

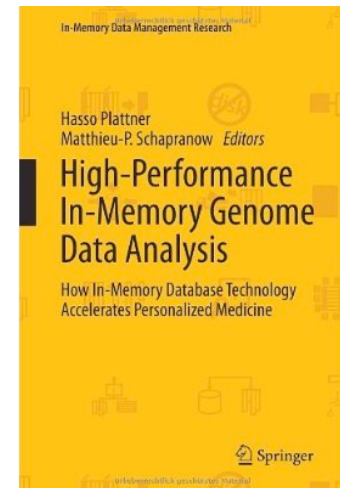


How Real-time Analysis turns Big Medical Data into Precision Medicine?

Dr. Matthieu-P. Schapranow
GLOBAL HEALTH, Rome, Italy
August 27, 2014

Important things first: Where to find additional information?

- Online: Visit <http://we.analyzegenomes.com> for latest research results, tools, and news
- Offline: Read more about it, e.g. High-Performance In-Memory Genome Data Analysis: How In-Memory Database Technology Accelerates Personalized Medicine, In-Memory Data Management Research, Springer, ISBN: 978-3-319-03034-0, 2014
- In Person: Join us for the **International Workshop on Big Data in Bioinformatics and Healthcare Informatics (BBH14)** in Washington D.C. on Oct 27, 2014 (<http://bbh14.analyzegenomes.com>)



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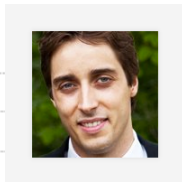
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Who you are dealing with?

158,952 km

This is the number of kilometres that you have already clocked up on your travels.

Flights around earth	3.966
Flights to moon	0.414
Shortest flight	FRA-AMS (367 km)
Longest flight	MUC-SFO (9,437 km)
Northernmost airport	Dublin (DUB)
Southernmost airport	Miami International, FL (MIA)




Dr.-Ing. Matthieu Schapranow
 Program Manager E-Health at Hasso Plattner Institute
 Berlin Area, Germany | Research

Previous Education Hasso Plattner Institute, SAP, Travel IQ
 Universität Potsdam

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441 connections

- Software Engineer by training (B.Sc., M.Sc., PhD)
- 2006-2014 with 
- Since 2007 at Chair of Prof. Hasso Plattner, HPI
- Since 2009 focusing on Life Sciences / E-Health

matthieu schapranow

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MatthieuSchapranow - Enterprise Platform and Integration ...
<https://epic.hpi.uni-potsdam.de/Home/MatthieuSchapranow>
 Dr. Matthieu-P. Schapranow received a PhD in Software Engineering from University of Potsdam in Germany in 2012. He also received BSc and MSc degrees in ...

Matthieu Schapranow presentations | SlideShare
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 Alle Präsentationen von Matthieu Schapranow ansehen.

Dr. Matthieu Schapranow, HPI - Speaker - CeBIT 2014
www.cebit.de/speaker/dr.-matthieu-schapranow-hpi/995
 Dr. Matthieu-P. Schapranow received a PhD in Software Engineering from University of Potsdam in Germany in 2012. He also received BSc and MSc degrees in ...

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Matthieu-P. Schapranow - ResearchGate
www.researchgate.net/profile/Matthieu-P_Schapranow
 Researcher » Matthieu-P. Schapranow, Hasso Plattner Institute, Research Group Enterprise Platform and Integration Concepts (EPIC), Germany, Databases, ...

[PDF] Real-time Analysis of Next Generation Sequencing Data
www.worldhealthsummit.org/.../Meinel_Christoph_Presentation_World...
 Real-time Analysis of Next Generation Sequencing Data. World Health Summit. Oct 24, 2012. Prof. Dr. Christoph Meinel. Matthieu Schapranow. Hasso Plattner ...

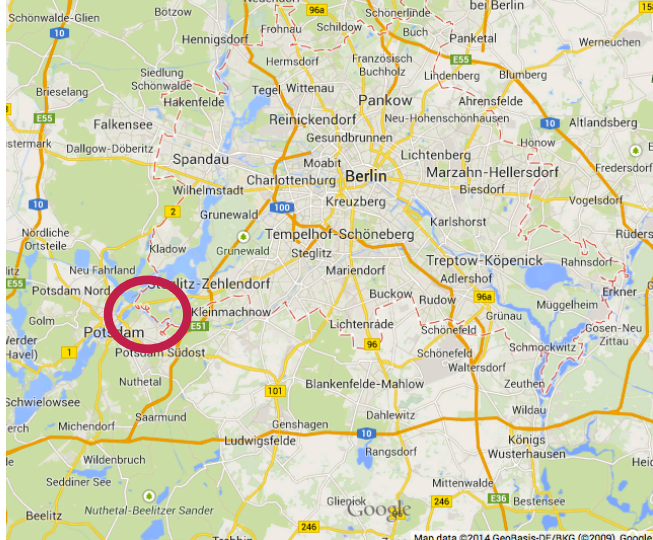
Dr. Matthieu-P. Schapranow - Google Scholar Citations
scholar.google.de/citations?user=0TDS0i0AAAAJ&hl=en
 Principal Investigator of In-Memory Technology for Life Sciences, Hasso Plattner Institute, Potsdam - hpi.uni-potsdam.de
 Security aspects in vulnerable RFID-aided supply chains. MP Schapranow, J Müller, A Zeier, H Plattner. RFID Systems and Technologies (RFID SysTech), 2009 ...



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Where do I work? Hasso Plattner Institute, Potsdam, Germany



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Hasso Plattner Institute Key Facts



- Founded as a public-private partnership in 1998 in Potsdam near Berlin, Germany
- Institute belongs to the University of Potsdam
- Ranked 1st in CHE since 2009
- 500 B.Sc. and M.Sc. students
- 10 professors, 150 PhD students

- Course of study: IT Systems Engineering



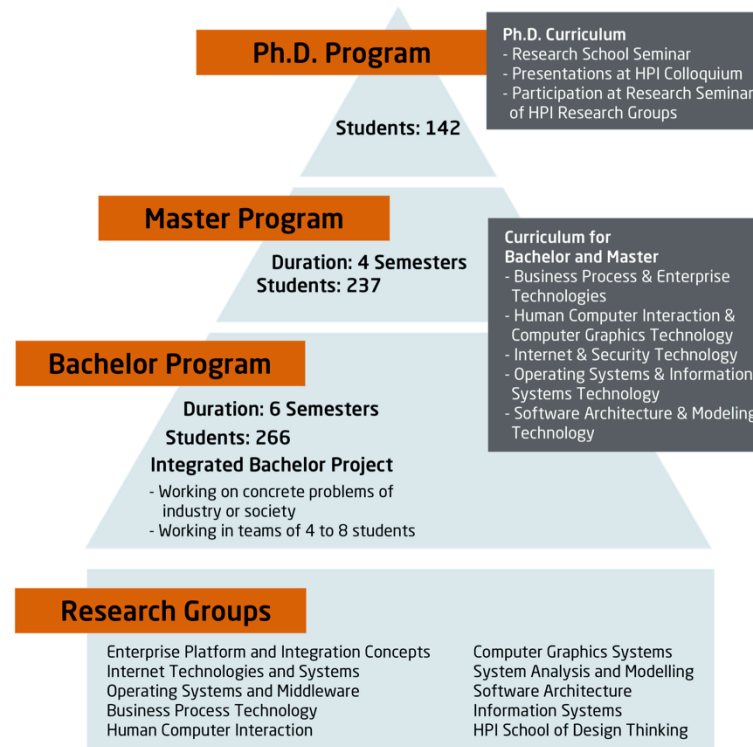
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Hasso Plattner Institute Programs



- Full university curriculum
- Bachelor (6 semesters)
- Master (4 semesters)
- Orthogonal Activities:
 - E-Health Consortium
 - School of Design Thinking
 - Research School



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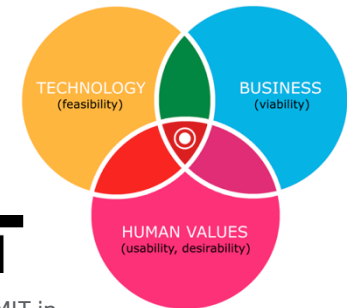
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Hasso Plattner Institute Enterprise Platform and Integration Concepts Group



Chair of Prof. Dr. h.c. Hasso Plattner

- Research focuses on the technical aspects of enterprise software and design of complex applications
 - In-Memory Data Management for Enterprise Applications
 - Enterprise Application Programming Model
 - **Scientific Data Management**
 - Human-Centered Software Design and Engineering
- Industry cooperations, e.g. SAP, Siemens, Audi, and EADS
- Research cooperations, e.g. Stanford, MIT, and Berkeley



Partner of Stanford
Center for Design
Research



Partner of MIT in
Supply Chain
Innovation and
CSAIL



Partner at
UC Berkeley
RAD / AMP Lab



Partner of SAP
AG

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The Setting Actors in Oncology

■ Patients



- Individual anamnesis, family history, and background
- Require fast access to individualized therapy

■ Clinicians



- Identify root and extent of disease using laboratory tests
- Evaluate therapy alternatives, adapt existing therapy

■ Researchers



- Conduct laboratory work, e.g. analyze patient samples
- Create new research findings and come-up with treatment alternatives

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Our Motivation

Make Precision Medicine Come Routine in Real Life



- Motivation: Can we enable **patients** to:
 - Understand and monitor their diseases to document the impact on their lives,
 - Receive latest information about their (chronic) diseases,
 - Cooperatively exchange with physicians and patients to improve quality of living

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Our Motivation

Make Precision Medicine Come Routine in Real Life (cont'd)



- Motivation: Can we enable **clinicians** to take their therapy decisions:
 - Incorporating all available specifics about each individual patient,
 - Referencing latest lab results and worldwide medical knowledge, and
 - Interactively during their ward round?

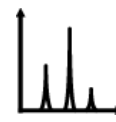
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IT Challenge: How to Integrate Distributed and Heterogeneous Sources of Big Medical Data



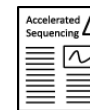
Human genome/biological data
600GB per full genome
15PB+ in databases of leading institutes



Human proteome
160M data points (2.4GB) per sample
>3TB raw proteome data in ProteomicsDB



Hospital information systems
Often more than 50GB



PubMed database
>23M articles



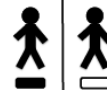
Cancer patient records
>160k records at NCT



Medical sensor data
Scan of a single organ in 1s
creates 10GB of raw data



Prescription data
1.5B records from 10,000 doctors and
10M Patients (100 GB)



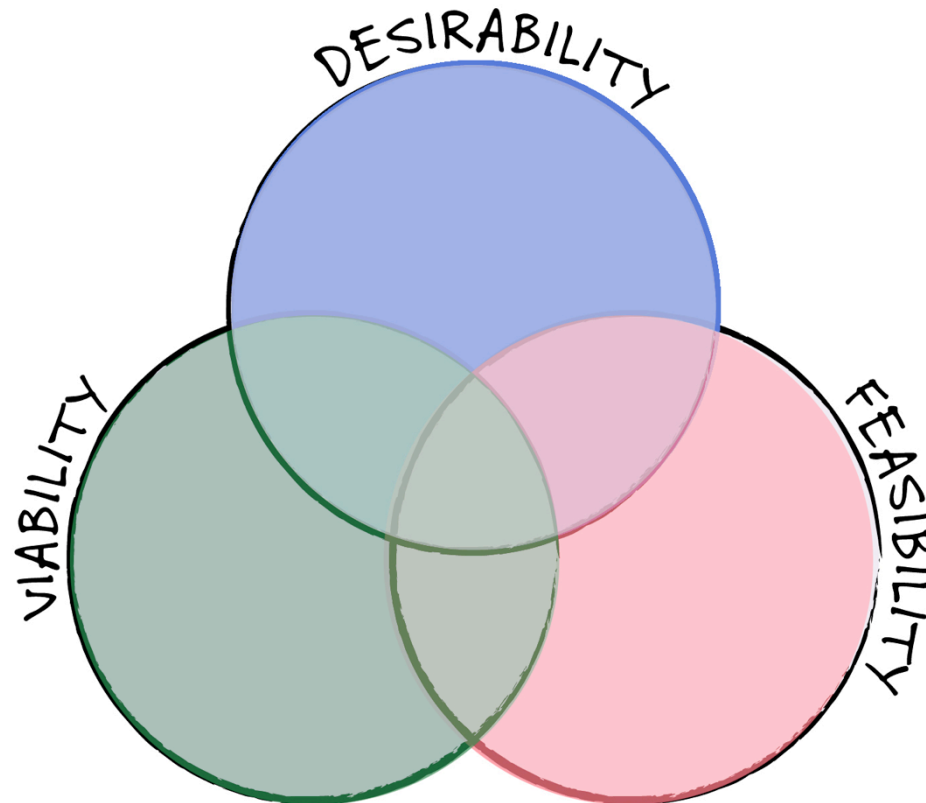
Clinical trials
Currently more than 30k
recruiting on ClinicalTrials.gov

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Our Methodology

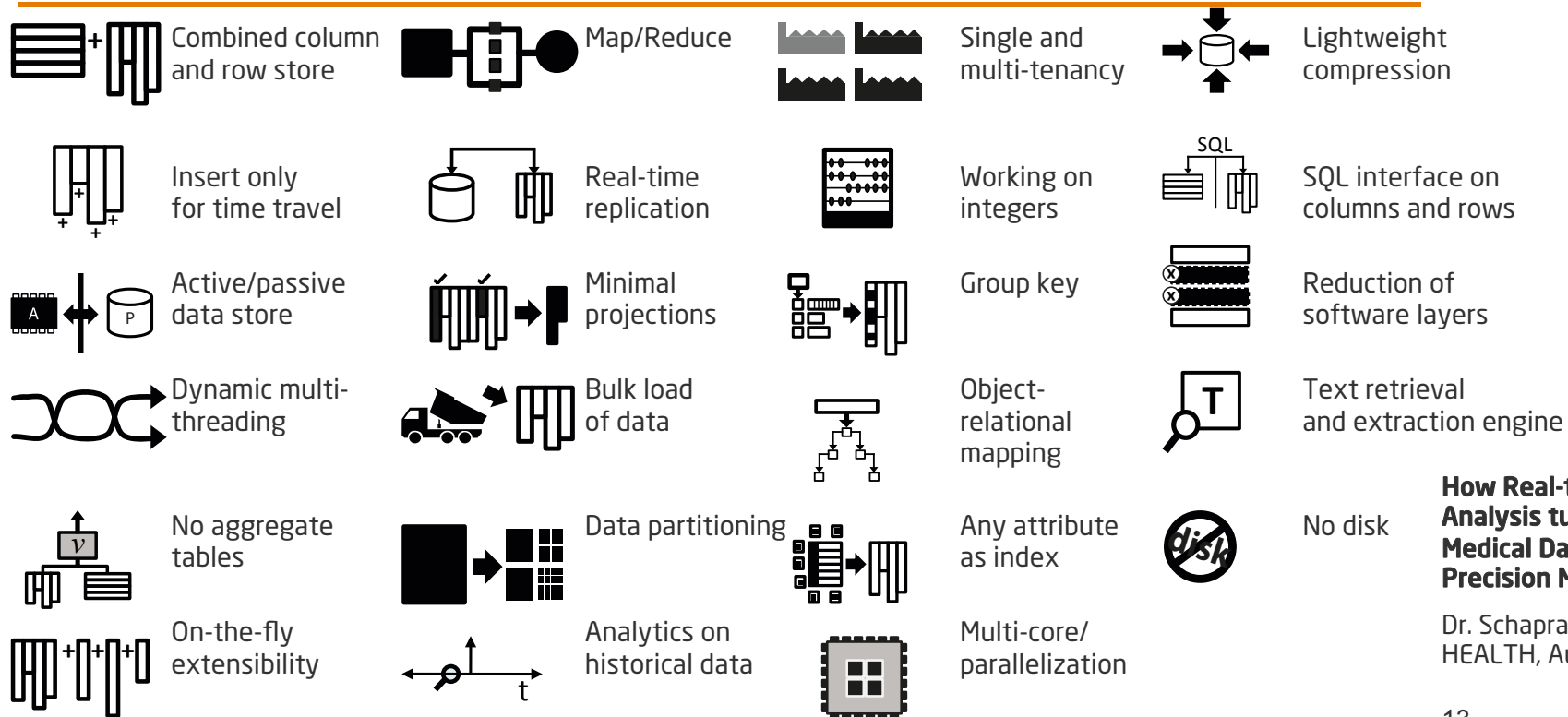
Design Thinking Methodology



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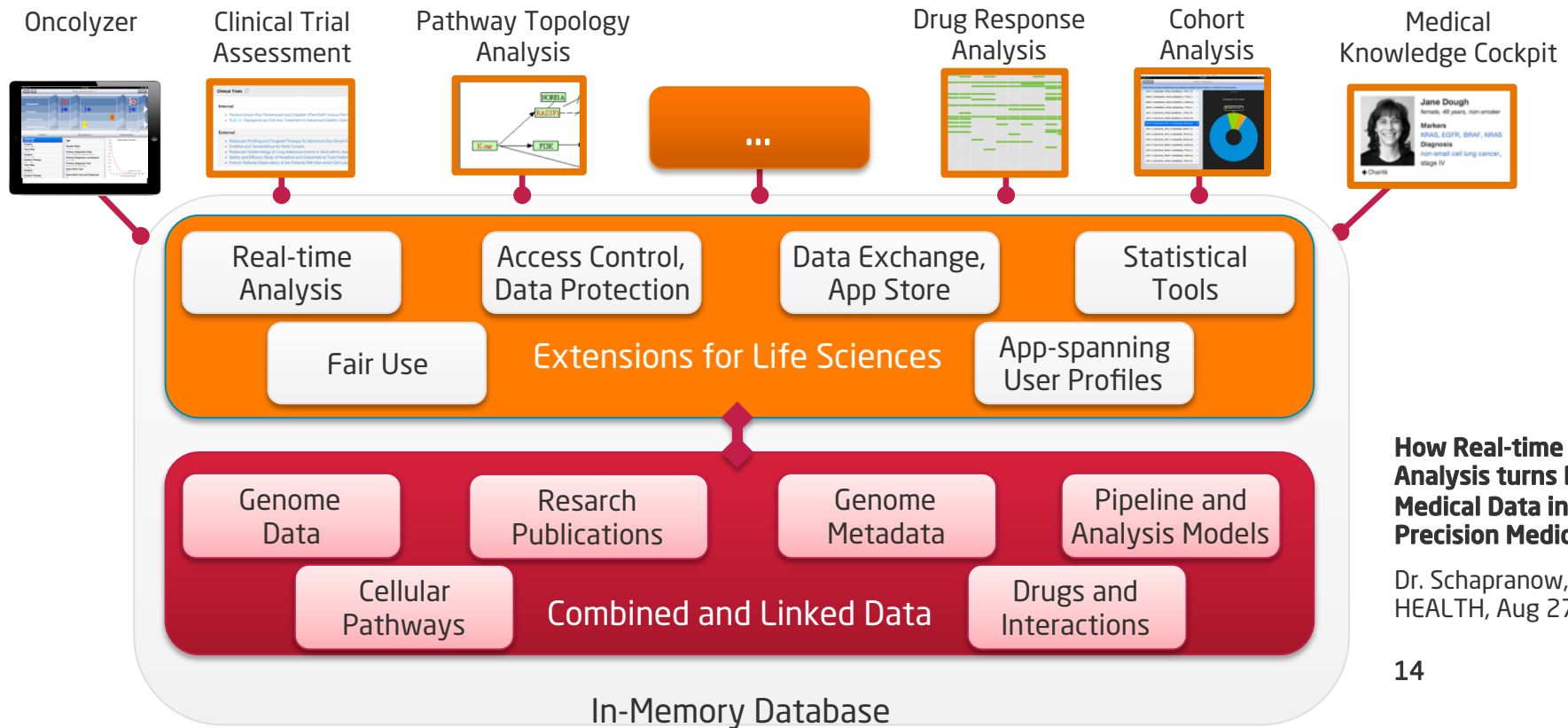
Our Technology: In-Memory Database Technology Enabling Real-time Data Analysis



How Real-time Analysis turns Big Medical Data into Precision Medicine?

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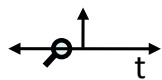
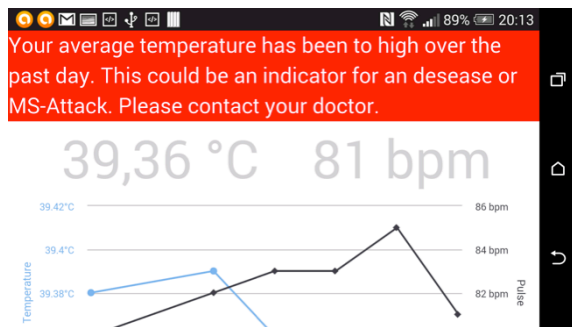
Our Approach: Analyze Genomes - A Cloud Platform Enabling Real-time Analysis of Big Medical Data



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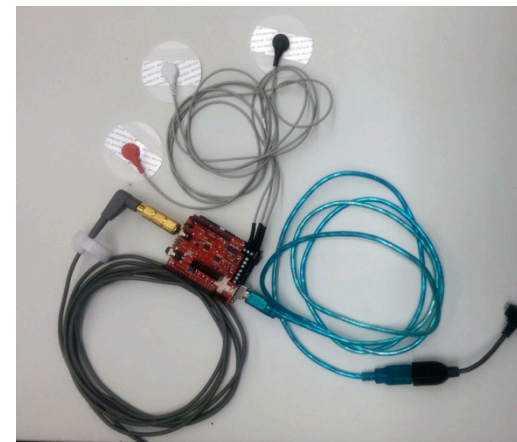
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Real-time Processing of Event Data from Medical Sensors



Comparison of waveform data with history of similar patients

- Processing of sensor data, e.g. from Intensive Care Units (ICUs) or wearable sensor devices (quantify self)
- Multi-modal real-time analysis to detect indicators for severe events, such as heart attacks or strokes
- Incorporates machine-learning algorithms to detect severe events and to inform clinical personnel in time
- Successfully tested with 100 Hz event rate, i.e. sufficient for ICU use



Harvard-MIT Health Sciences & Technology



Future SOC Lab

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Drug Safety

Statistical Analysis of Drug Side Effects Data

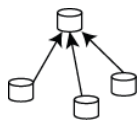
Side Effects ARM

Min Support: 0.002, Min Confidence: 0.002, Max Length Prerule: 2, Max Length Postrule: 2

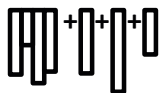
Results for Side Effects ARM

Drugs	Side Effects	Support	Confidence	LIFT
DARVON + Darvocet	Nervous system disorder	0.003784	1.00	158.24
DARVON + PROPOXYPHENE NAPHSYLATE AND ACETAMINOPHEN	Nervous system disorder	0.004371	0.88	139.66
Darvocet + PROPOXYPHENE NAPHSYLATE AND ACETAMINOPHEN	Nervous system disorder	0.003784	1.00	158.24
DARVON + Darvocet	Movement disorder	0.003784	1.00	167.81
DARVON + PROPOXYPHENE NAPHSYLATE AND ACETAMINOPHEN	Movement disorder	0.004371	0.88	146.11
DARVON + Darvocet	Cardiovascular disorder	0.003784	1.00	158.64
DARVON + PROPOXYPHENE NAPHSYLATE AND ACETAMINOPHEN	Cardiovascular disorder	0.004366	0.88	139.85
Darvocet + PROPOXYPHENE NAPHSYLATE AND ACETAMINOPHEN	Movement disorder	0.003784	1.00	167.81
Darvocet + PROPOXYPHENE NAPHSYLATE AND ACETAMINOPHEN	Cardiovascular disorder	0.003784	1.00	158.64
DARVON + Darvocet	Nervous system disorder + Movement disorder	0.003784	1.00	218.04

- Combines confirmed side effect data from different data sources
- Interactive statistical analysis, e.g. apriori rules, to discover still unknown interactions
- Integrates personal prescription data and directly report side effects
- Work together with your doctor to prevent interaction with already prescribed drugs



Unified access to international side effect data

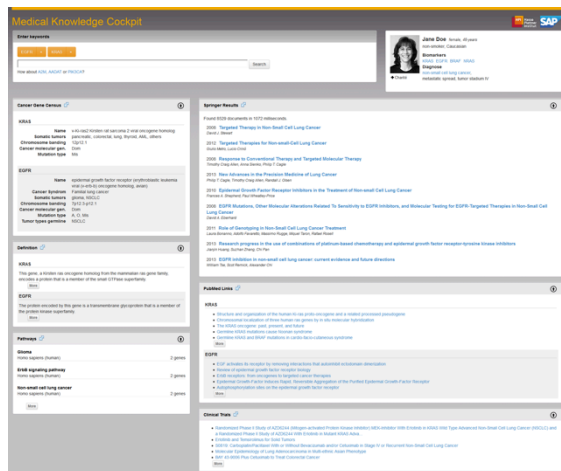


On-the-fly extension of database schema to add side effect databases

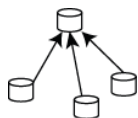
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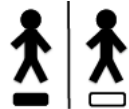
Medical Knowledge Cockpit



- Search for affected genes in distributed and heterogeneous data sources
- Immediate exploration of relevant information, such as
 - Gene descriptions,
 - Molecular impact and related pathways,
 - Scientific publications, and
 - Suitable clinical trials.



Unified access to structured and un-structured data sources



Automatic clinical trial matching build on text analysis features

- No manual searching for hours or days: In-memory technology translates searching into interactive finding!

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Medical Knowledge Cockpit Publications



The screenshot displays two side-by-side panels from the Medical Knowledge Cockpit. The left panel, titled 'Cancer Gene Census', shows details for the KRAS gene, including somatic tumors (pancreatic, colorectal, lung, thyroid, AML, others), name (v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog), chromosome banding (12p12.1), cancer molecular gen. (Dom), mutation type (Mis), and a list of associated genes like EGFR and BRAF. The right panel, titled 'Springer Results', shows a list of 223 relevant documents, including titles like 'Identification of driver mutations in lung cancer: first step in personalized cancer' and 'Adenocarcinoma', along with author names and years.

- In-place preview of relevant data, such as publications and publication meta data
- Incorporating individual filter settings, e.g. additional search terms

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Medical Knowledge Cockpit Latest Clinical Trials



The screenshot displays a 'Medical Knowledge Cockpit' interface. On the left, a 'Pathways' sidebar lists various cancer-related pathways with their associated species and gene counts:

Pathway	Species	Gene Count
Non-small cell lung cancer	Homo sapiens (human)	5 genes
Prostate cancer	Homo sapiens (human)	5 genes
ErbB signaling pathway	Homo sapiens (human)	5 genes
Endometrial cancer	Homo sapiens (human)	5 genes
Pathways in cancer	Homo sapiens (human)	5 genes
Bladder cancer	Homo sapiens (human)	5 genes
Glioma	Homo sapiens (human)	4 genes
Melanoma	Homo sapiens (human)	4 genes

The main 'Clinical Trials' panel is divided into 'Internal' and 'External' sections. The 'Internal' section lists one trial: 'FLO +/- Pazopanib as First-line Treatment in Advanced Gastric Cancer (PaFLO)'. The 'External' section, which includes a 'Less' button, lists multiple trials related to lung cancer, such as 'Molecular Profiling and Targeted Therapy for Advanced Non-Small Cell Lung Cancer, Small Cell Lung Cancer, and Thymic Malignancies' and 'Randomized Phase II Study of AZD6244 (Mitogen-activated Protein Kinase Inhibitor) MEK-Inhibitor With Erlotinib in KRAS Wild Type Advanced Non-Small Cell Lung Cancer (NSCLC) and a Randomized Phase II Study of AZD6244 With Erlotinib in Mutant KRAS Adva...'. Other trials listed include 'Lung Cancer in Women Treated With Anti-oestrogens and Inhibitors of EGFR (LADIE)', 'Ad/HER2/Neu Dendritic Cell Cancer Vaccine Testing', 'S0819: Carboplatin/Paclitaxel With or Without Bevacizumab and/or Cetuximab in Stage IV or Recurrent Non-Small Cell Lung Cancer', 'Single Nucleotide Polymorphism(SNP)Study', 'PF-00299804 in Treating Patients With Stage IIIB or Stage IV Non-Small Cell Lung Cancer That Has Not Responded to Standard Therapy for Advanced or Metastatic Cancer', and 'Erlotinib Plus Tivantinib (ARQ 197) Versus Single Agent Chemotherapy in Locally Advanced or Metastatic Non-Small Cell Lung Cancer'.

- Personalized clinical trials, e.g. by incorporating patient specifics
- Classification of internal/external trials based on treating institute

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Medical Knowledge Seamless Integration of Patient Specifics



A screenshot of the "Medical Knowledge Cockpit" web interface. The interface has a dark grey header with the title "Medical Knowledge Cockpit" in orange. On the right side of the header are logos for HPI Hasso Plattner Institut and SAP. Below the header is a search bar with the placeholder text "Enter search terms" and a "Search" button. Below the search bar, there is a suggestion: "How about A2M, AADAT or PIK3CA?". Below that, there are several filter buttons: "NRAS" (orange), "BRAF" (orange), "EGFR" (orange), "KRAS" (orange), and "non-small cell lung cancer" (grey). Each button has a small "x" icon to its right. The interface also displays a patient profile for "Jane Dough", a female, 48 years old, non-smoker. Her markers are listed as "KRAS, EGFR, BRAF, NRAS" and her diagnosis is "non-small cell lung cancer, stage IV". There is a small "Charité" logo below her profile picture.

- Google-like user interface for searching data
- Seamless integration of individual EMR data
- Search various sources for biomarkers, literature, and diseases

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Medical Knowledge Cockpit Publications



Search

Springer Link
powered by SAP HANA

Molecular Pathology of Lung Cancer, 2012
Molecular Targeted Therapy of Lung Cancer
Sanja Dacic

Page: 1

Receptor Tyrosine Kinases
EGFR

The EGFR (HER-1/ErbB1) is a member of the ErbB family of tyrosine-kinase receptors (TK), which includes HER-1/ErbB1, HER-2/neu/ErbB2, HER-3/ErbB3, and HER-4/ErbB4. It is composed of extracellular (ligand binding), transmembrane and intracellular (tyrosine-kinase) domain. Upon ligand binding and receptor homo- or hetero-dimerization and activation, activated EGFR signals downstream to the PI3K/AKT and RAS/RAF/MAPK pathways (Fig. 10.1). These intracellular signaling pathways regulate key processes such as apoptosis and proliferation.

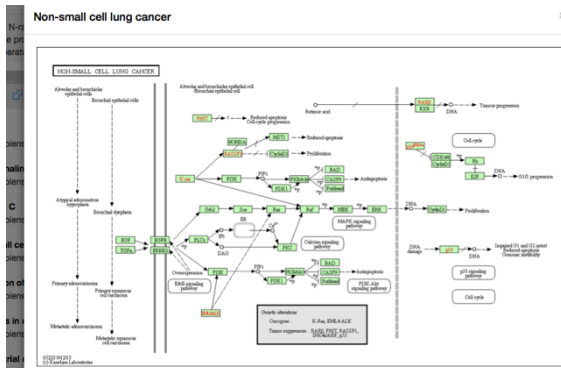
Therapies Targeting EGFR Pathway
Two treatment strategies targeting EGFR have been developed: monoclonal antibodies directed against the extracellular ligand-binding domain of the EGFR (e.g., cetuximab) and small molecule TK inhibitors (e.g., gefitinib [Iressa] and

- Interactively explore relevant publications, e.g. PDFs
- Improved ease of exploration, e.g. by highlighted medical terms and relevant concepts

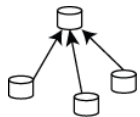
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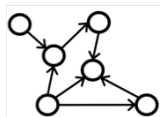
Medical Knowledge Cockpit Pathway Topology Analysis



- Search in pathways is limited to “is a certain element contained” today
- Integrated >1,5k pathways from international sources, e.g. KEGG, HumanCyc, and WikiPathways, into HANA
- Implemented graph-based topology exploration and ranking based on patient specifics
- Enables interactive identification of possible dysfunctions affecting the course of a therapy before its start



Unified access to multiple formerly disjoint data sources



Pathway analysis of genetic variants with graph engine

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Medical Knowledge Cockpit

Search in Structured and Unstructured Medical Data



Clinical Trials

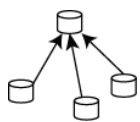
Internal

- Panitumumab Plus Pemetrexed and Cisplatin (PemCisP) Versus Pemetrexed and Cisplatin
- FLO +/- Pazopanib as First-line Treatment in Advanced Gastric Cancer

External

- Molecular Profiling and Targeted Therapy for Advanced Non-Small Cell Lung Cancer
- Erlotinib and Temezirolimus for Solid Tumors
- Molecular Epidemiology of Lung Adenocarcinoma in Multi-ethnic Asia
- Safety and Efficacy Study of Neratinib and Cetuximab to Treat Patients with Metastatic Breast Cancer
- French National Observatory of the Patients With Non-small Cell Lung Cancer

- Extended text analysis feature by medical terminology
 - Genes (122,975 + 186,771 synonyms)
 - Medical terms and categories (98,886 diseases, 47 categories)
 - Pharmaceutical ingredients (7,099)
- Indexed clinicaltrials.gov database (145k trials/30,138 recruiting)
- Extracted, e.g., 320k genes, 161k ingredients, 30k periods
- Select studies based on multiple filters in less than 500ms



Unified access to structured and unstructured data sources



Clinical trial matching using text analysis features

How Real-time Analysis turns Big Medical Data into Precision Medicine?

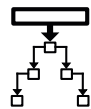
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Cloud-based Services for Processing of DNA Data



Hasso Plattner Institut

ID	Progress	Pipeline	Results	Cost
1458	Completed in 00065e05	BENCH_128.fastq.baac_25	50132	Free
1457	Completed in 00085e05	BENCH_64.fastq.baac_25	82271	Free
1456	Completed in 00012e05	BENCH_32.fastq.baac_25	124164	Free
1455	Completed in 00017e05	BENCH_16.fastq.baac_25	196209	Free
1454	Completed in 00029e05	BENCH_8.fastq.baac_25	286502	Free
1453	Completed in 00000e05	BENCH_4.fastq.baac_25	440512	Free
1452	Completed in 00007e05	BENCH_128.fastq.baac_10	50132	Free
1451	Completed in 00007e05	BENCH_64.fastq.baac_10	82271	Free
1450	Completed in 00012e05	BENCH_32.fastq.baac_10	124163	Free
1449	Completed in 00019e05	BENCH_16.fastq.baac_10	196301	Free
1448	Completed in 00027e05	BENCH_8.fastq.baac_10	286500	Free
1447	Completed in 00020e05	BENCH_4.fastq.baac_10	440512	Free
1446	Completed in 00005e05	BENCH_128.fastq.baac_5	50132	Free
1445	Completed in 00007e05	BENCH_64.fastq.baac_5	82272	Free
1444	Completed in 00019e05	BENCH_32.fastq.baac_5	124163	Free
1443	Completed in 00017e05	BENCH_16.fastq.baac_5	196303	Free
1442	Completed in 00032e05	BENCH_8.fastq.baac_5	286504	Free



Standardized Modeling and runtime environment for analysis pipelines

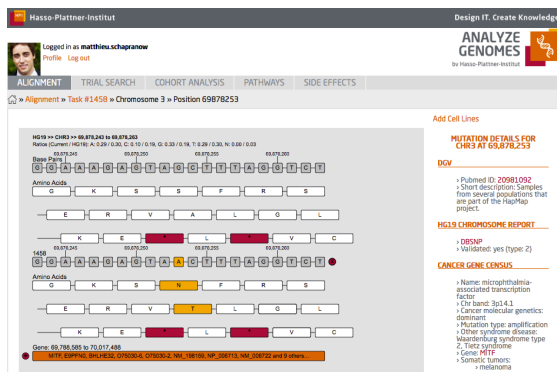
- Control center for processing of raw DNA data, such as FASTQ, SAM, and VCF
- Personal user profile guarantees privacy of uploaded and processed data
- Supports reproducible research process by storing all relevant process parameters
- Implements prioritized data processing and fair use, e.g. per department or per institute
- Supports additional service, such as data annotations, billing, and sharing for all Analyze Genomes services
- Honored by the 2014 European Life Science Award



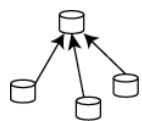
How Real-time Analysis turns Big Medical Data into Precision Medicine?

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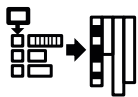
Interactive Genome Browser



- Genome Browser enables interactive comparison of multiple genomes
- Combined knowledge by integrating latest international annotations and literature, e.g. from NCBI, dbSNP, and UCSC
- Detailed exploration of genome locations and existing associations
- Ranked variants, e.g. accordingly to known diseases
- Links always back to primary data sources to guarantee validity of discovered findings



Unified access to multiple formerly disjoint data sources

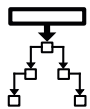
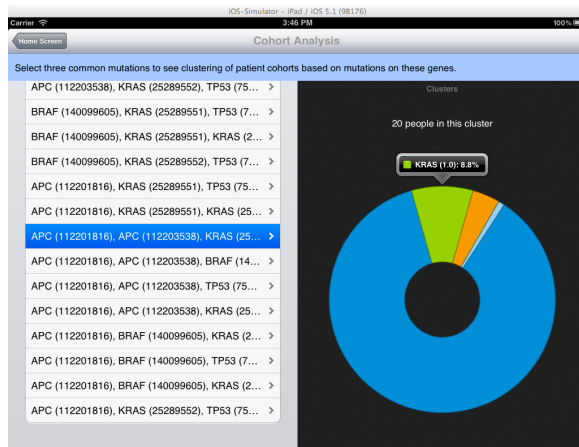


Matching of genetic variants and relevant annotations

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Analysis of Patient Cohorts



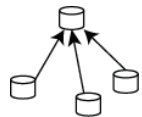
Fast clustering directly performed within the in-memory database

- In a patient cohort, a subset does not respond to therapy - why?
- Clustering using various statistical algorithms, such as k-means or hierarchical clustering
- Calculation of all locus combinations in which at least 5% of all TCGA participants have mutations: 200ms for top 20 combinations
- Individual clusters are calculated in parallel directly within the database
- K-means algorithm: 50ms (PAL) vs. 500ms (R)

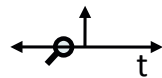
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Oncolyzer



Unified access to formerly disjoint oncological data sources



Flexible analysis on patient's longitudinal data

- Research initiative for exchanging relevant tumor data to improve personalized treatment
- Real-time analysis of tumor data in seconds instead of hours
- Information available at your fingertips: In-memory technology on mobile devices, e.g. iPad
- Interdisciplinary cooperation between clinicians, clinical researchers, and software engineers
- Honored with the 2012 Innovation Award of the German Capitol Region

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Oncolyzer Patient Details Screen

- Combines patient's longitudinal time series data with individual analysis results
- Real-time analysis across hospital-wide data using always latest data when details screen is accessed
- <http://epic.hpi.uni-potsdam.de/Home/HanaOncolyzer>

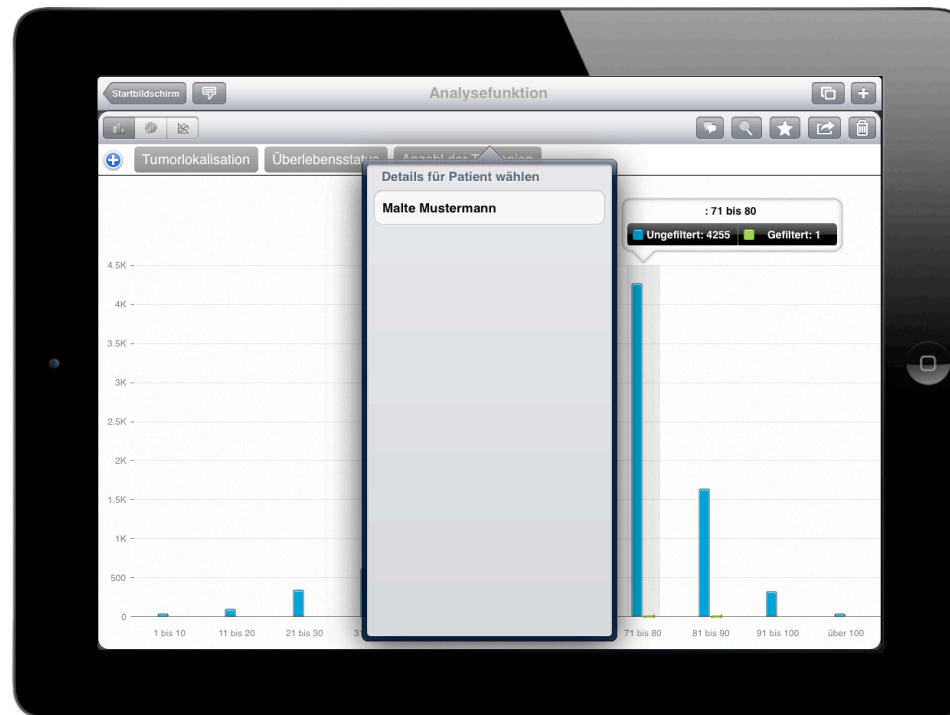


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Oncolyzer Patient Analysis Screen

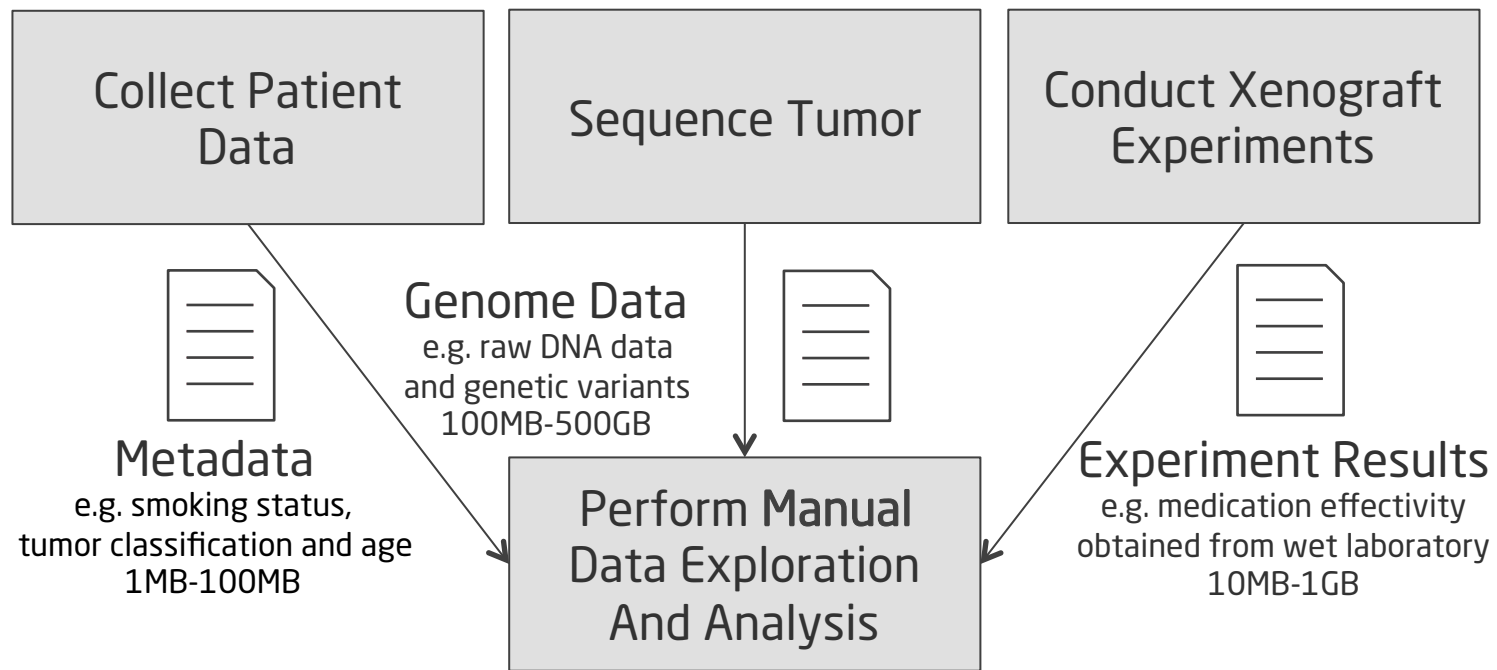
- Allows real-time analysis on complete patient cohort
- Supports identification of clinical trial participants based on their individual anamnesis
- Flexible filters and various chart types allow graphical exploration of data on mobile devices



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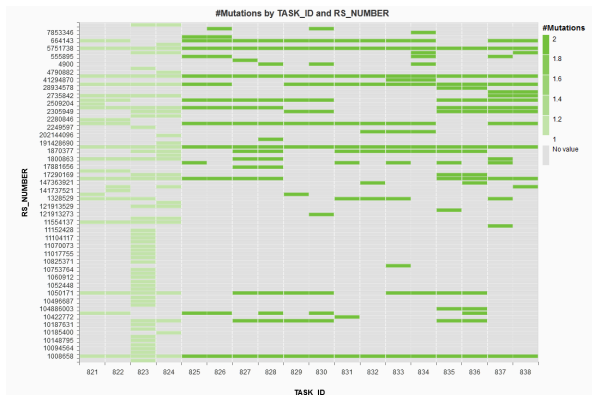
Drug Response Analysis Data Sources and Matching



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Drug Response Analysis Interactive Data Exploration



- Drug response depends on individual genetic variants of tumors
- Challenge: Identification of relevant genetic variants and their impact on drug response is a ongoing research activity, e.g. Xenograft models
- Exploration of experiment results is time-consuming and Excel-driven
- In-memory technology enables interactive exploration of experiment data to leverage new scientific insights



Interactive analysis of correlations between drugs and genetic variants

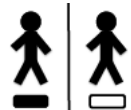
Interactive Clinical Trial Recruitment



cytolon



- Switch from trial-centric to patient-centric clinical trials
- Real-time matching and clustering of patients and clinical trial inclusion/exclusion criteria
- No manual pre-screening of patients for months: In-memory technology enables interactive pre-screening process
- Reassessment of already screened or already participating patient reduces recruitment costs



Assessment of patients preconditions for clinical trials

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Join us for upcoming projects!



- Analysis of waveform data from intensive care stations (MIT)
- Design and discovery of clinical trials (Cytolon)
- Discovery of new drugs (Bayer)
- Detect cardiovascular diseases and evaluate treatment options (BMBF)
- Use health insurance data to improve health care (BMWi)
- Processing of big medical data (Bachelor's project)



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What to take home?

Test-drive it yourself: <http://we.AnalyzeGenomes.com>

■ For patients



- Identify relevant clinical trials and medical experts
- Start most appropriate therapy as early as possible

■ For clinicians



- Preventive diagnostics to identify risk patients early
- Indicate pharmacokinetic correlations
- Scan for similar patient cases, e.g. to evaluate therapy

■ For researchers



- Enable real-time analysis of medical data and its assessment, e.g. assess pathways to identify impact of detected variants
- Combined free-text search in publications, diagnosis, and EMR data, i.e. structured and unstructured data

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Keep in contact with us after returning from Rome



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