PRIVGEN

Privacy-preserving sharing and processing of genetic data

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Motivation

Genetic data and applications

Genetic data applications

- **Patient Care** (Diagnosis; Therapeutic choice).
- **Research** (Genome-Wide Association Studies)
  - Needs for international sharing of genetic data to increase sample sizes and achieve sufficient power
- **Legal and forensics** (criminal forensics, contested paternity…)
- **Direct-to-Consumer Services** (genealogy, Disease susceptibility risks …)

International/national projects for genomic data sharing

- **Global Alliance for Genomics & Health** (beacons)
- **Disease specific databases** (e.g. Sickkids)
- **Plan France Médecine Génomique 2025**

Motivation

Security and privacy of genetic data

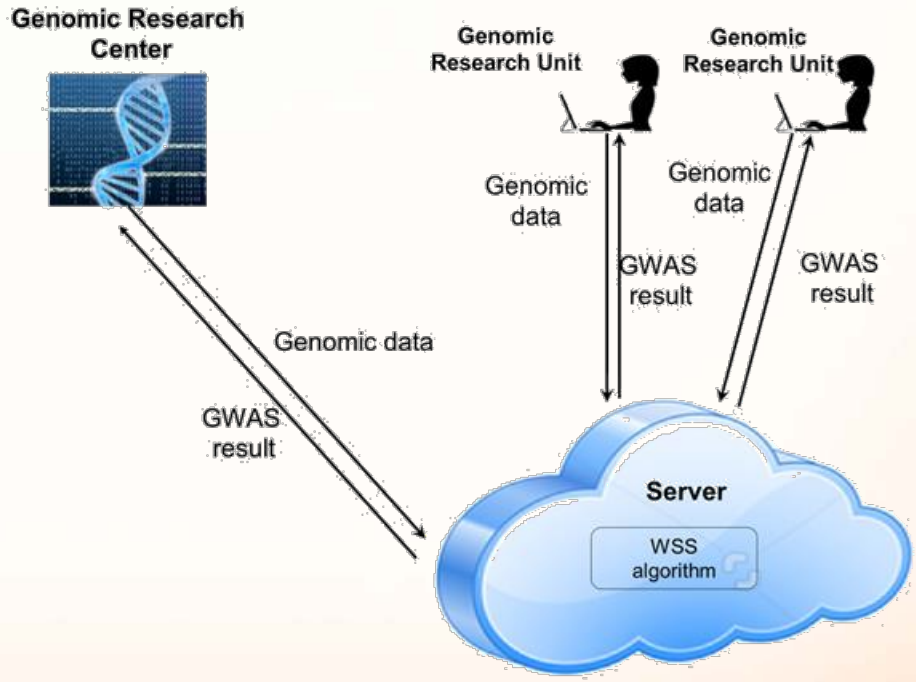
Genetic data are extremely sensitive data –

- They can allow identification and are partly shared with relatives, they can inform about health/behavior of the individual but also of his/her relatives.
- Sensitive genomic characteristics are crucial for most applications
- They have their own deontological and legislative frameworks, and beyond common medical regulations:
  - **International Declaration on Human Genetic Data, UNESCO, 2003** - Article 14§(a) - Countries should endeavor to protect the privacy of individuals and the confidentiality of genetic data …
  - **GDPR** - Article 4- defines genetic data as personal data - Article 9- genetic data processing treatments must be carried out in agreement with data owner and respecting his privacy and data's confidentiality

Motivation

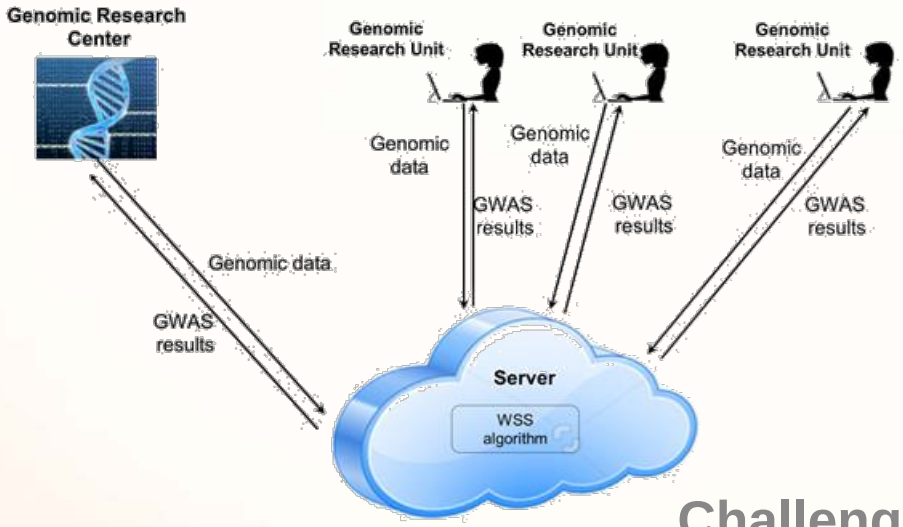
Genome-Wide Association Studies threats (examples)

- Owners loose the control on their data:
  - Confidentiality concerns
  - Traceability, intellectual/scientific ownership protection
    - Illegal redistribution / re-routing of the information (information leaks)
  - Integrity concerns
    - Falsification of data to interfere with statistical studies
    - Integrity of outsourced computations



- Privacy concerns
  - Identification of the presence of an individual in an anonymized public database
  - Reconstruction of individual sample without a priori knowledge
  - Identification of the GWAS objective (interest for a specific gene)
- …

Research activities of PRIVGEN



Challenge 1 - Mechanisms for a continuous digital content protection

***Objective**: Merge different security mechanisms into one digital content protection tool for continuous and multipurpose security objectives*

Challenge 2 - Composition of security and privacy-protection mechanisms

***Objective**: a compositional development approach for secure and privacy-preserving distributed genetic application*

Challenge 3 - Distributed processing and sharing of genetic data

***Objective**: a platform to perform association testing against a reference panel of healthy individuals that are compared against patients*

Ch1 - Mechanisms for a continuous digital content protection

Secure externalized Genome-Wide Association Studies

- Identification of the constraints and limits of actual secure GWAS:
  - Mainly secured with differential privacy, homomorphic encryption, secure multiparty computations …
  - Do not consider sharing of patient data but of aggregated data
  - Are not compliant with iterative algorithms for large data sets
- Proposition of different secure GWAS algorithms based on externalized data
  - Secure externalized $\chi 2$ test and collapsing test
  - 1rst secure neural network able to learn on encrypted data
    - Input, output and trained parameter are all encrypted
    - No approximation of the neuron activation function
    - No interactions with the user during the training phase
    - Loss of accuracy due to the need to work with integer values
  - A secure framework for iterative algorithms based on a original proxy strategy along with cryptographic hashing and pretty good privacy (PGP).

D. Niyitegeka et al. ***Secure Collapsing Method Based on Fully Homomorphic Encryption****, Studies in Health, Submitted.*
R. Bellafqira et al., ***Secure Multilayer Perceptron Based on Homomorphic Encryption****. Digital Forensics and Watermarking, IWDW 2018, LNCS Vol. 11378, pp. 322-336, 2019.*

Ch1 - Mechanisms for a continuous digital content protection

Crypto-watermarking tools for outsourced genetic data

- First watermarking modulations for genetic data compliant with VCF and WSS files (GWAS file formats)
  - DNA Watermarking methods have been proposed for steganography purposes or copyright protection of synthetic or living cell DNA
  - Solutions we proposed are robust or reversible and do not interfere with GWAS algorithms

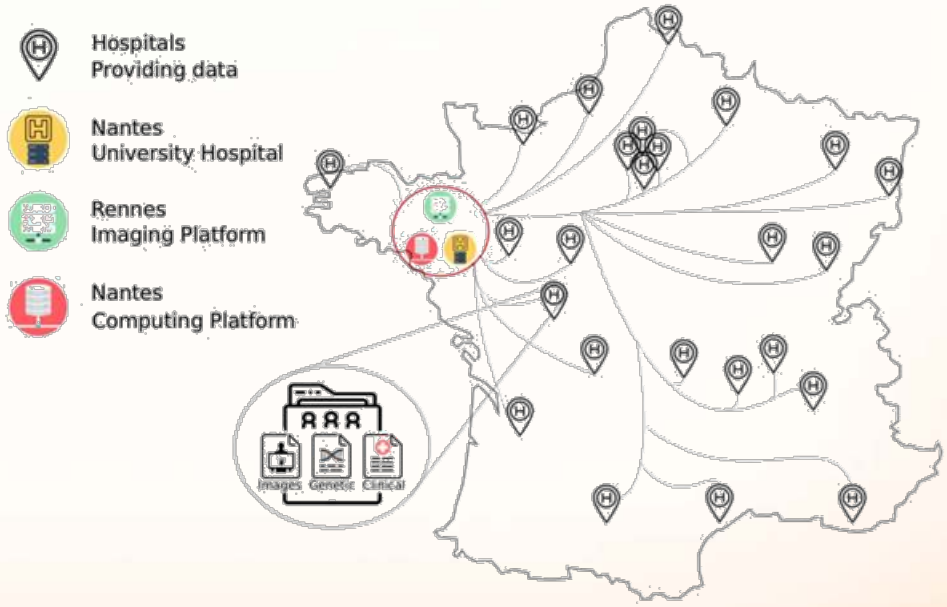
- Proposition of a dynamic HE crypto-watermarking system. Allows the cloud to protect in terms of integrity HE encrypted data and identify modified data.
  - Dynamic - protected database can be updated by the data-owners, the cloud does not have to re-watermark the whole data base.
  - Tampered data (modified, deleted and/or added) can be identified

R. Bellafqira et al., ***Robust watermarking for genetic data traceability in externalized GWAS frameworks****. IEEE/ACM transactions on computational biology and bioinformatics, submitted.*
G. Coatrieux et al., ***Lossless watermarking for genomic data****. IEEE Transactions on Information Forensics and Security, submitted*
D. Niyitegeka et al. ***Dynamic Watermarking-Based Integrity Protection of Homomorphically Encrypted Databases****. Digital Forensics and Watermarking, IWDW 2018, LNCS Vol. 11378, pp. 151-166, 2019.*
J.F. Contreras et al., ***Protection of Relational Databases by Means of Watermarking: Recent Advances and Challenges****. Chapter, book Advances in Security in Computing and Communications, , pp.101-121 , 2017*

Ch 2 - Composition of security and privacy-protection mechanisms

Motivation: Distributed analyses

- General trend: geographically distributed data and computation
- I-CAN project (ex.): 34 French hospitals (+ future foreign cooperations)



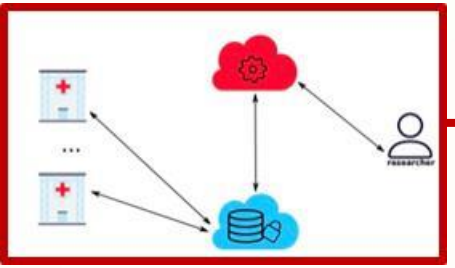
- Future:
  - Large distribution of massive data and computations
  - Different admin/legal domains

*Garzon, Südholt, Benavides: "**An overview of distributed biomedical analyses and data analytics tools"**, to be submitted in January 2020.*

Ch 2 - Composition of security and privacy-protection mechanisms

Development approach

1. Requirements analysis



2. Architecture selection

Set of predefined architectures

→ **Associated scalability, security/ privacy properties (watermarking, encry., …)**

3. Data/workflow definition

Security/privacy operators (watermarking, encry., …)

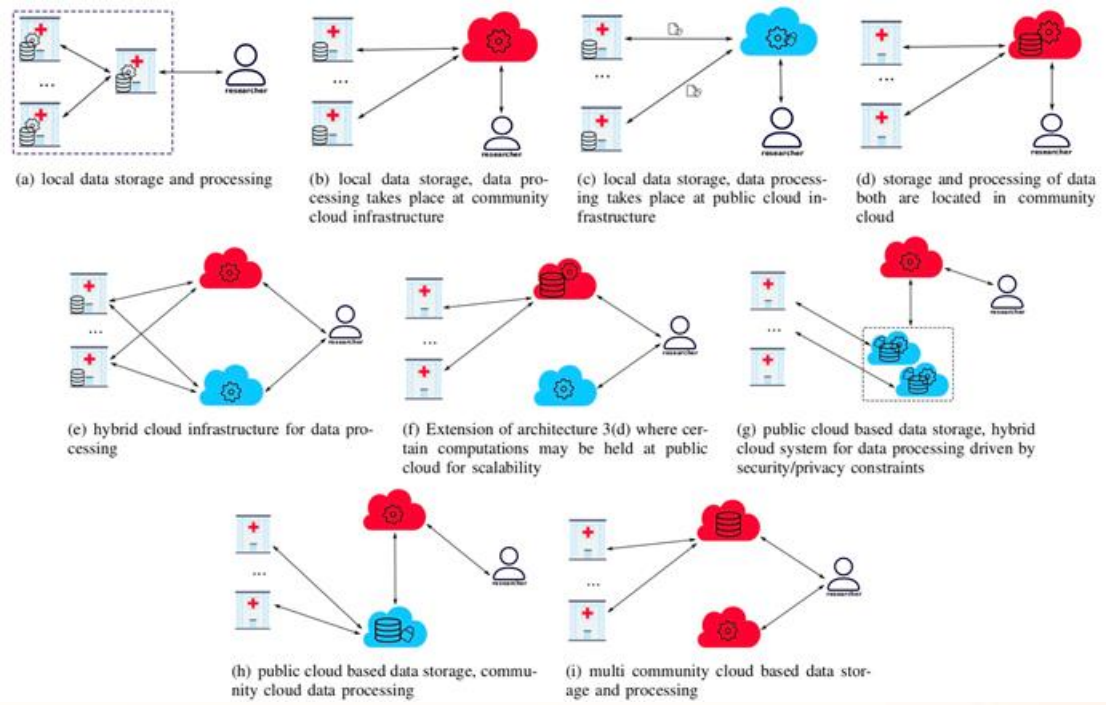
→ **Enforcement of security/ privacy props (watermarking, encry., …)**

4. Analysis deployment & execution

Java framework, Cloud deployment

Ch 2 - Composition of security and privacy-protection mechanisms

- **Architecture level** : set of architectures for biomedical analyses derived from existing analysis



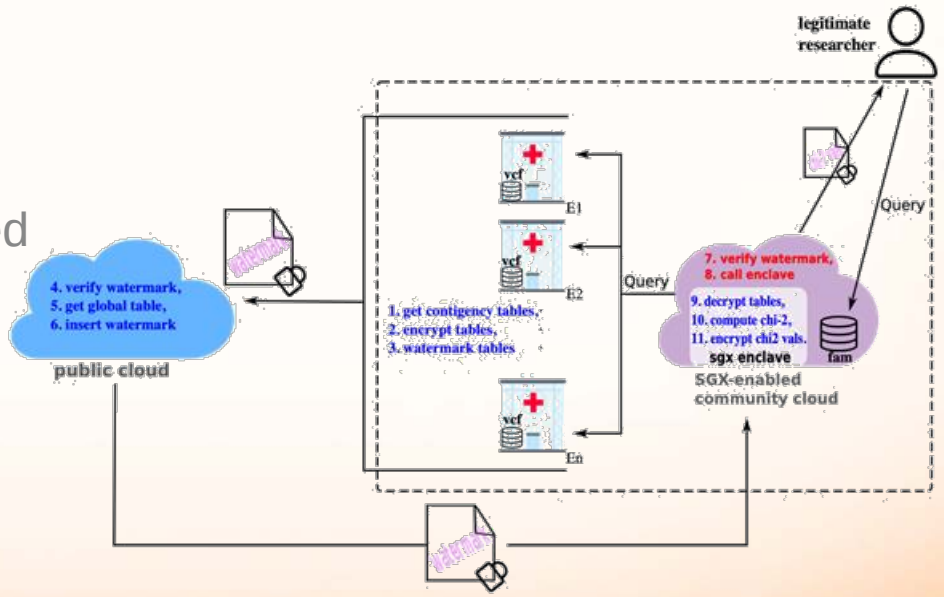
- **Composition support: Programming-level operators**
  - Operators for homomorphic/ a/symmetric/ attribute-based encryption, fragmentation, third-party/localized computations, watermarking
  - Definition as Idris functions
    - Composition through higher-order functions
    - Type-based correctness support
  - Second definition as java framework

F.-z. Boujdad, A. Gaignard, M. Südholt, et al: "**On distributed collaboration for biomedical analyses**"; CCGrid-Life, May 2019.

F.-z. Boujdad, M. Südholt: "**Constructive Privacy for Shared Genetic Data**"; 8th Int. Conf. on Cloud Computing and Services Science (CLOSER 2018); ScitePress; Madeira, March 2018.

Challenge 3 - two platforms for distributed processing and sharing of genetic data

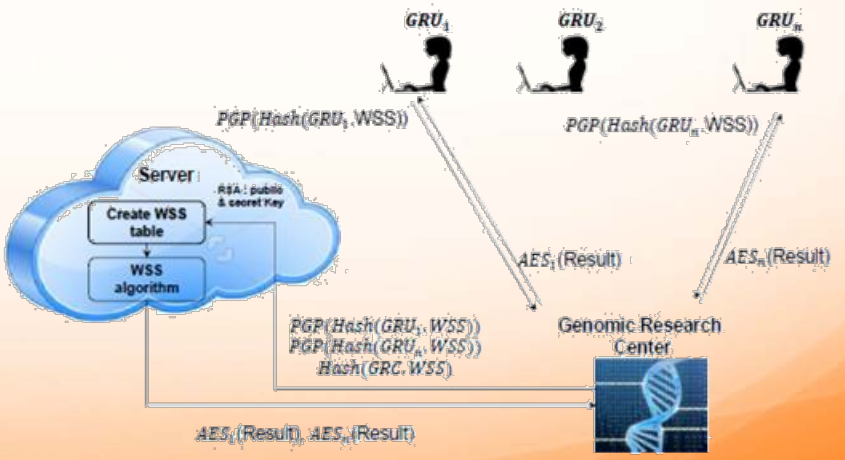
- **Platform 1 :** PrivGen cloud platform
  - PrivGen cloud platform
    - Java implementation + deployment/execution scripts
  - Deployment on Grid 5000
    - Large-scale CS grid/cluster-based infrastructure
  - Direct transfert to biomedical infrastructures (IFB, Bird)
  - Hybrid cloud, use of SGX



*Boujdad, Coatrieux, Genin, Niyitegeka, Südholt et al.: "**A Hybrid Cloud Architecture for Performing Privacy-Preserving Genome-Wide Association Studies**", to be submitted end of Nov. 2019.*

Challenge 3 - two platforms for distributed processing and sharing of genetic data

- **Platform 2 :** PRIVAS - A tool to perform Privacy-Preserving Association Studies
  - A complete secured GWAS framework – allows several research units to share their data in the cloud without breaching privacy and to conduct “iterative” GWAS without computation complexity overhead
  - Framework implemented with Weighted-Sum Statistic (WSS) algorithm as illustration but generic to all GWAS algorithms similar to WSS (see challenge 1)
  - Proof Of Concept Platform deployed on Datarmor supercomputer of IFREMER
  - POC to be made available to the international community.



R. Bellafqira et al.. ***Privacy-preserving genome-wide association study for rare mutations - a secure framework for externalized statistical analysis***. *IEEE Access, submitted, 2020.*

T.E. Ludwig, et al., ***PrivAS: a tool to perform Privacy-Preserving Association Studies***. *Jobim, 2019.*