Rejuvenated Medical Visualization

From Single-Patient to Cohort Study Data

Steffen Oeltze-Jafra

Tutorial Outline

Welcome

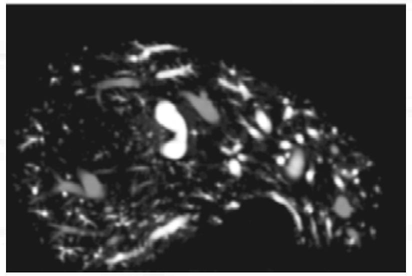
- Interactive Visualization of Whole-Body Medical Volume Data
  Ynnerman (40 min)
- From Static to Dynamic – Visualizing Real-Time Imaging Data
  Bruckner (40 min)

Coffee break (20min)

- From Anatomy to Physiology
  Hauser (35 min)
- From Single-Patient to Cohort Study Data
  Oeltze-Jafra (35min)
- Closing Words and Discussion
  All Presenters (30min)

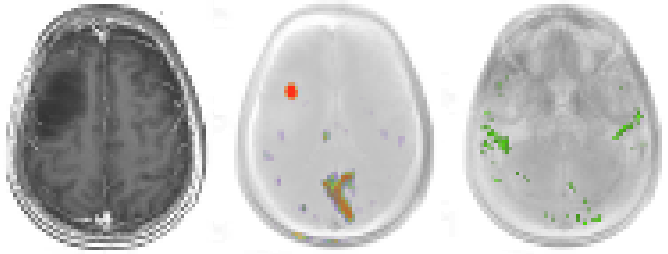
From Single-Patient to Cohort Study Data

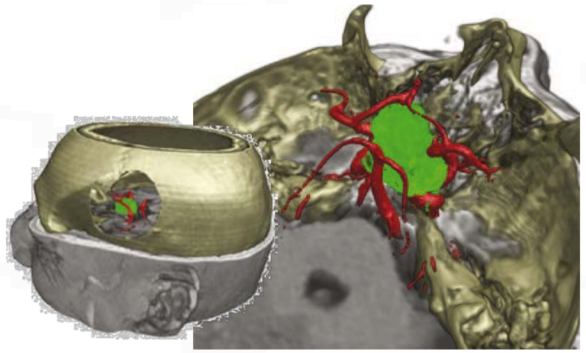
Single patient,
single body part



[Selle01]

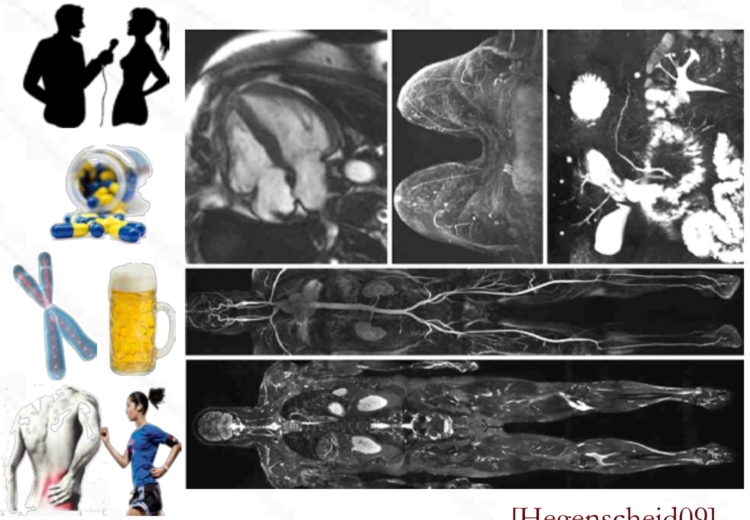
Single patient,
single body part,
multimodality or time-varying data





[Beyer07]

Thousands of subjects, longitudinal **non-image** (100s of variables) **and image data** (***whole-body*** and body parts, multi-modality, time-varying)



[Hegenscheid09]

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Cohort Studies in Epidemiology

- Epidemiology investigates
  - Health-related events in defined populations (cohorts)
  - Factors contributing to disease outbreaks in individuals
  - Effectiveness of therapies and screening programs
- Investigation based on cohort studies
  - Often, carried out in waves over years (longitudinal)
  - Comprising thousands of individuals
  - Collecting hundreds of socio-demographic and biomedical variables for each individual

Modern Epidemiology

- Employs also *medical image data*, gene sequence data, blood and urine samples, ECG data as well as tissue samples
- These data are acquired efficiently, in large scale and high quality
- For ethical reasons, non-invasive imaging techniques are employed for largely healthy populations, e.g., MRI and US

Goals of Epidemiologic Research

1. Examination of *incidence* and *prevalence* of diseases
2. Identification of risk factors
3. Efficiency evaluation of preventive and therapeutic measures
4. Determination of differences between *healthy aging* and *pathologies in an early stage*

- No purely academic endeavor but has huge consequences
- Examples: passive smoking protection, safer sex campaigns, vaccination programs, cancer screening,…

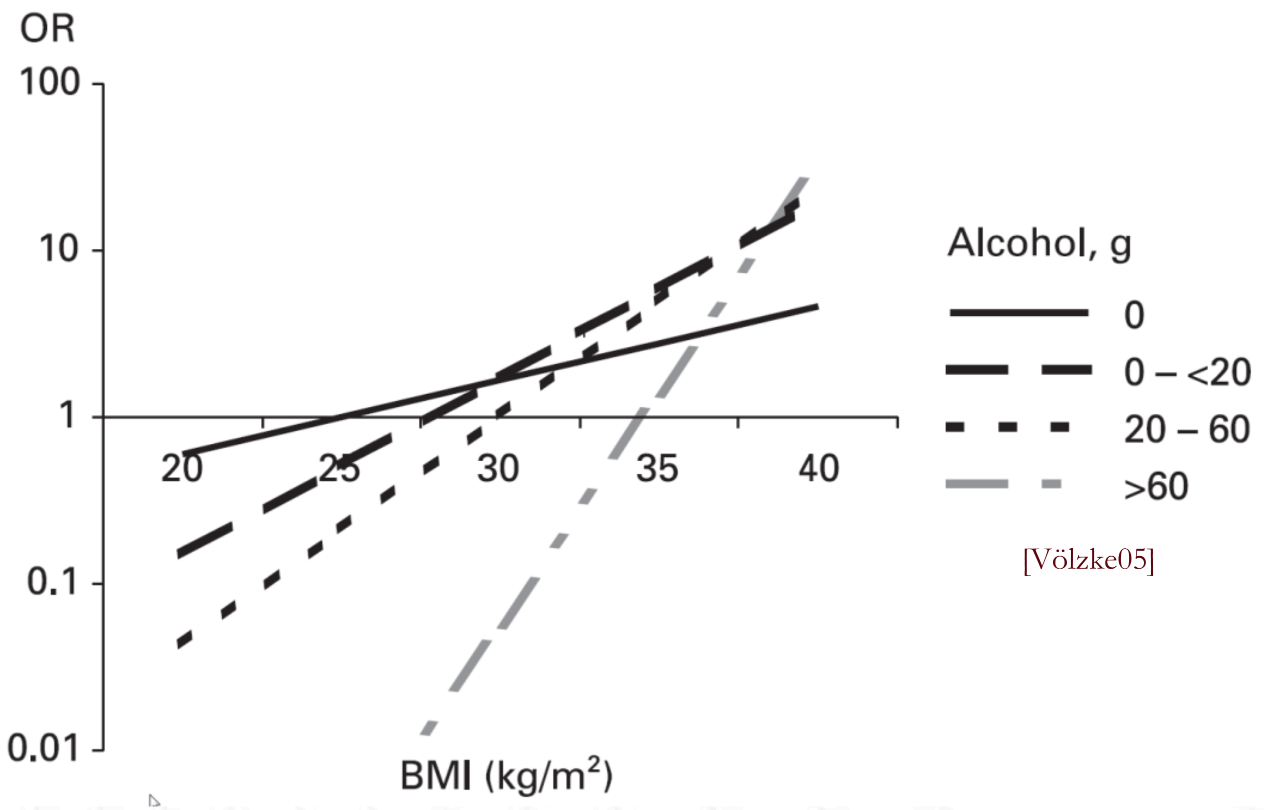
Some Results

- Breast cancer should not be operated in a radical manner in early stages of the disease.
- Radiation treatment may cause subsequent cancer diseases, in particular when children are treated. Limit the amount of radiation!
- Some risk factors depend linearly on a variable such as radiation dose or nicotine intake while others exhibit U- or J-shaped relations, e.g., the risk of mental disorders related to alcohol consumption or sleeping duration.

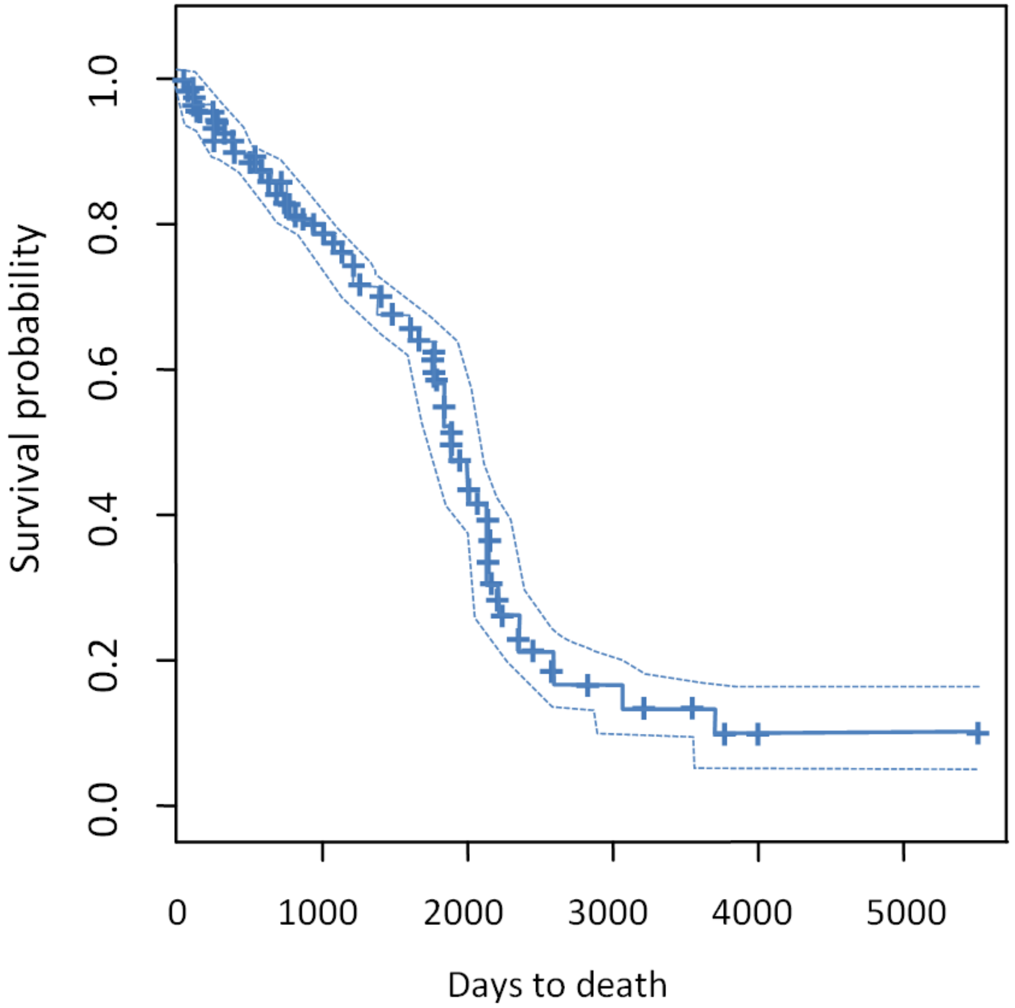
Data Characteristics

- Massive amount of heterogeneous data
- Different domains and aggregation levels
- (Different) variables per individual, organ, organ part
- Time-dependent and static variables
- Never perfectly reliable (consumption of alcohol, tobacco, …)
- Often sparse (treatment of diabetes),
- Often incomplete (not all people agree to the MRI exam)
- Dichotomous variables (presence of back pain)

Standard Visualizations



[Völzke05]



[Preim15]

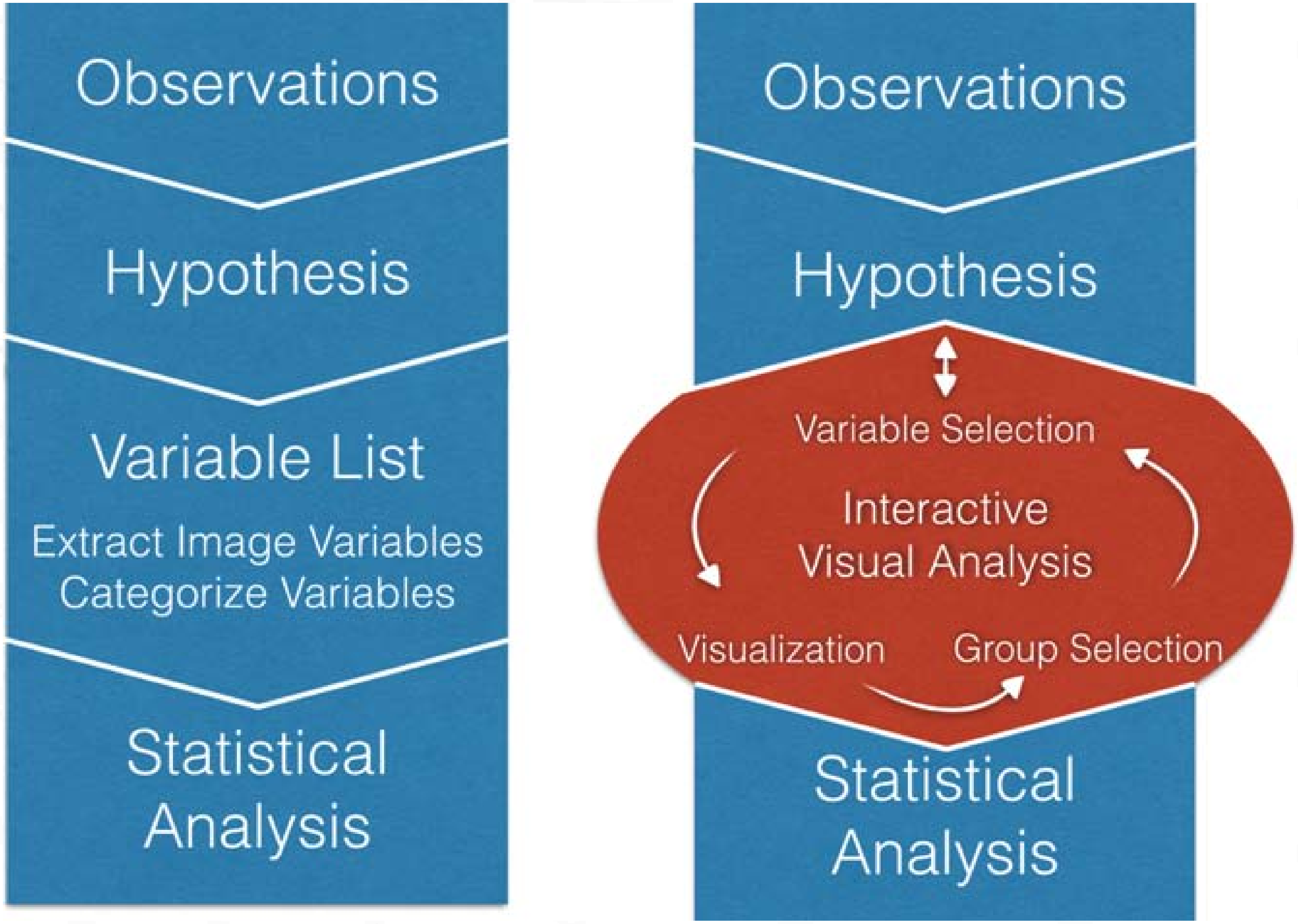
Left: *Interaction Term* describing the relative risk for the development of gall stones depending on body mass index (BMI) and alcohol consumption

Right: *Kaplan-Meier Curve* (including uncertainty) to characterize prognosis

Visual Analytics Approaches

Standard Analysis vs. Visual Analytics

- Old and new workflow in epidemiology
- Visual analytics allows for a more flexible and interactive selection of variables, a data-driven definition of groups and subgroups, and for the generation of new hypotheses



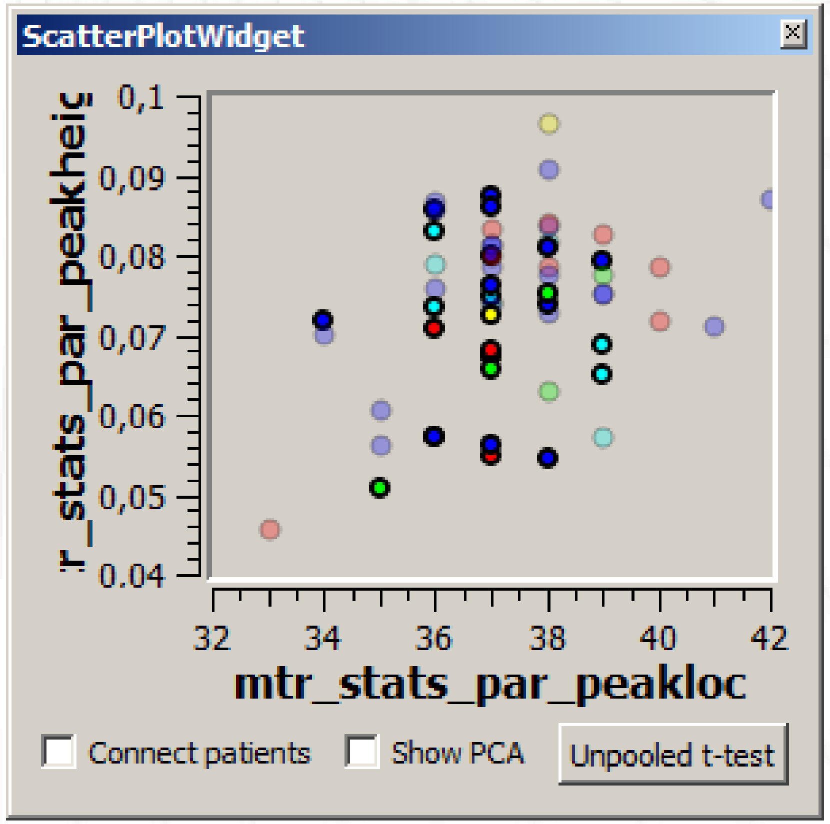
[Klemm14]

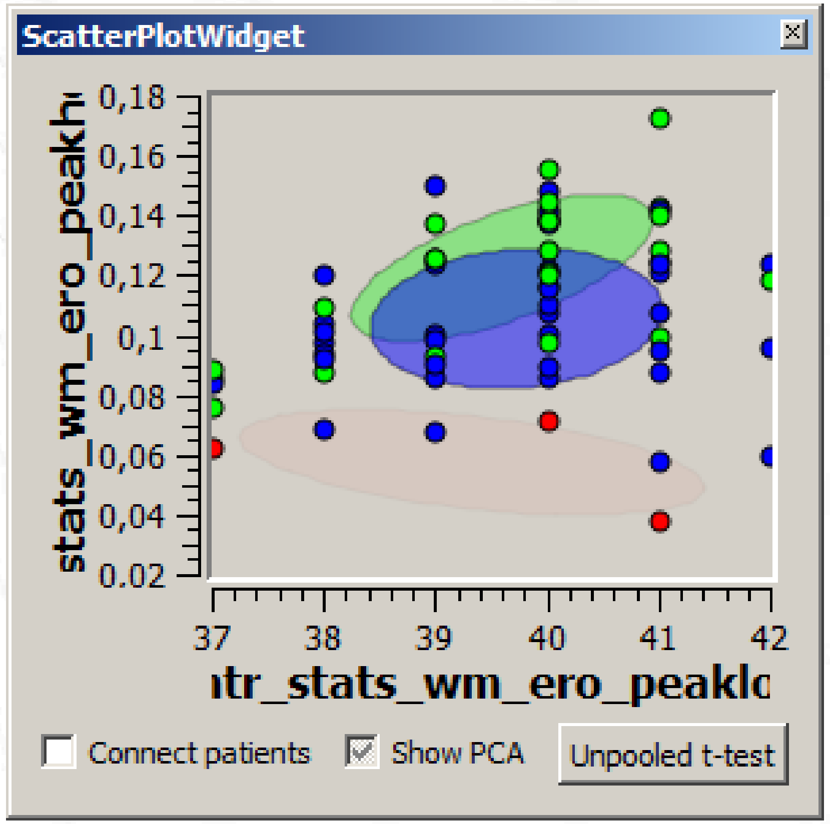
Potential of Visual Analytics

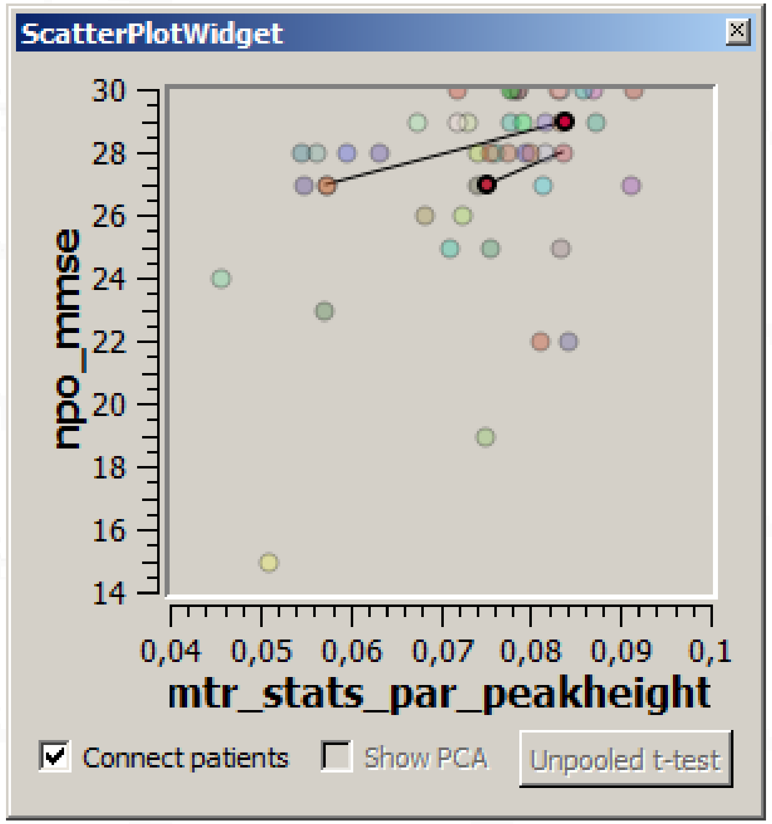
- Integration of data mining and interactive visual exploration
- **Data Mining**: machine learning techniques, such as pattern mining, classifiers, clustering, supervised learning techniques (Neural networks, support vector machines), dimension reduction
- **Interactive Visual Exploration**: visual queries, brushing and linking, multiple coordinated views, parallel coordinates, scatter plots, glyph-based displays, time-lines, graphs, and treemaps.
- **Integration**: analytics is not just a preprocess, but carefully integrated in the exploration, thus loops between visualization, exploration, and data mining are supported.

Examples of Visual Analytics Approaches

- Statistics is main research vehicle of epidemiologists
- Scatter plots with overlaid clusters and (local) regression lines



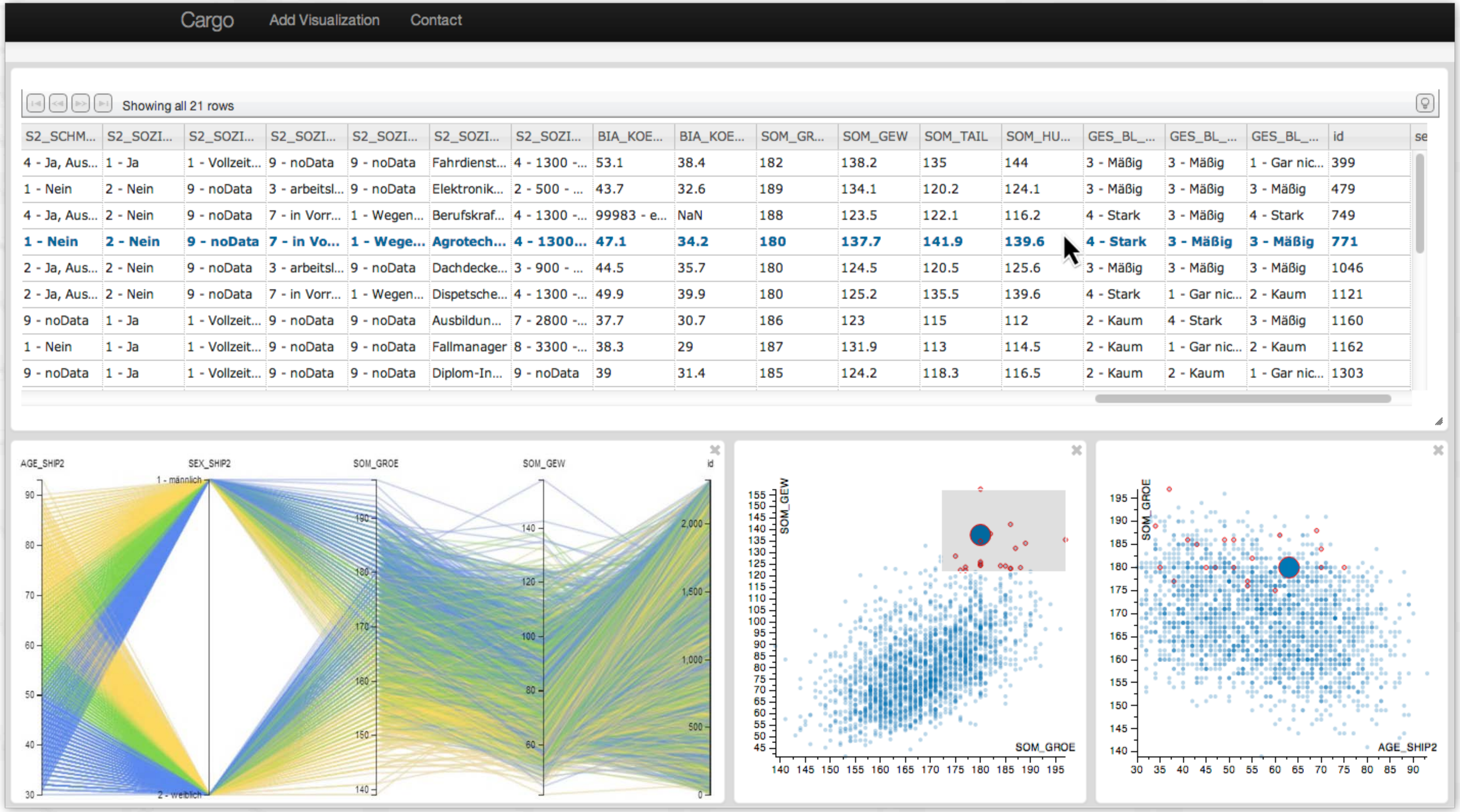




[Steenwijk10]

Examples of Visual Analytics Approaches

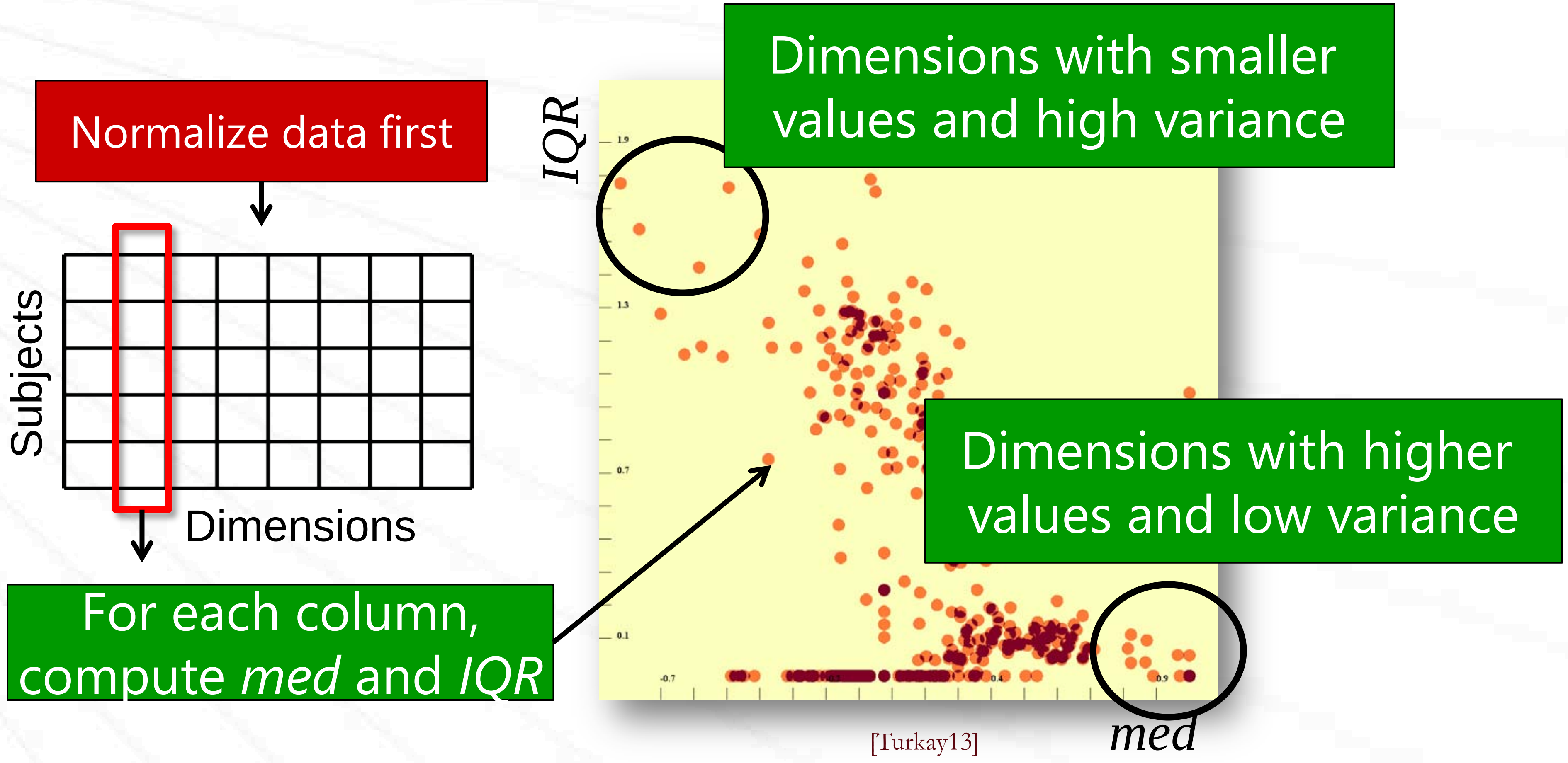
- Multiple Coordinated Views System
- Brushing & linking
- Clustering for data-driven definition of sub-groups



[Klemm14]

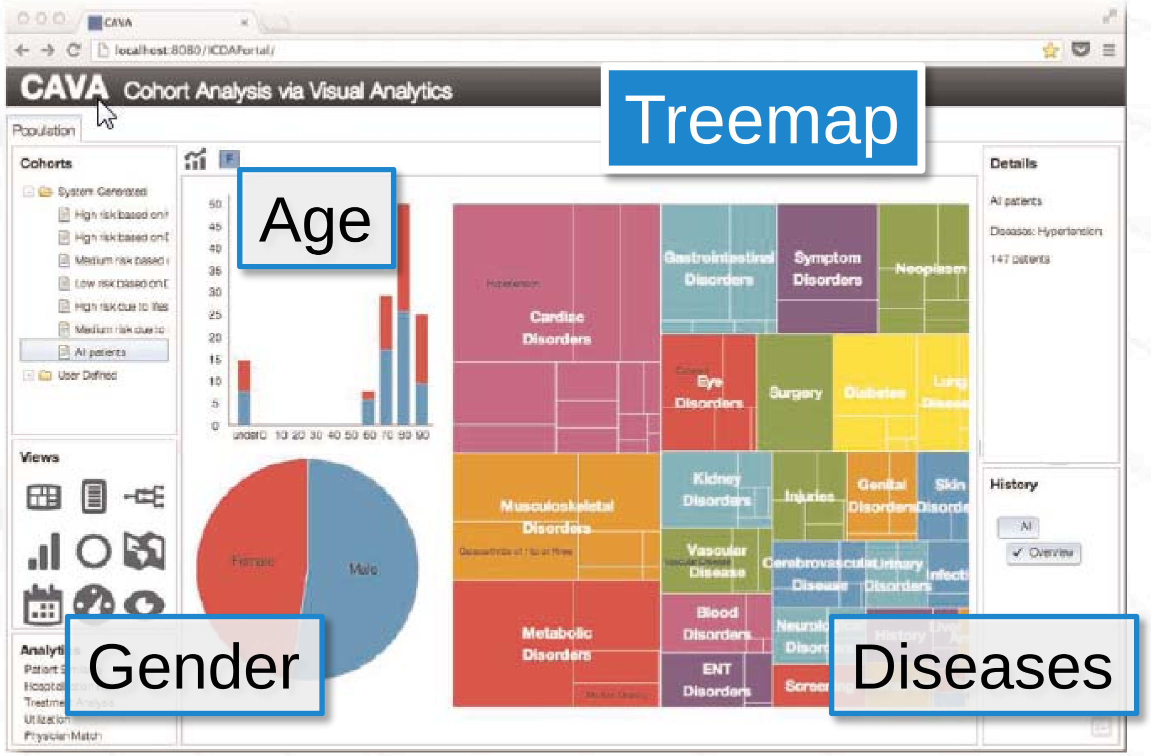
Examples of Visual Analytics Approaches

- Treat dimensions, NOT subjects, as first-order analysis objects [Turkay11]
- Compute statistics for each dimension, e.g., median, IQR, skewness, kurtosis
- Oppose statistics in plots and brush



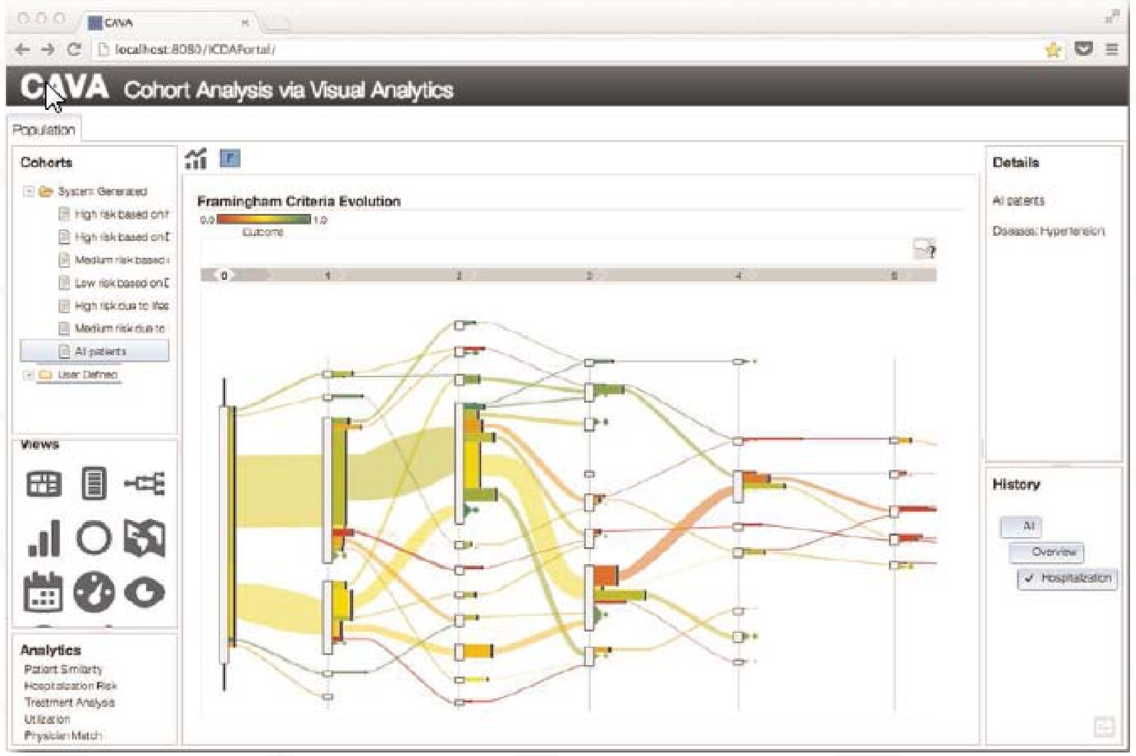
Examples of Visual Analytics Approaches

- Visualization techniques suitable for categorical data
- Time-oriented visualizations of events in longitudinal studies



[Zhang15]

Overview of a cohort

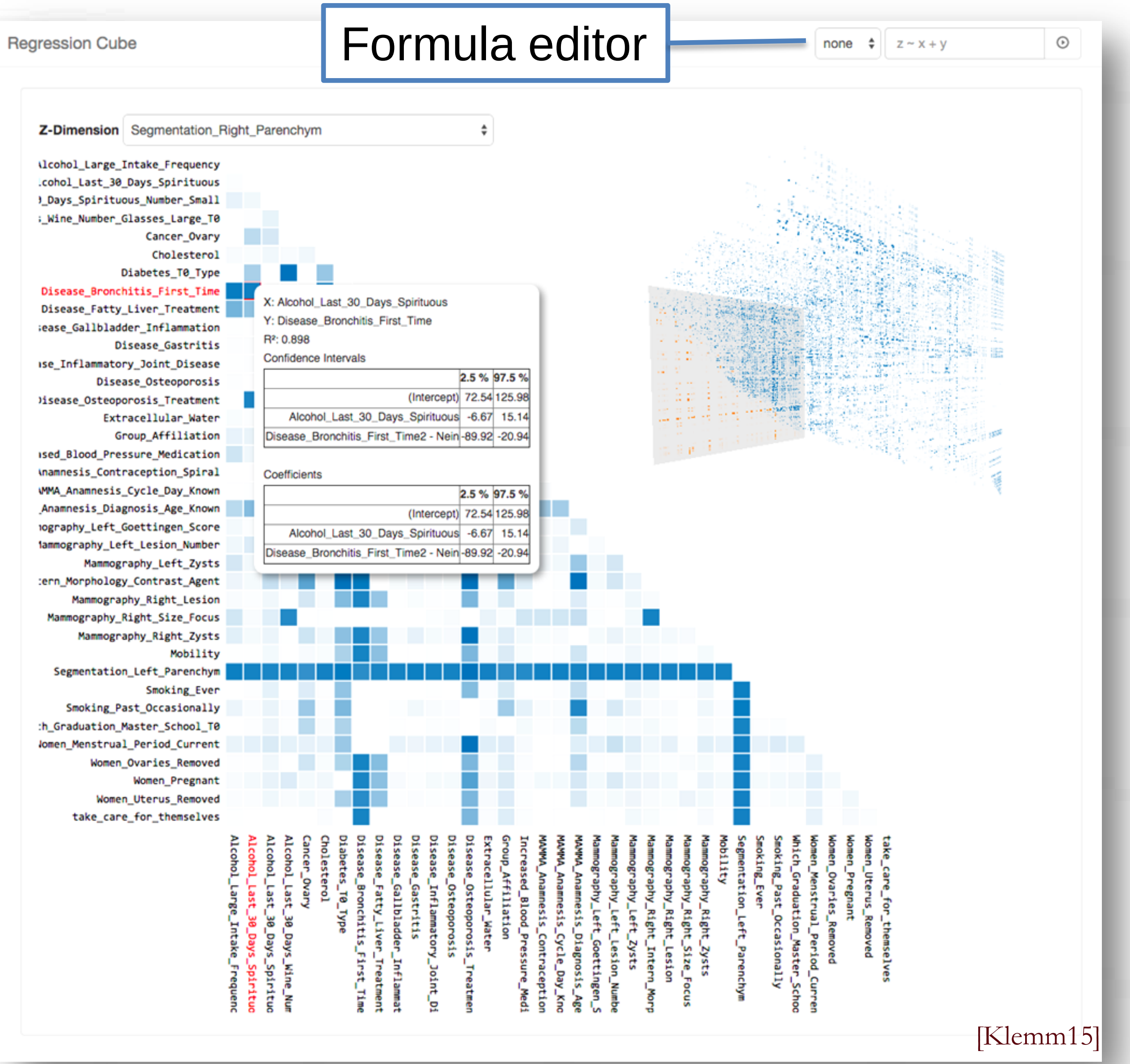


[Zhang15]

Symptom progression pathways

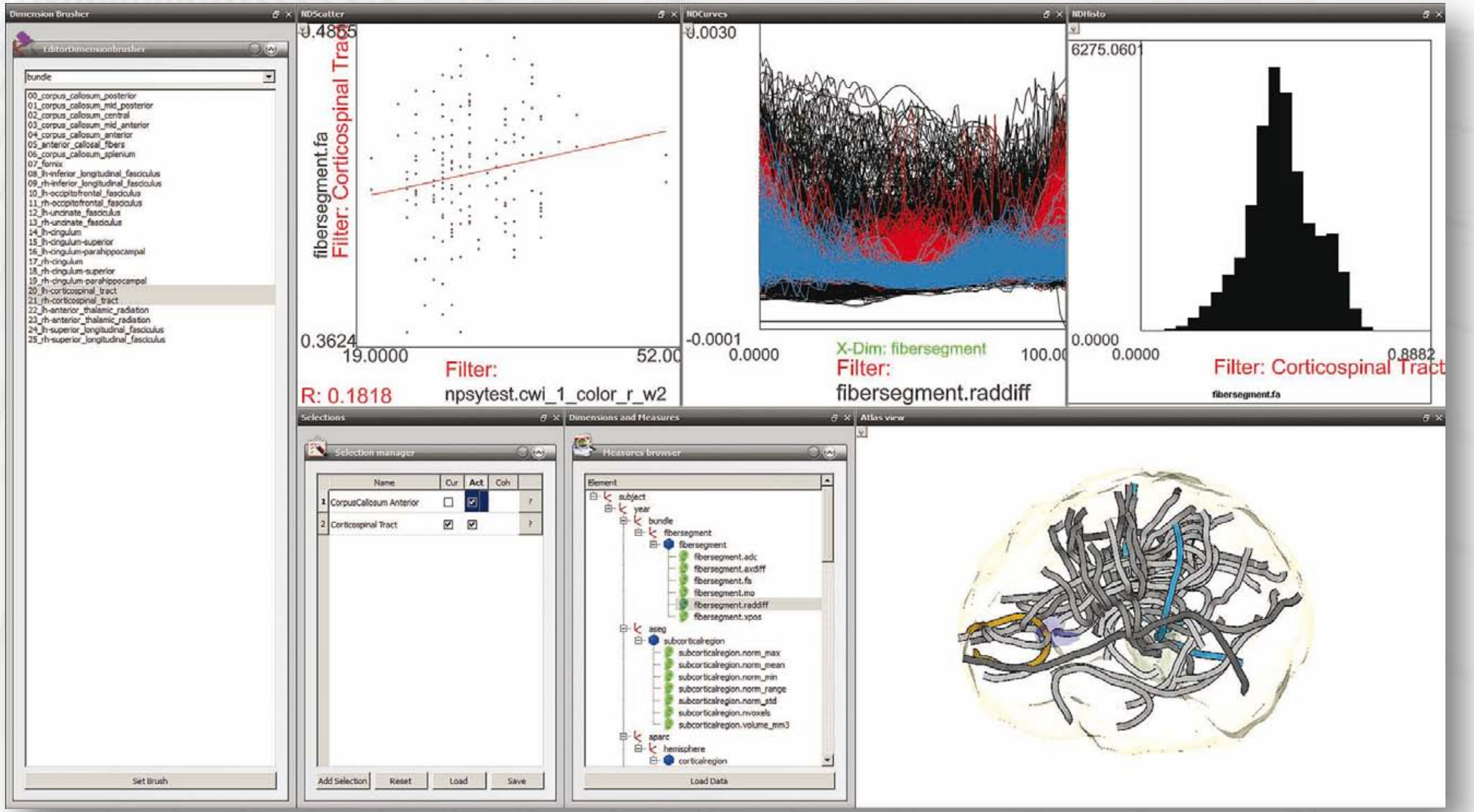
Regression-Based Visual Analytics

- **Key idea**: User specifies a target variable, usually a pathology, and combinations of (2 or 3) variables are checked w.r.t. a possible correlation (hypothesis-free)
- Regression cube for visualization
- Saturation encodes strength of correlation
- Come and see Paul's talk on Wed., 28th, VAST session at 8:30-10:10 in Room "Red"



[Klemm15]

Special Data Structures



[Angelelli14]

- Data cube model for seamless integration of entities with only partially overlapping dimensions
- Example: Fiber tracts and cortical regions with shared IDs of subject and study wave but disjoint sets of fractional anisotropy and cortical thickness measures
- Come and see Paolo's talk on Thurs., 29th, CG&A session at 14:00-15:40 in Room "Empire"

Visual Analytics: The Patent

- „Iterative Refinement of Cohorts Using Visual Exploration and Data Analytics“ (D. Gotz, A. Perer, Z. Zhang, IBM, granted 4/2014)
- **Preamble**: „A need exists for an integrated system that combines visual exploration and data analytics to ... refine cohorts ... and make new discoveries.“
- **Selected Claims** (out of 11):
  - Reduce cohort using one or more visual filters,
  - Visualize selected cohort using a selected view,
  - Expand current cohort by one or more analytical methods,
  - Modify current cohort using one or more additional reductions and extensions

Visual Analytics Prototyping

- Prototyping using modern web technologies allows for a fast feedback loop between computer scientists and epidemiologists
- Client-Server structure to outsource heavy computations on a server machine, keeping system requirements on the client low

[Klemm14]

Image-Centric Cohort Studies

Potential of Image Data

- Depiction of the vital organs of a large population
- Representation of the broad variability in anatomy and physiology
- Characterization of health and disease
- Differentiation between effects of normal aging and pathologies

Disclaimer:

The individual is of less interest to epidemiologists, just like the realistic, high-quality visualization of its specific image data.

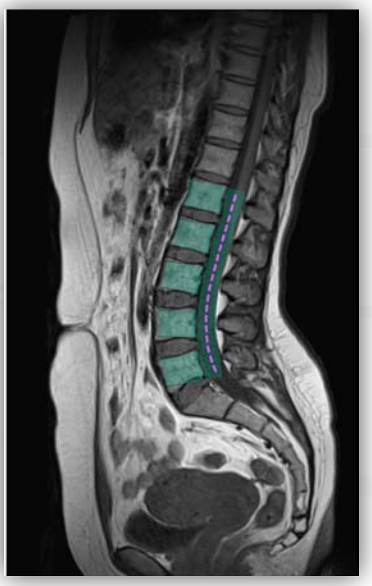
Data Acquisition

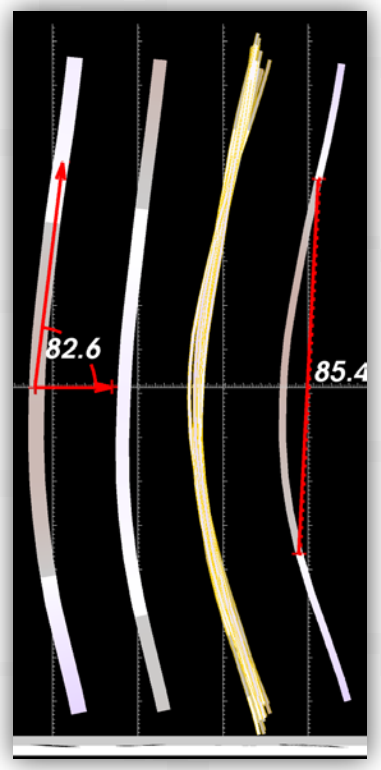
- All *epidemiological instruments* need to be applied in a highly standardized manner → minimize intra-observer variability
- Scanners, sequences and protocols are highly standardized
- No updates are allowed in the whole (>5 year!) cycle
- Ethical and economic aspects are essential
  - Primarily Ultrasound and MRI

Problem: not all people may agree to acquisition or may be eligible for it, e.g., pacemaker patients in MRI

Data Processing

- Image data itself are too complex
- Epidemiologists are interested in derived measures related to:
    - Shape, Size, Angle,
    - Location, neighborhood,
    - Tissue density,…
- Huge amount of data requires segmentation and quantification to be as automatic and reproducible as possible





Example Studies

- SHiP (Study of Health in Pomerania), Longitudinal study in 3 waves, wide range of diseases, focus: diabetes, cardio vascular diseases, diseases of the bile duct and liver
- Rotterdam Study (Focus: elderly persons (>55 years) and cardio vascular diseases, Start: 1990, >900 PubMed publications)
- UK Biobank (500.000 persons, 2006-2010)
- Cognitive Aging Study (Bergen, Norway) [Ystad09]
- Nationale Kohorte (Germany, Start: 2014) [GNC14]
  - 200.000 test persons (aged 20-69, 20% intensified level 2 examination)
  - ~30.000 MRI data will be acquired in 5 centers
  - Automatic quality control and normalization as essential aspects (MR scanners do not have perfectly the same characteristics)

Study of Health in Pomerania (SHiP)

Study in 3 waves [Völzke11]

- SHiP-0: 1997-2001, n=4308 (f/m), age: 20-79
- SHiP-1: 5-year-follow up, n=3300
- SHiP-2: 12-year follow-up, n=2500
  (less participants as always; drop out)
  SHiP-Trend: new sample drawn, n=8016

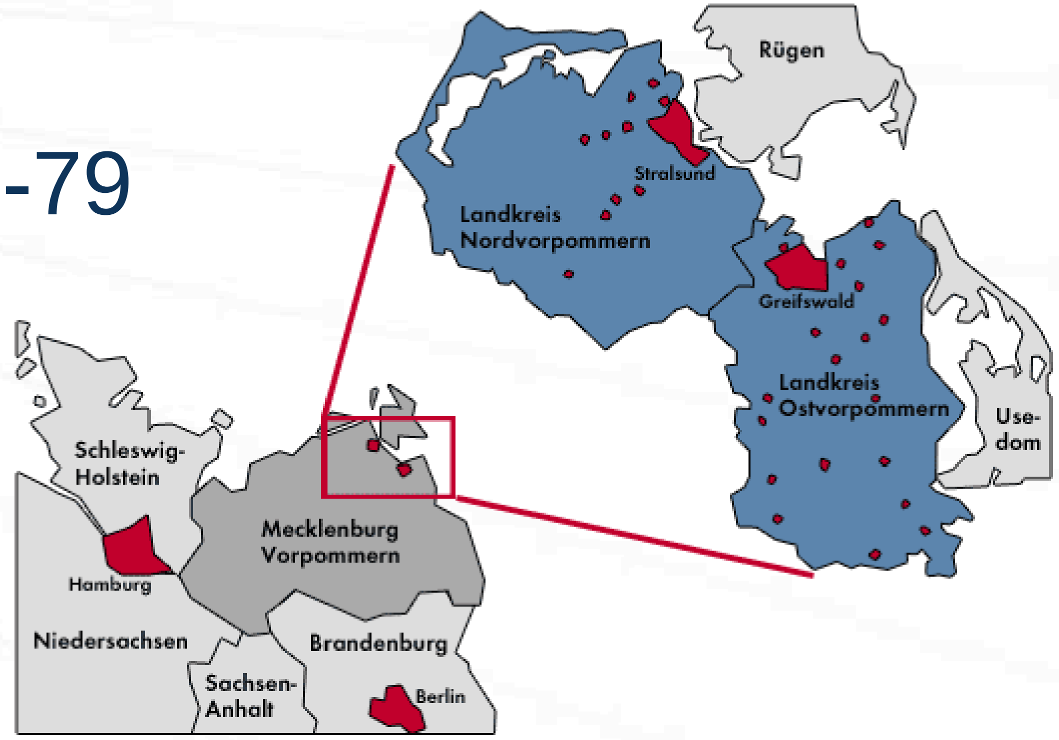


Image Data [Hegenscheid09]

- Whole-body MRI: 1.5 Tesla, basis program + contrast-enhanced cardio MRI + MRA for men and MR Mammography for women (up to 40 datasets per study participant)

Case Study: Analysis of Lower Back Pain

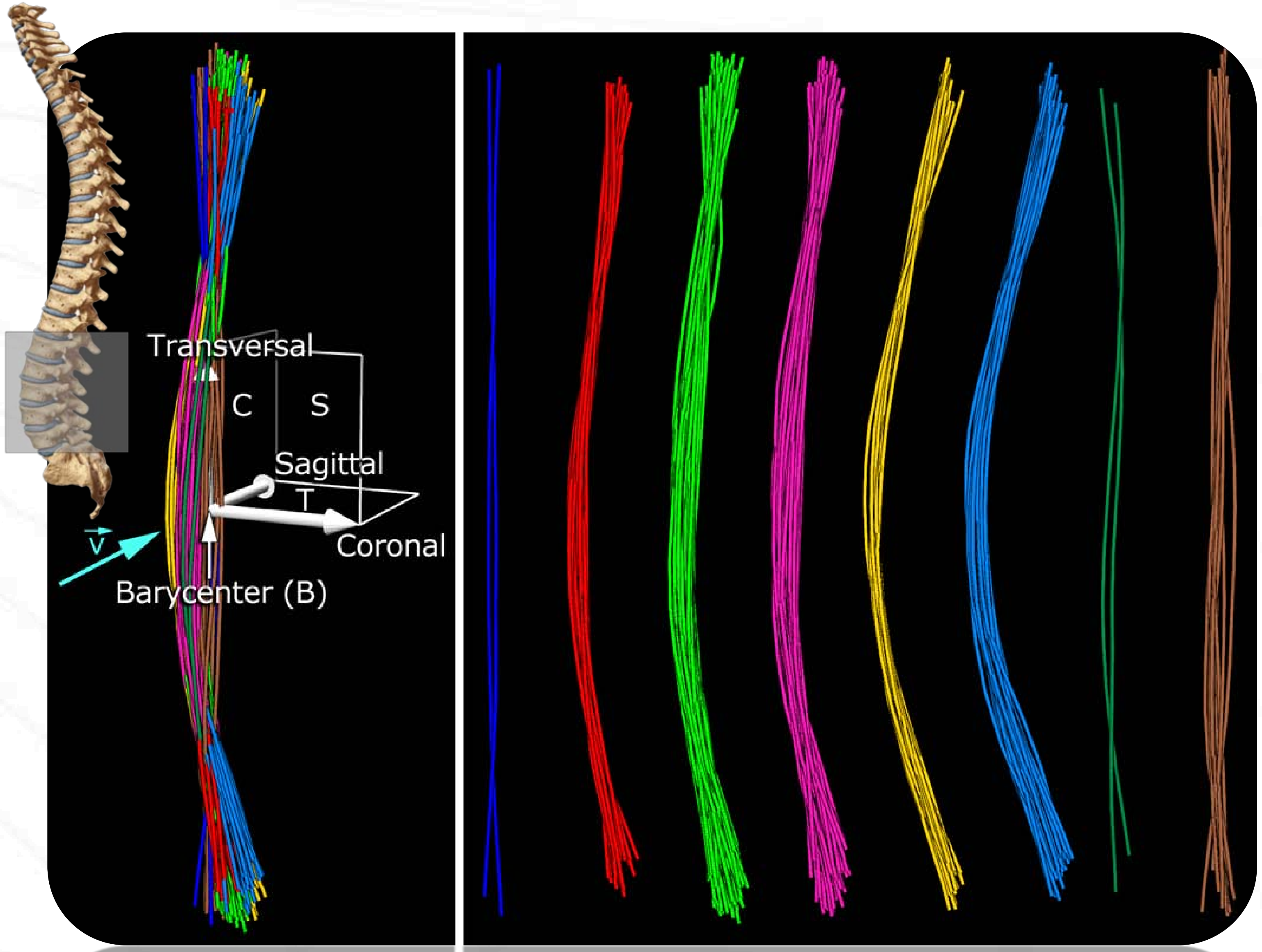
- 129 variables (only 15 scalar) of SHiP are possibly related to back pain
- Image data: T1/T2-weighted MRI data, rather low res (1.1x1.1x4 mm)
- Known correlations:
  - Back pain is related to age, depression, physical stress, smoker status [Manek05]
  - Curvature of spine is related to age, body height, weight
- Visual Analytics goals:
  - Confirm known or assumed correlations
  - Identify new correlations
  - Differentiate between pathological and age-related deformations of the spine

Case Study: Analysis of Lower Back Pain

- Task: robust, automatic detection of the spine
- Hierarchical Finite Element method applied to >2000 patients [Rak13]
- Detection combined with centerline extraction (repr. by 100 vertices)
- Successful in ~80 percent

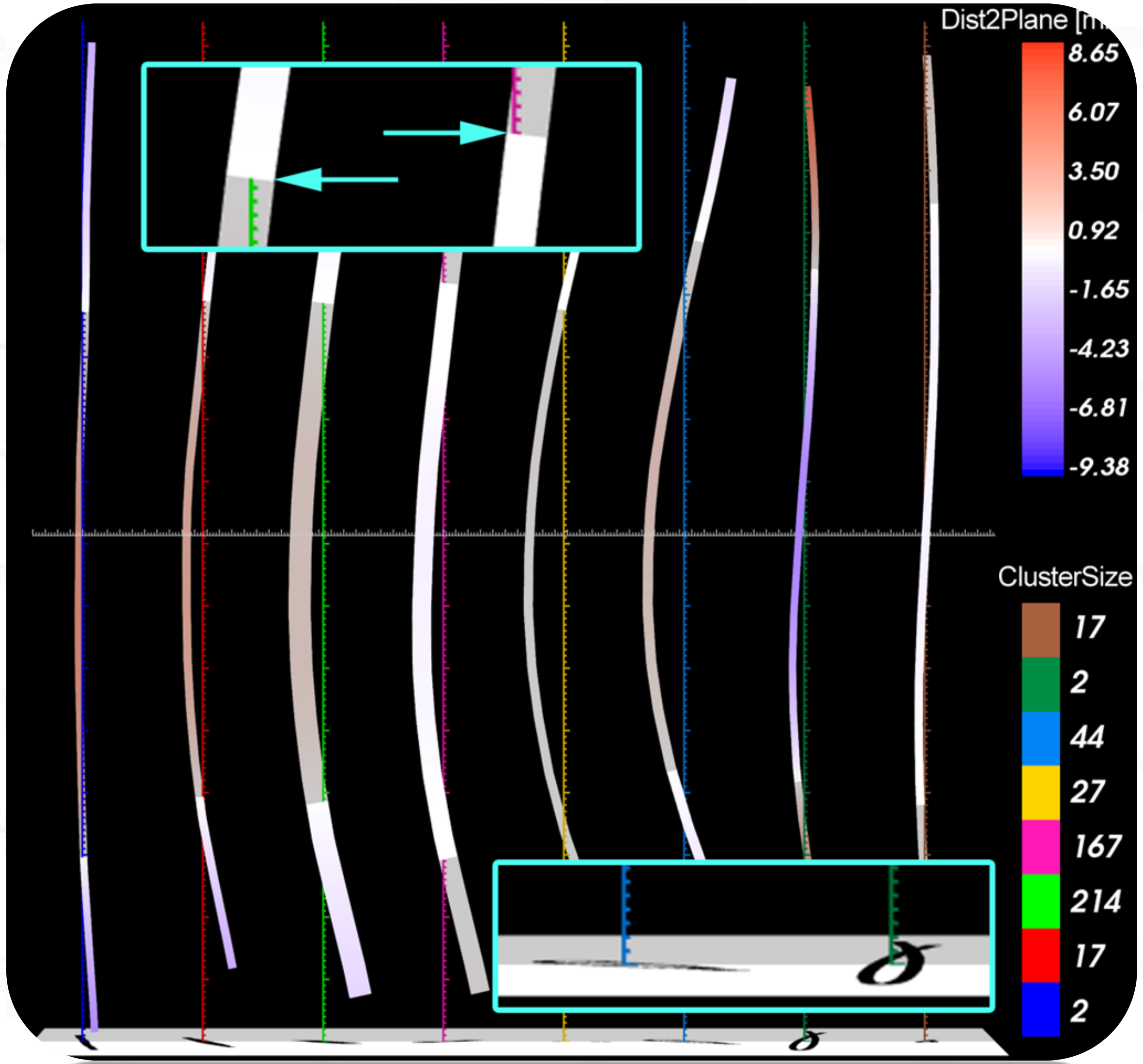
Case Study: Analysis of Lower Back Pain

- Task: identification of sub-groups of participants with similar spine canal bending
- Agglomerative Hierarchical Clustering approach [Klemm13]
- Automatic determination of number of clusters [Salvador04]



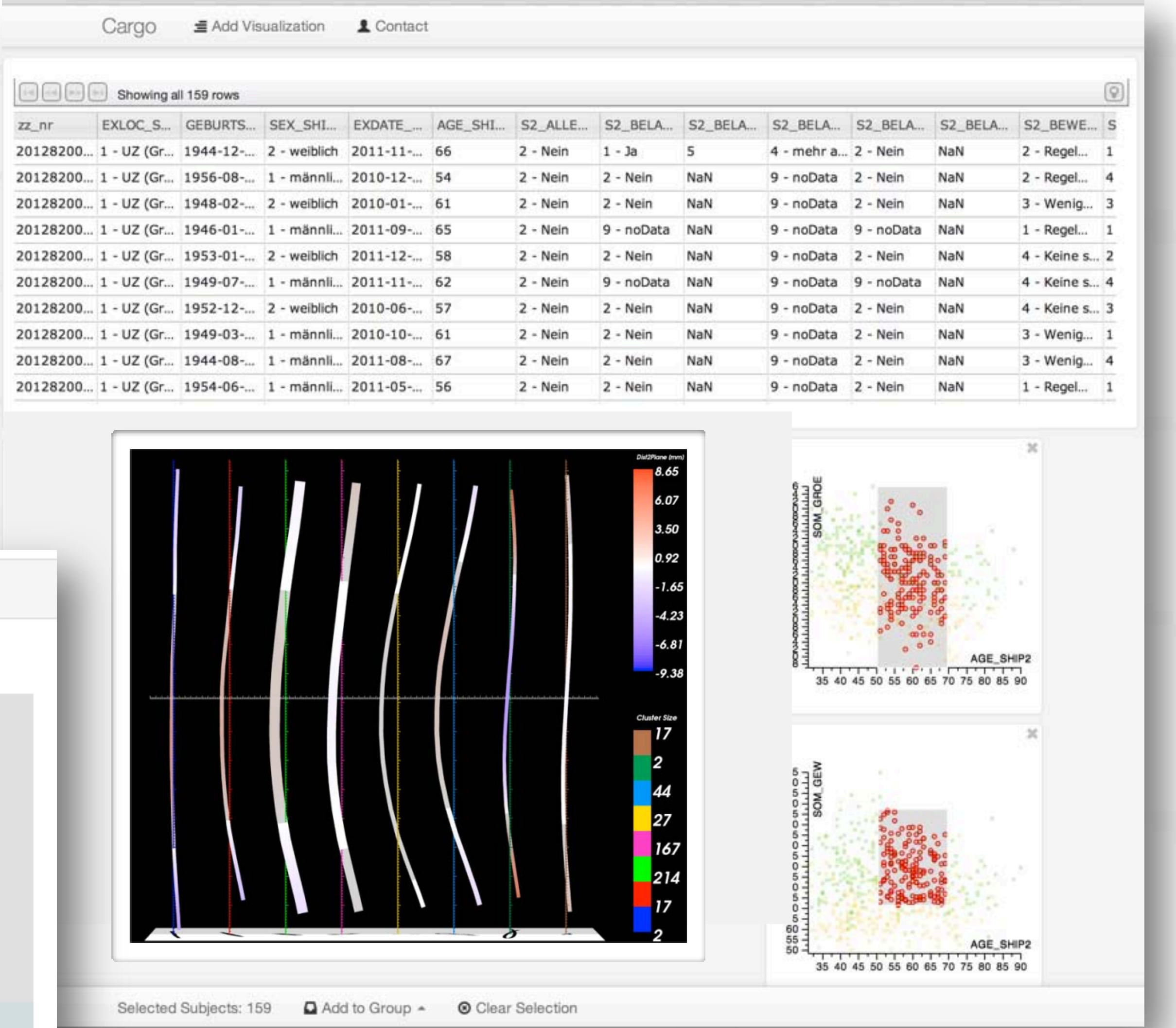
Case Study: Analysis of Lower Back Pain

- Task: display of clustering results
- Ribbon-based visualization of cluster representatives
- Width encodes cluster size
- Color encodes distance to midsagittal plane
- Shadows on projection plane indicate bending strength orthogonal to midsagittal plane



Case Study: Analysis of Lower Back Pain

- Tasks: relation of clusters to cohort variables and search for correlations
- Integration of 3D view into framework
- Bidirectional linking between 3D view and all other views
- Augmentation of InfoVis plots by mean shapes of lumbar spine



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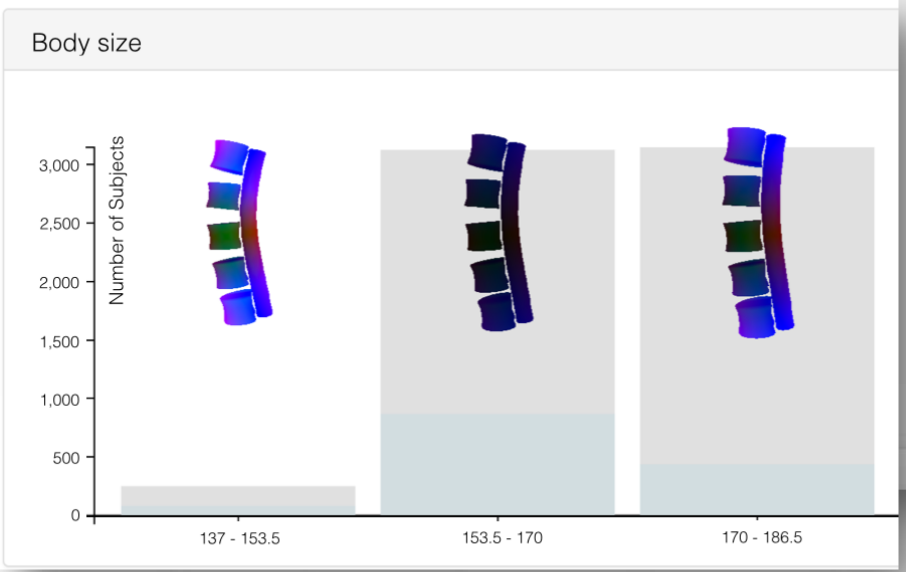

Case Study: Analysis of Lower Back Pain

- Analysis revealed correlations of lower back pain with
  - leg fatigue,
  - physically heavy work,
  - body weight,
  - dyspnoea, and
  - headache intensity (particularly interesting)
- Analysis, so far, is restricted to the overall spine shape
- Further insights are expected when the following is considered:
  - The shape and size of individual vertebrae
  - The angle between the central spine axis and the vertebrae
  - The distance between individual vertebrae

Concluding Remarks

- Visual analytics approach is subject to discussions, e.g., the value of clustering, subspace-clustering? Parameter sensitivity?
- *Hypothesis generation* using *interactive visual* analysis of the *entire* data pool is a new concept to epidemiologists
- Integration of statistics and statistical graphics is essential to increase acceptance of new concepts, tools, and views
- When working with epidemiologists there is no direct influence on patient care but potentially a large indirect influence by the refinement of guidelines for diagnosis and treatment processes.

Outlook

- Pair analytics
  - Expert and computer scientist cooperatively analyze epidemiological data
  - Localized or distributed (analysis performed at one or separate locations)
  - Consequence: one workspace or two separate workspaces, each with input devices, requiring synchronization and an appropriate GUI-design

- Uncertainty-aware visual analytics
  - Ambiguous subgroup definition yields uncertain statistics
  - Measurement inaccuracies, e.g. of blood pressure, or unreliable self reports, e.g. on eating and drinking habits, yield uncertain variables
  - Consequence: model uncertainties, consider them in the analysis, and convey them in the visualization

Acknowledgements

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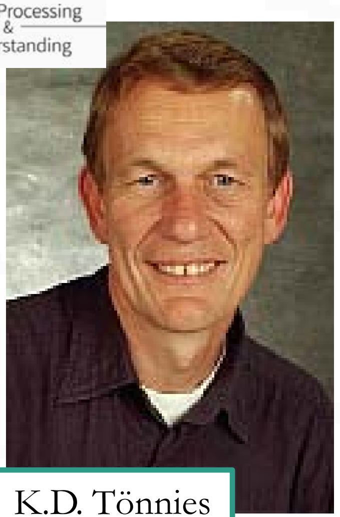
K.D. Tönnies

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