2
• Cufflinks

One container with everything
• Pros:
  • One image
• Cons:
  • Potential incompatible dependencies
  • Large image size
  • Changing individual components tricky

External workflow that orchestrate containers
• Pros:
  • Containers can be mixed and matched
• Cons:
  • Workflow system must be supported
  • Reproducibility concerns

Slide credit: Kevin Sayers, SPHN DCC
Enabling edge computing

“Bringing the algorithm to the data”

2018

Securely transfer data to a BioMedIT node for analysis

2019

Provide single sign on (SSO) to access BioMedIT nodes where data is located

2020

Federation that abstracts the underlying BioMedIT infrastructure

Slide credit: Kevin Sayers, SPHN DCC
BioMedIT Project status

Regulations
- SPHN Ethical framework (2017)

IT infrastructure
- Infrastructure implementation ongoing on different sites (Zürich, Basel, Lausanne)
- Support to SPHN/PHRT projects ongoing (preparatory phase)
- Identity federation in development (Swiss EduID)

Workflow interoperability
- Proof-of-concept workflow interoperability completed (genomics)
- Workflow infrastructure (e.g. container repositories) and standards in development
- Workflow federation in development

Data interoperability
- Proof-of-concept node-to-node data transfers completed
- Technologies to link hospitals tested
- Key infrastructure, registries and automation in development
- Data catalogs, secondary data reuse in early development
Collaborations

Global Alliance for Genomics & Health
Collaborate. Innovate. Accelerate.

SPHN: a driver project for GA4GH (February 2019)

Elixir collaborations on selected technology developments
Outlook into 2021-2024

- Extend network to regional hospitals and private clinics
- Expand range of data collected (hospitals and platforms), consolidate semantics
- Integrate healthy citizen data
- Strengthen role of ELSIag and foster engagement of patients and citizens
- Establish PPPs (public-private partnerships) and international consortia
- Establish concepts for sustainable national center for PH research post 2024 (governance and technology)
More information

SPHN / BioMedIT

https://www.sphn.ch/
https://dcc.sib.swiss/

Documents
SPHN Glossary
SPHN Ethical Framework
SPHN Information Security Policy
SPHN Data Use Agreement Template
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Kevin Sayers (SIB, DCC)
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Martin Fox
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Sofia Georgakopoulou (Uni Basel)

BioMedIT network collaborators
University hospitals, represented by:
Christian Lovis (HUG, also chair semantics)
Nicolas Rosat (CHUV)
Alexander Leichtle (Insel)
Markus Obreiter (USB)
Roland Naef, Cornelia Kruschel-Weber (USZ)

All PIs and collaborators of SPHN projects
Questions?
Technical interoperability

“Cloud-of-services” federation

- Middleware-infrastructure agnostic (OpenStack, OpenNebula)
- Harmonization at the level of services

<table>
<thead>
<tr>
<th>Project management (registry)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identity and access control</td>
</tr>
<tr>
<td>Data access and data management</td>
</tr>
<tr>
<td>Workflow execution</td>
</tr>
</tbody>
</table>
The General Data Protection Regulation (GDPR) imposes new rules on organizations that offer goods and services to people in the European Union (EU), or that collect and analyze data tied to EU residents, no matter where they are located.

- **Enhanced** personal privacy rights
- **Increased** duty for protecting data
- **Mandatory** breach reporting
- **Significant** penalties for non-compliance
GDPR overview

Consent (5)  Notice (3)

Data subjects rights (16)  Data governance (5)

Privacy by design (2)  Data security (5)

Breach response (3)  Data transfer (4)

Also applies to medical and research data

Business Processes & User Controls

Applications & Processing Controls

IT Infrastructure Controls

Internal Audits

GDPR Regulation (261 pages)

Also applies to medical and research data
BioMedIT data transfer protocol

Two encryption layers:
- Transport encryption (SFTP)
- Project-level data encryption

Distinct asymmetric key pairs
SPHN/BioMedIT data flows

Controlled web access

Primary BioMedIT node

Project data mgmt (e.g. shared registry, cohort mgmt, ...)

Data analysis

Transfer BioMedIT node

Feasibility query interface
Data export procedure
Pseudonymized data only

Hospital IT

Primary repository (clinical system with identifiable patient data)

Hospital 1

Reidentification framework

Raw data
Semantic mappings
Deidentification

Clinical research data mgmt system

Hospital 2

Software, API, process
Storage system

Primary data (clinical, raw)
Deidentified research data
Project research clinical data
Data analysis (data, algorithms)

Generic description of data flows in SPHN
Container issues

TECHNOLOGY

Hackers mined $90,000 worth of Monero with a simple Docker Hub trick

- Pulling random containers can result in pulling something malicious
- Public repositories often lack vulnerability scanning
- Even if there is no malicious intent, no guarantee container functions as expected

Kromtech finds malicious code hiding in enterprise upstart's repositories of software

By Thomas Claburn in San Francisco 14 Jun 2018 at 07:01 3

Slide credit: Kevin Sayers, SPHN DCC
Addressing the concerns

• Host a private SPHN repository
  • Local Gitlab can be used to build the images

• Utilize tools that scan repositories for image vulnerabilities

• Manual review of Dockerfile or Singularity files

• Container signing from developers

Slide credit: Kevin Sayers, SPHN DCC
EnhanceR Singularity tests

- Representative bioinformatics workflow in a Singularity container
- Demonstrated functionality in BioMedIT nodes
- Demonstrated analysis reproducibility
- White paper available

Collaboration: ETHZ, Uni Basel, Uni Zürich, Uni Bern, SIB
## EnhanceR Singularity test matrix

<table>
<thead>
<tr>
<th>Milestone</th>
<th>UniBe</th>
<th>sciCORE UniBas</th>
<th>S3IT UZH</th>
<th>VitalHT / SIB</th>
<th>SIS ETHZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singularity installed</td>
<td>☑</td>
<td>☑</td>
<td>v2.3-dist</td>
<td>(v2.2.1 and v2.3)</td>
<td>(v2.3)</td>
</tr>
<tr>
<td>&quot;hello world&quot; pipeline building</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>(from Dockerfile)</td>
<td>(from Dockerfile)</td>
</tr>
<tr>
<td>&quot;hello world&quot; pipeline running</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>(from Singularity image)</td>
<td>☑</td>
</tr>
<tr>
<td>sciCORE pipeline1 &amp; pipeline2 building</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>(from Dockerfile)</td>
<td>(from Dockerfile)</td>
</tr>
<tr>
<td>sciCORE pipeline1 &amp; pipeline2 running</td>
<td>☑</td>
<td>☑</td>
<td>-</td>
<td>(only pipeline 2, pipeline1 is too big to run in home directory (quota issue))</td>
<td>☑</td>
</tr>
<tr>
<td>Docker -&gt; Singularity conversion via Dockerfile</td>
<td>☑ (with &quot;hello world&quot; pipeline)</td>
<td>☑</td>
<td>☑</td>
<td>(with SIB-publications pipeline)</td>
<td>☑</td>
</tr>
<tr>
<td>Docker -&gt; Singularity conversion via Dockerhub</td>
<td>☑ (with &quot;whalesay&quot; container)</td>
<td>☑ (with custom Dockerfiles for pipeline1 &amp; pipeline2)</td>
<td>☑</td>
<td>pdodrka/lab/fmr/prep</td>
<td>(with &quot;whalesay&quot; container and custom Dockerfiles)</td>
</tr>
<tr>
<td>Docker -&gt; Singularity conversion via &quot;private&quot; Gitlab</td>
<td>☑ (with &quot;hello world&quot; pipeline, no auth)</td>
<td>☑</td>
<td>-</td>
<td>not planned</td>
<td>(from private GitHub)</td>
</tr>
<tr>
<td>Runner script</td>
<td>☑ (pipeline.py)</td>
<td>☑ (pipeline.py from UniBe)</td>
<td>-</td>
<td>not planned</td>
<td>☑</td>
</tr>
<tr>
<td>Guideline document</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>all details are in: README.md and in final report</td>
<td>☑</td>
</tr>
</tbody>
</table>