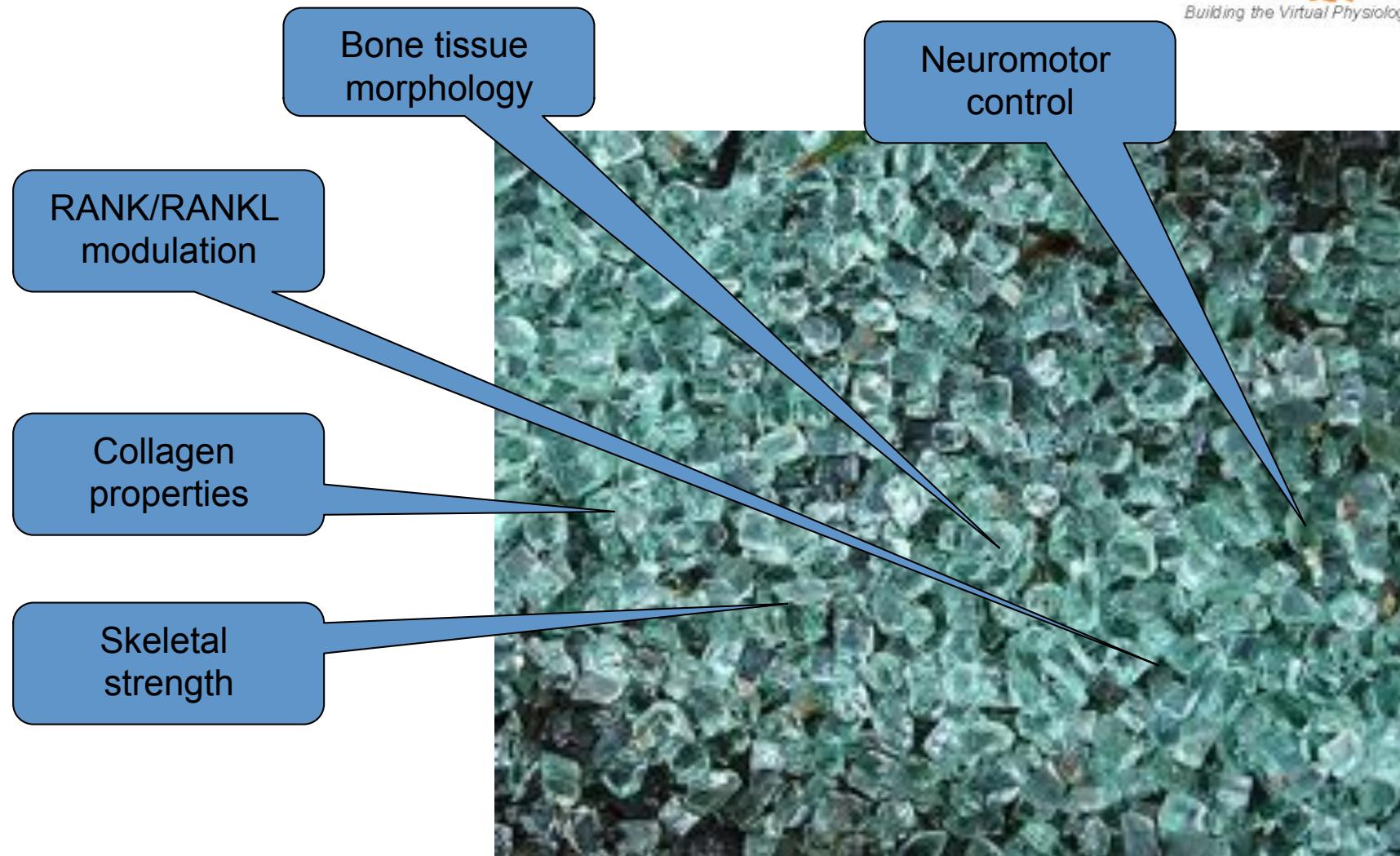


# Collaborative Modeling and Simulation: the Virtual Physiological Human vision

Marco Viceconti

VPH Institute & Istituto Ortopedico Rizzoli

# Like a shattered glass

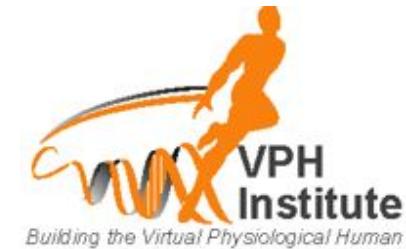


# The Human Jigsaw

- The human body is currently investigated as if it is a jigsaw puzzle made of a trillion pieces
- We are trying to understand the whole picture by looking at a single piece, or at a few closely interconnected pieces
- We do need a frame, within which we can finally start to place the pieces all together, and the glue that connects them
- The frame is not the whole picture, but is the only way we might hope to see it one day



# Integrative research



The Integrative Research approach requires  
a **radical** transformation on the way  
biomedical research is conducted

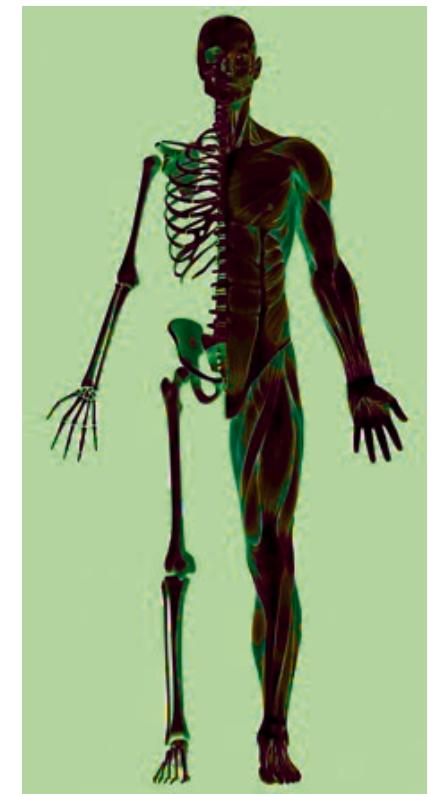
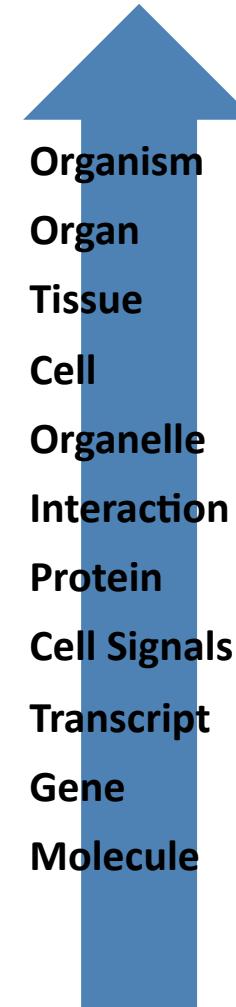
That is why it is necessary to create a  
framework made of technology and  
methods

This framework is called  
**Virtual Physiological Human**

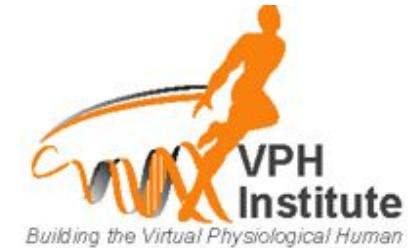
# What is the VPH?



The Virtual Physiological Human is a methodological and technological framework that once established will enable the investigation of the human body as a single complex system.



# Why predictive models?



Capture  
knowledge

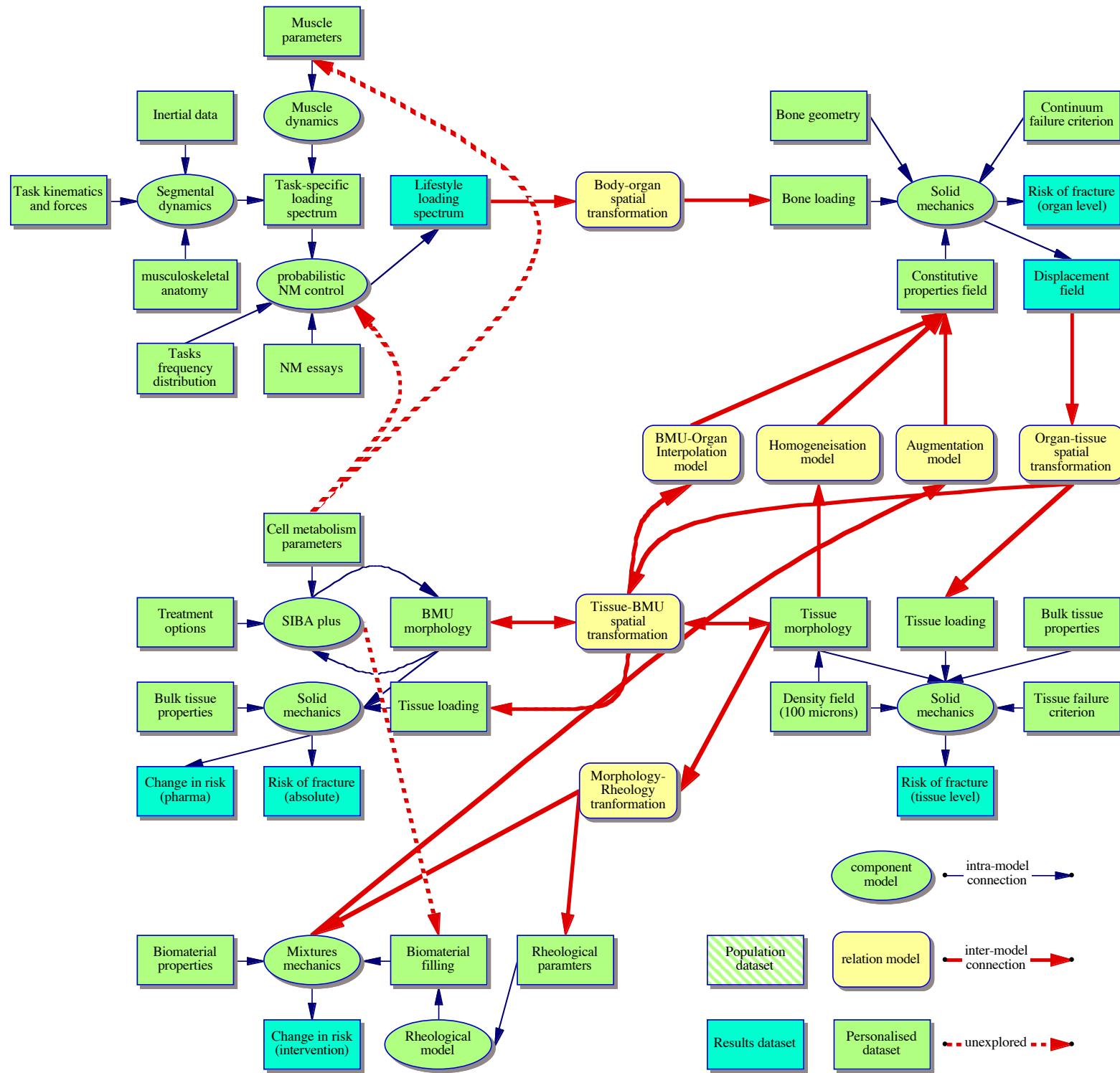
Reusable

Predictive  
models

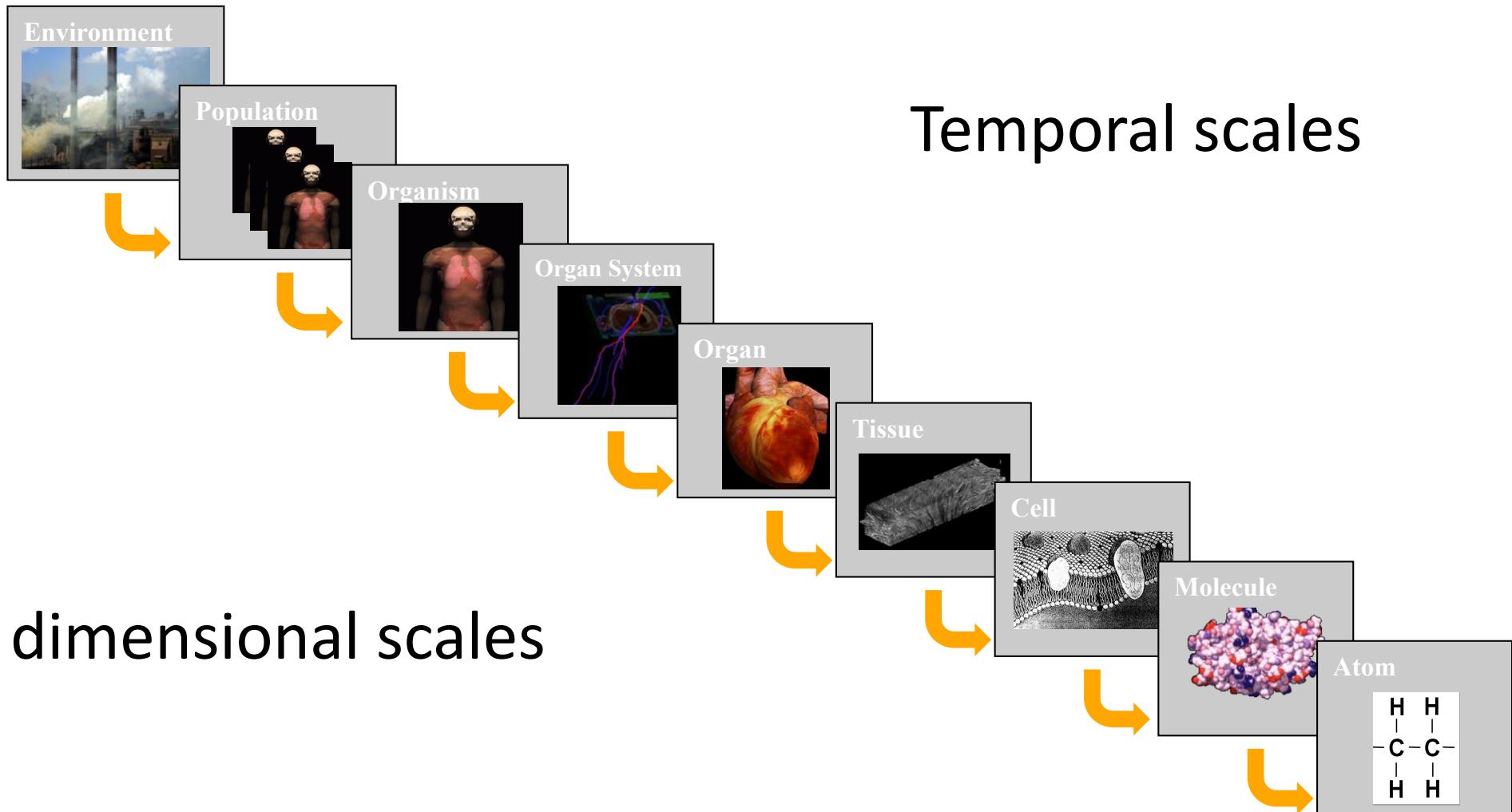
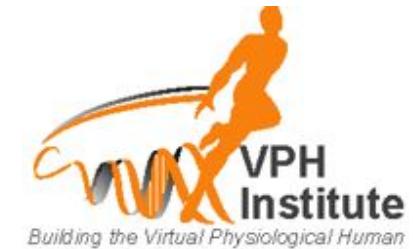
Subject  
Specific

Digital Artefacts

Integrable

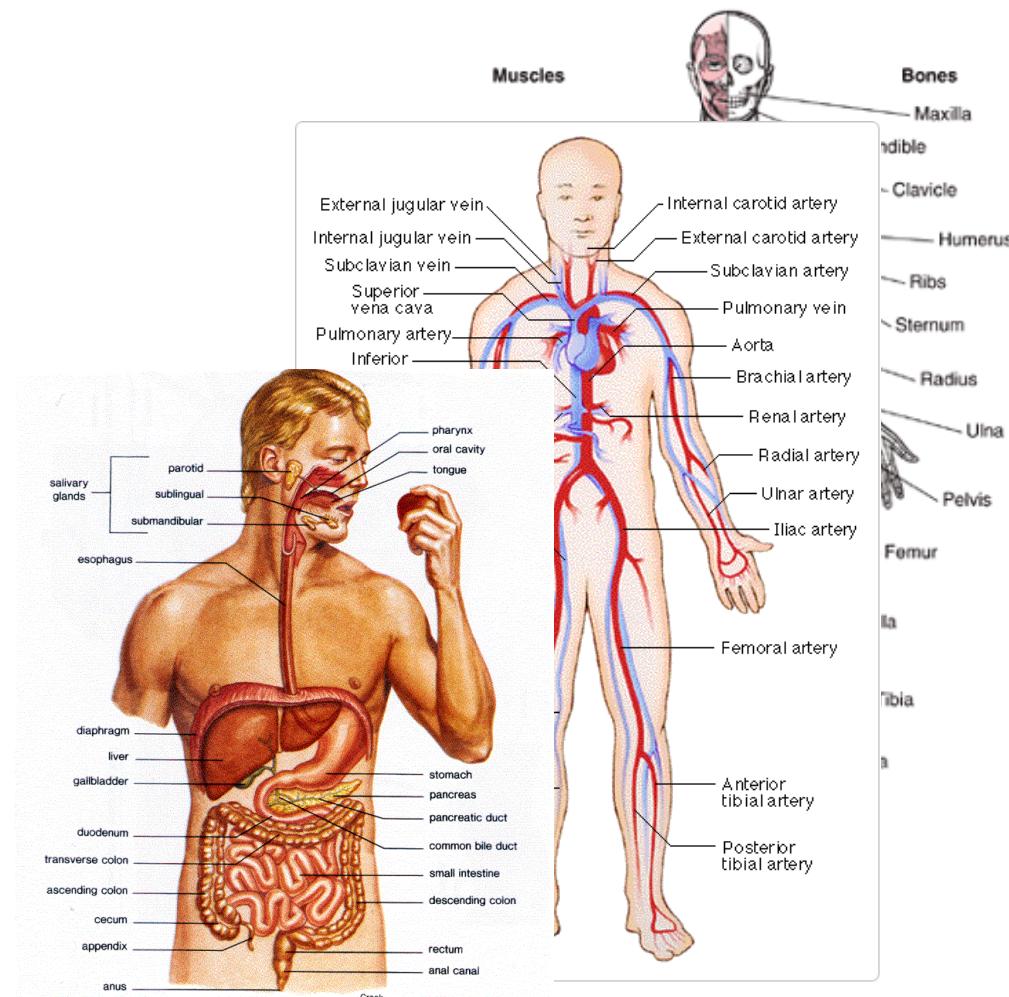


# Integration across...

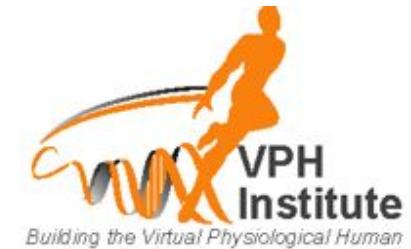


# Integration across...

## Organ systems



# Integration across...

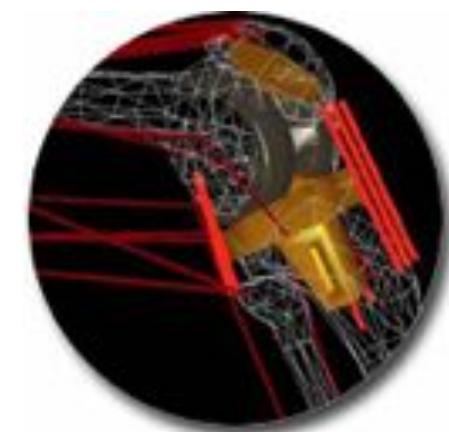


Medicine

## Knowledge domains

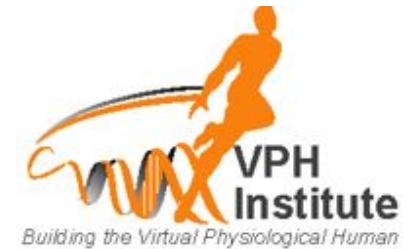


Biology



BioEngineering

# Where the VPH began



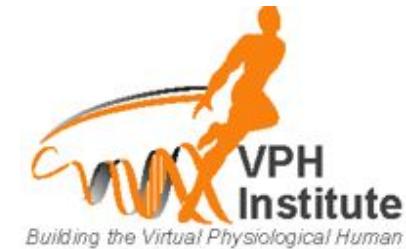
Final document of the Workshop:  
“Towards virtual physiological human: Multilevel  
modelling and simulation of the human anatomy  
and physiology”  
Barcelona, 1-2 June 2005



FP6 ***STEP: A Strategy for the EuroPhysiome.***  
Outcome of consultation/STEP roadmap  
document was FP7 call 2 Objective ICT-2007.5.3:  
**Virtual Physiological Human**



# VPH Network of Excellence

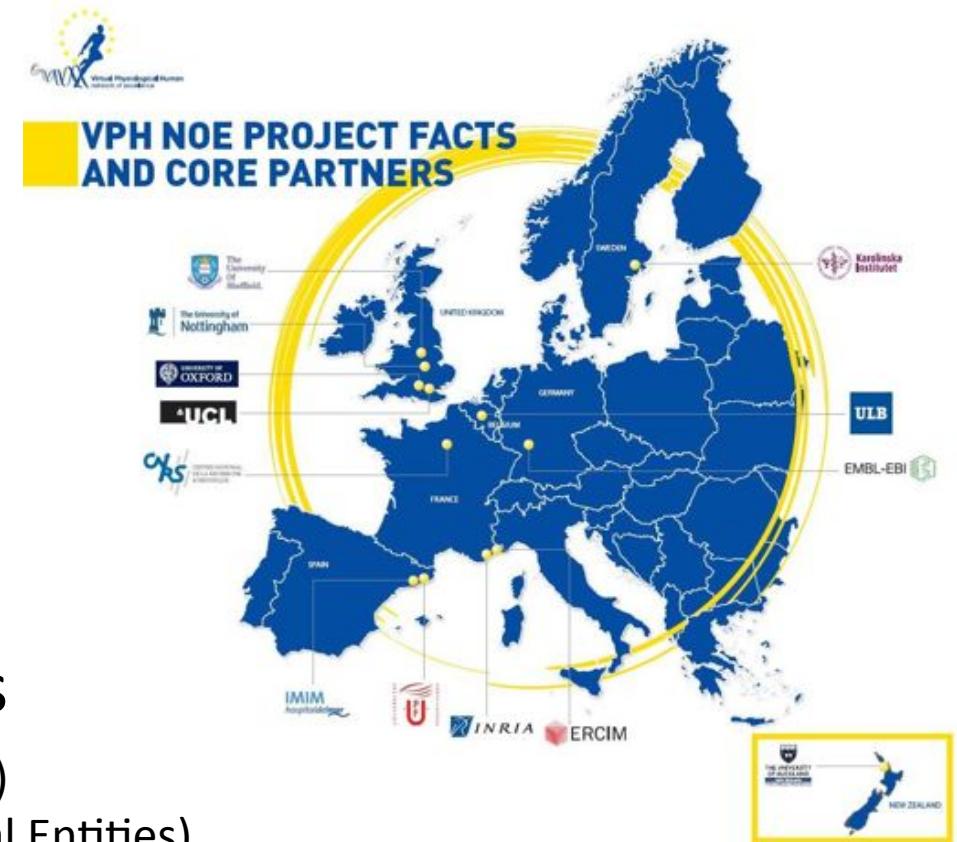


- **14 Core Partners**

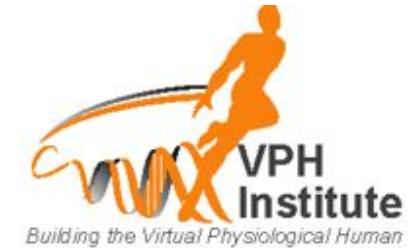
- 4 UK (UCL, UOXF, UNOTT, USFD)
- 3 France (CNRS, INRIA, ERCIM)
- 2 Spain (UPF, IMIM)
- 1 Germany (EMBL [EBI])
- 1 Sweden (KI)
- 1 Belgium (ULB)
- 1 New Zealand (UOA)
- 1 Italy (IOR)

- **Associate / General Members**

- 33 General Members (Academic Institutions)
- 9 Associate Members (Commerical/Industrial Entities)
- ... and growing



# FP7 call 2 projects



CV/ Atherosclerosis IP



Heart/ LVD surgery  
STREP



Oral cancer/ BM  
D&T STREP



Heart /CV disease  
IP



Vascular/ AVF &  
haemodialysis STREP



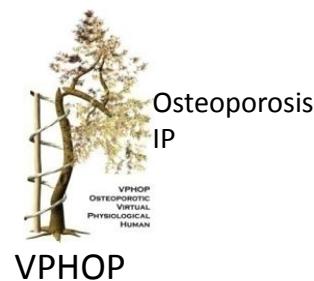
Heart /CV disease  
STREP



Grid access CA



Liver surgery STREP



Networking  
NoE



Cancer STREP



Alzheimer's/ BM &  
diagnosis STREP

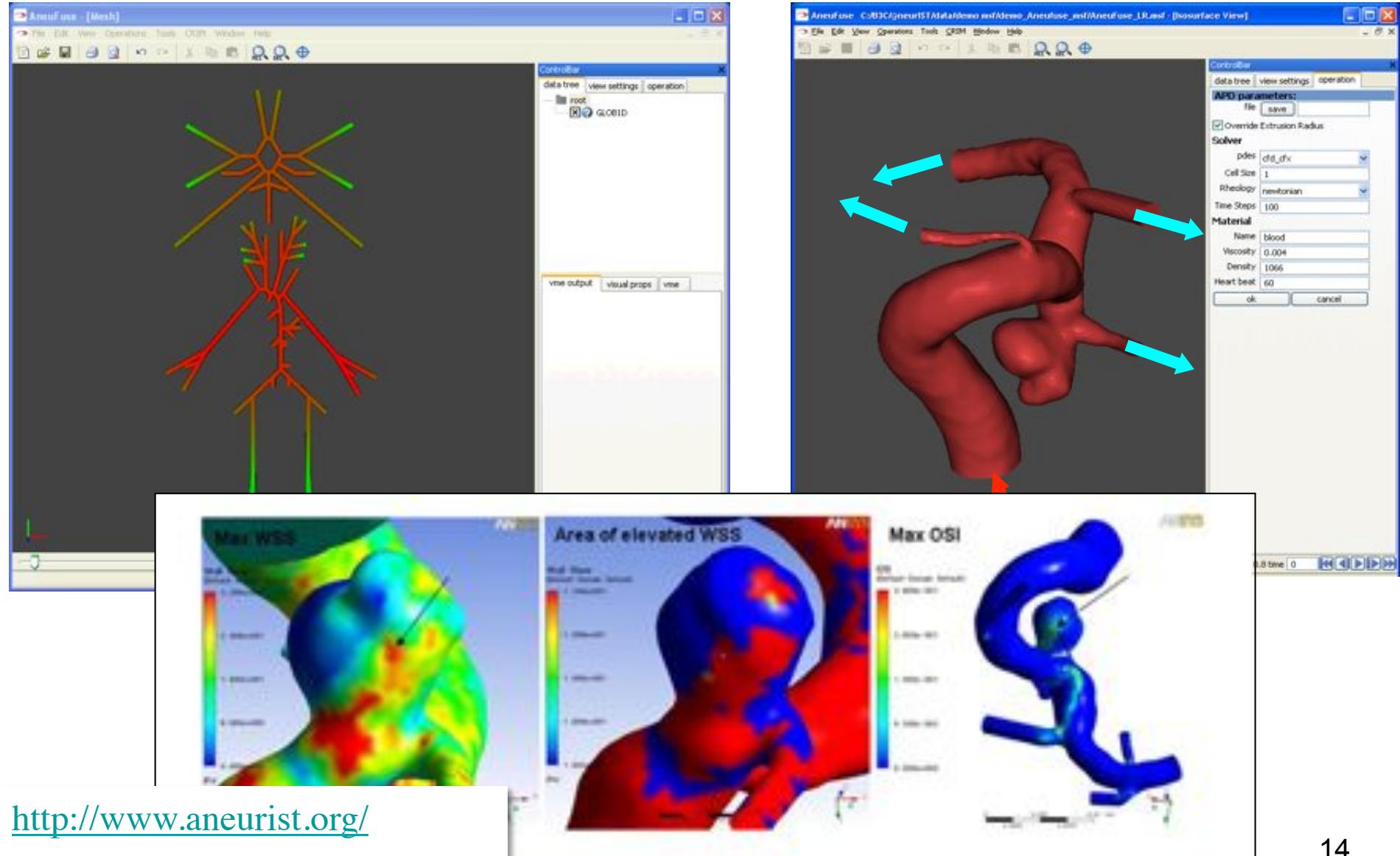


Security and  
Privacy in VPH CA



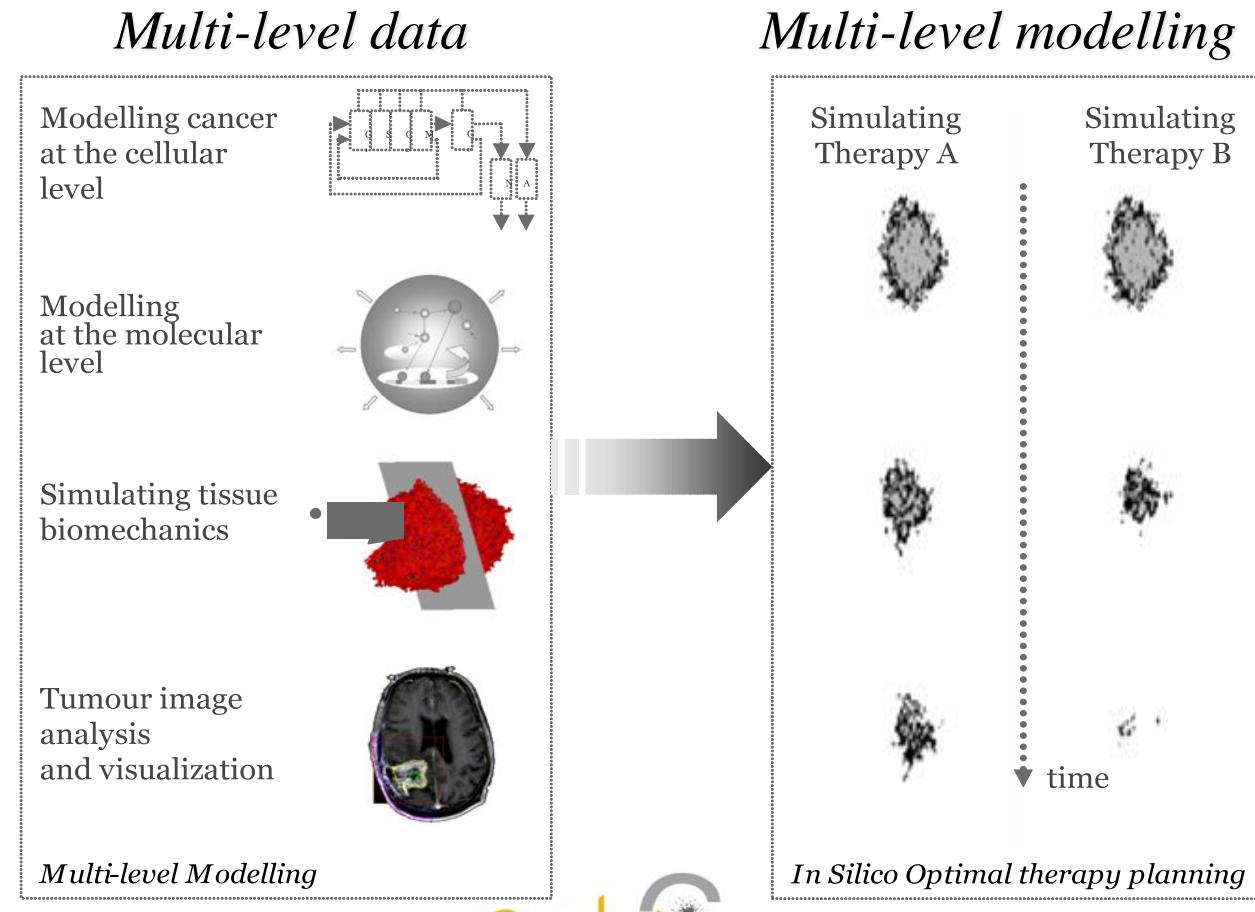
# aneurist

Integrated biomedical informatics for the management of cerebral aneurysms



- ContraCancrum will integrate molecular, cellular, tissue and higher level modelling concepts into a single technological entity that will simulate therapy outcome based on the individual patient information.
- This could serve as a powerful weapon to better understand and fight cancer. The most important IT challenge is to integrate across different scales into an integrated cancer therapy/growth simulator.
- The primary clinical challenge is to gather histopathology, microarrays and multi-modal imaging exams (e.g. DT-MRI, CT, etc) of the same patient.
- A significant validation on lung and brain cancer cases will demonstrate the added value of modelling assisted cancer therapy design and will pave the way for its future clinical use.

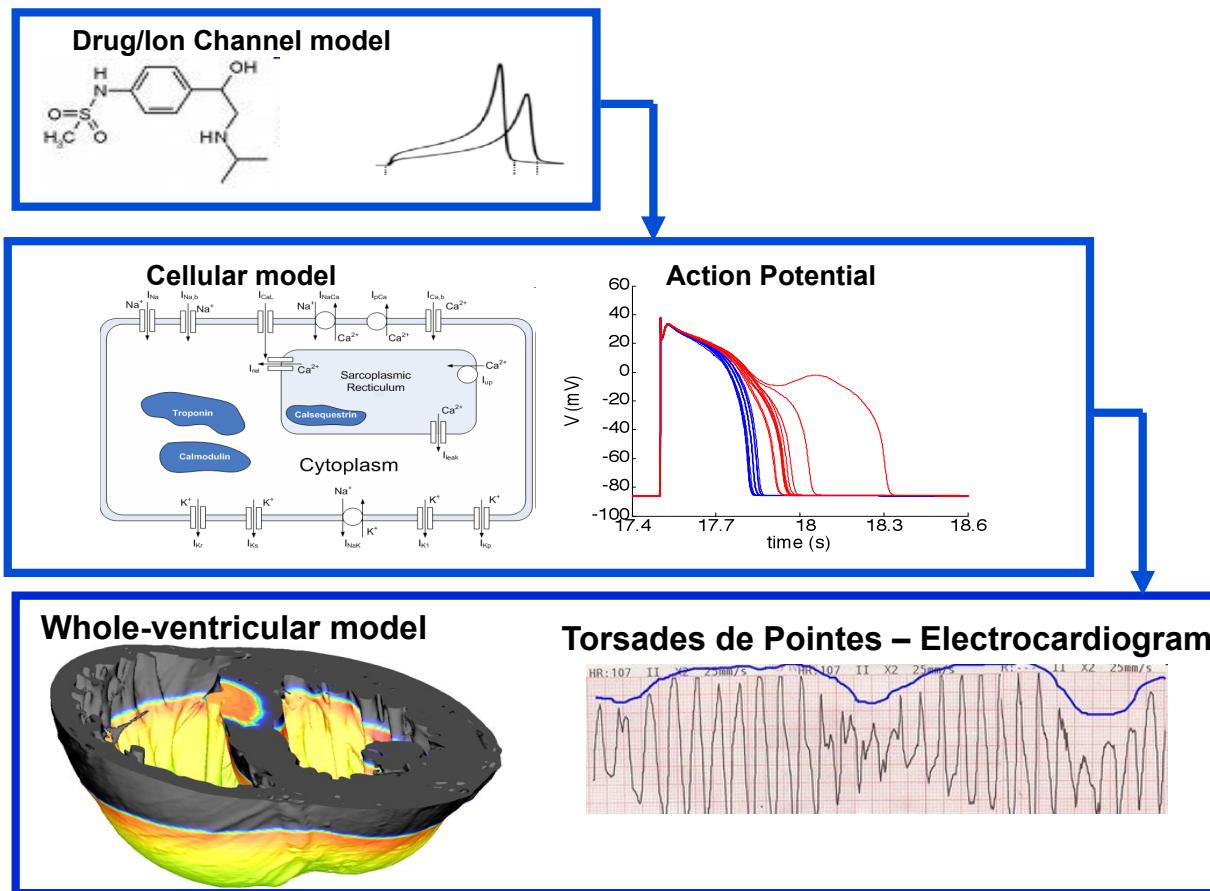
# Clinically Oriented Translational Cancer Multilevel Modelling



# PreDiCT: Computational Prediction of Drug Cardiac Toxicity



**Aim:** to identify **new biomarkers of drug-induced cardiotoxicity** using computational modelling and simulation techniques





## A Major National Initiative

Funded by the German Federal Ministry  
of Education and Research

www.virtual-liver.de



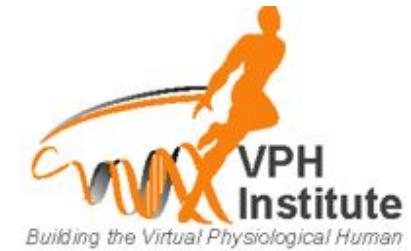
Bundesministerium  
für Bildung  
und Forschung

www.bmbf.de



Federal Ministry  
of Education  
and Research

# What is VPH?



- Cover all organ systems, all scales.
- Large-scale research initiative.
- Started in 2005, > €200m funding, > 2000 researchers in Europe.
- International ramifications in USA, Japan, Korea, Australia, China, etc.
- A network of Excellence, a congress, three special issues on TRS, *a virtual institute*



# Join the VPH Institute today!

**2011 membership is free**

<https://www.biomedtown.org/vphinstitute/>

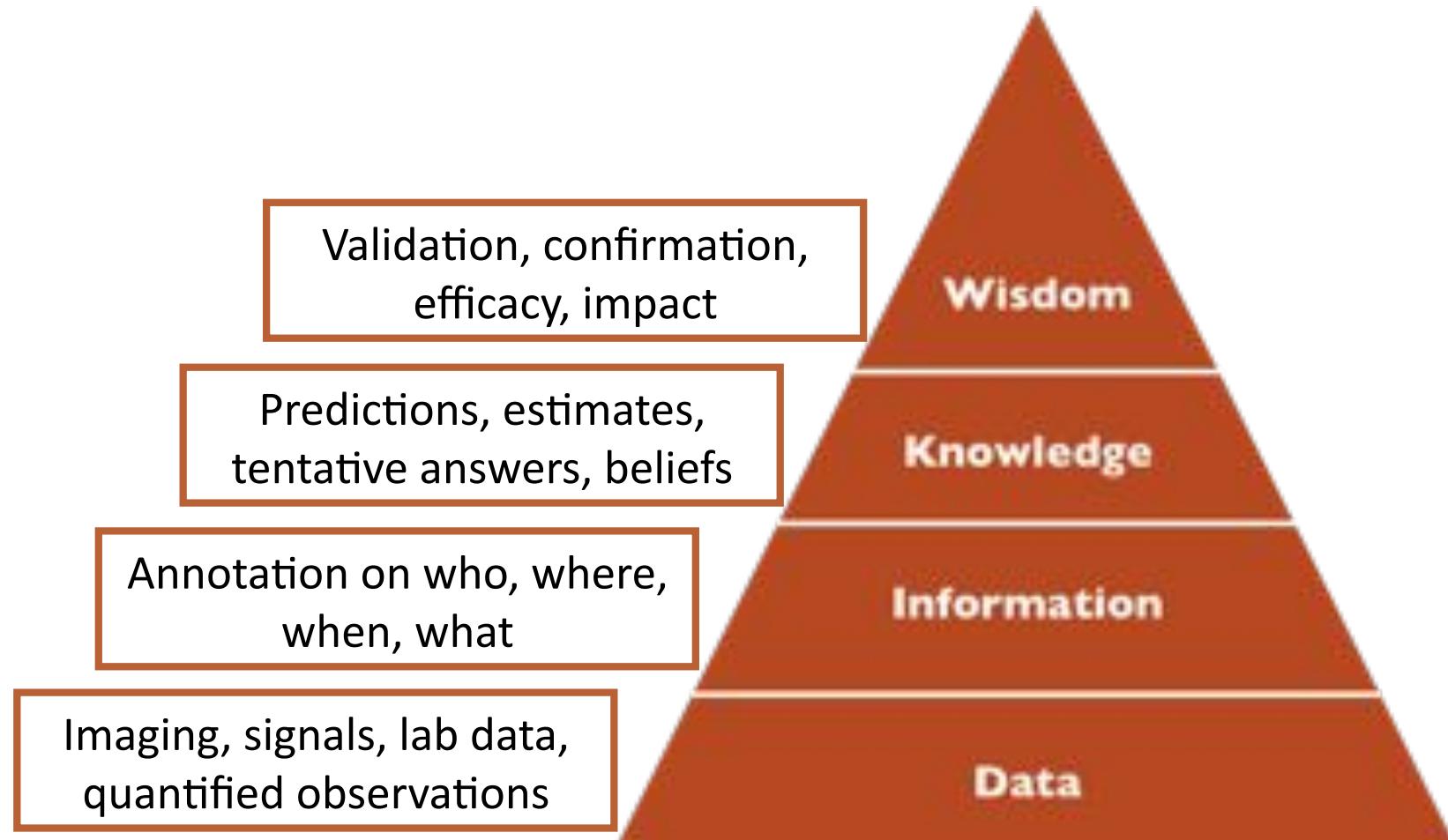
First General Assembly:  
28 September 2011  
Universitat Pompeu Fabra



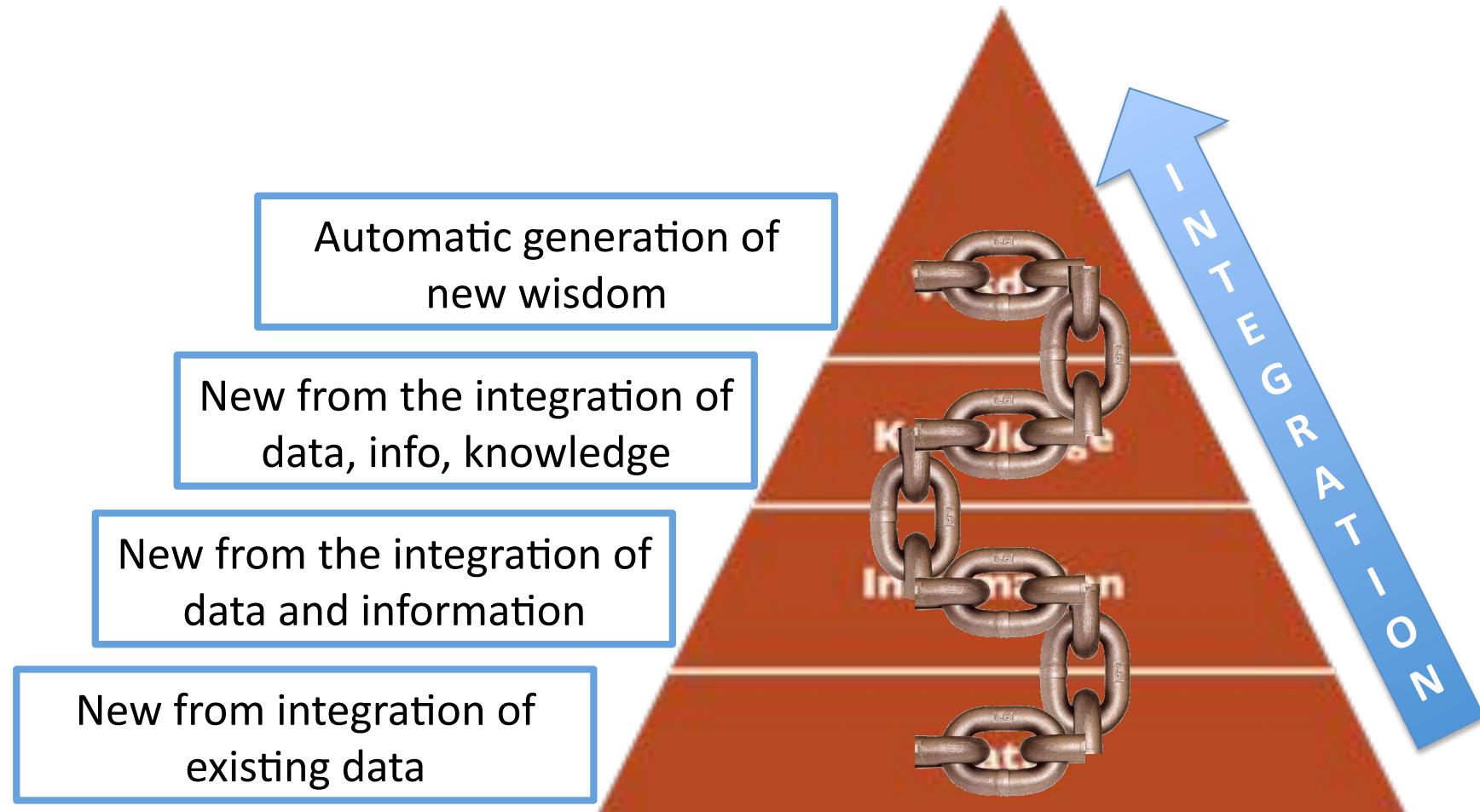
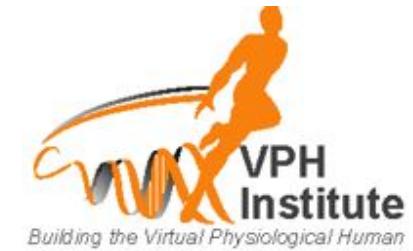


# Collaborative production of integrative knowledge

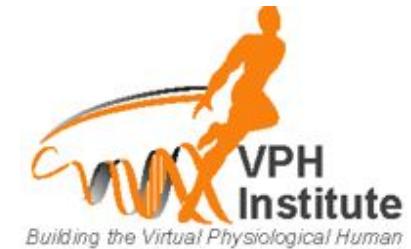
# DIKW Pyramid



# VPH Infostructure



# VPH Infostructure



- From data to information → **Secure Health Data Cloud**
  - all health data (clinical, personal, research, industrial) into a single cloud virtually accessible from anywhere, but under strict access control
- From information to knowledge → **Personalised models**
  - process data into subject-specific predictive models to assist prevention, diagnosis, planning, treatment, and rehabilitation
- From knowledge to wisdom → **A web of predictive models**
  - all predictive models into an integrative cloud that represents the infinitely complex system of life



You are here: Home

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- [Users Forum](#)
- [The last News](#)
- [Suggest a new Feature](#)
- [Submit a bug](#)

- [The BML data collections](#)
- [The LML data collections](#)
- [Ad Repository](#)

PhysiomeSpace is the digital library service designed to help researchers to share their biomedical data and models.



The service is aimed at helping researchers to share their biomedical data and models. PhysiomeSpace has just completed its beta implementation and it is now open to beta users willing to start using it and to provide suggestions for further improvements.

[Start now](#)



## JOIN THE BETA PROGRAM!

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(you must log in)

HOME PAGE



## Getting Started

The access to the beta program is free, thus to get access you should:

- [Subscribe to PhysiomeSpace](#)
- [Now you can access the service](#)
- [Download the client application - Members only](#)



## Documentation

- [Read the user's manual - Members only](#)
- [See the list of reported bugs](#)
- [See the new features section](#)
- [Read the terms of use](#)

IN BRIEF



## public repository

you are here: Home → public repository

- Recent:
  - 1000 VMEs & VMs posted Jan 13, 2011
  - 1000 VMEs & VMs posted Jan 28, 2010
- Import:
  - Add existing documents

- Recent:
  - Import 10 VMEs
- Import:
  - Add existing documents

Total Quality: 1000 VMEs  
Total Agreements: 1000 VMEs  
Agreements: 1000 VMEs  
Pending: 1000 VMEs

## Public Repository

Maximum items per page: 10 20 50 100

Quality index: Default Quality Index

Order by: name owner quality date

< prev 1 2 next >

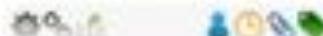
mat\_test\_import\_export\_VME



mat\_test\_import\_export\_VME



mat\_test\_import\_export\_VME



test\_vulture



series\_IC\_6\_320x240x4



PUBLIC  
REPOSITORY

There are public data collection. These VMEs are shared with all members of PhysiomeSpace

13, 2011

In 3D  
model

28, 2010

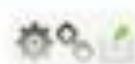
Maximum items per page:

Quality index:

Order by:

< prev 1 2 next >

-  Execution Webservice
-  [mif test import export VMI](#)
-  DataSource Link
-  Request for sharing
-  res\_CT\_0\_238x184x84



DataSource Owner

DataSource upload date

Binary size

Metadata quality

PUBLIC  
REPOSITORY

© 2011 SCS



## public repository

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**Recent**

[After plasma & reseeding](#)  
Paper ID: 1  
Sep 13, 2011

[Comparing Between 2D  
Systolic pressure related  
available on  
PhysiomeSpace](#)  
Sep 28, 2010

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PUBLIC  
REPOSITORY  
#1 New request

[Maria Rizzo](#) Log out My timeline My saved My dashboard

## Public Repository

Maximum items per page: [10](#) [20](#) [50](#) [100](#)

Quality index: [Default quality index](#) [Review](#)

Order by: [Title](#) [Owner](#) [Quality](#) [Last updated](#)

[page 1](#) [2](#) [Next >](#)

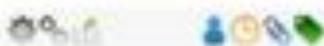
[mf\\_test\\_import\\_export\\_VME](#)



[mf\\_test\\_import\\_export\\_VME](#)



[mf\\_test\\_import\\_export\\_VME](#)



[test\\_valence](#)



[www\\_1CT\\_0\\_228x100x84](#)



Click here to send a  
request for sharing to the  
dataresource owner



## user's repository

you are here: [home](#) > [users](#) > [mario Rossi](#)

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### New

[View version 3.0: Simiology](#)

Report ID:

Jan 13, 2011

[View complete dataset 100](#)

Dataset maximum width:

available for:

PhysiomeSpace

Jun 28, 2010

[More details](#)

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PUBLIC  
REPOSITORY  
#5 New request

**Info** Requested DataResource(s) added to your basket.

## Mario Rossi's Basket

Maximum items per page:

1

Order by:

[Title](#)

[Author](#)

[Quality](#)

[+ date](#)

[+ years](#)

1

[years +](#)

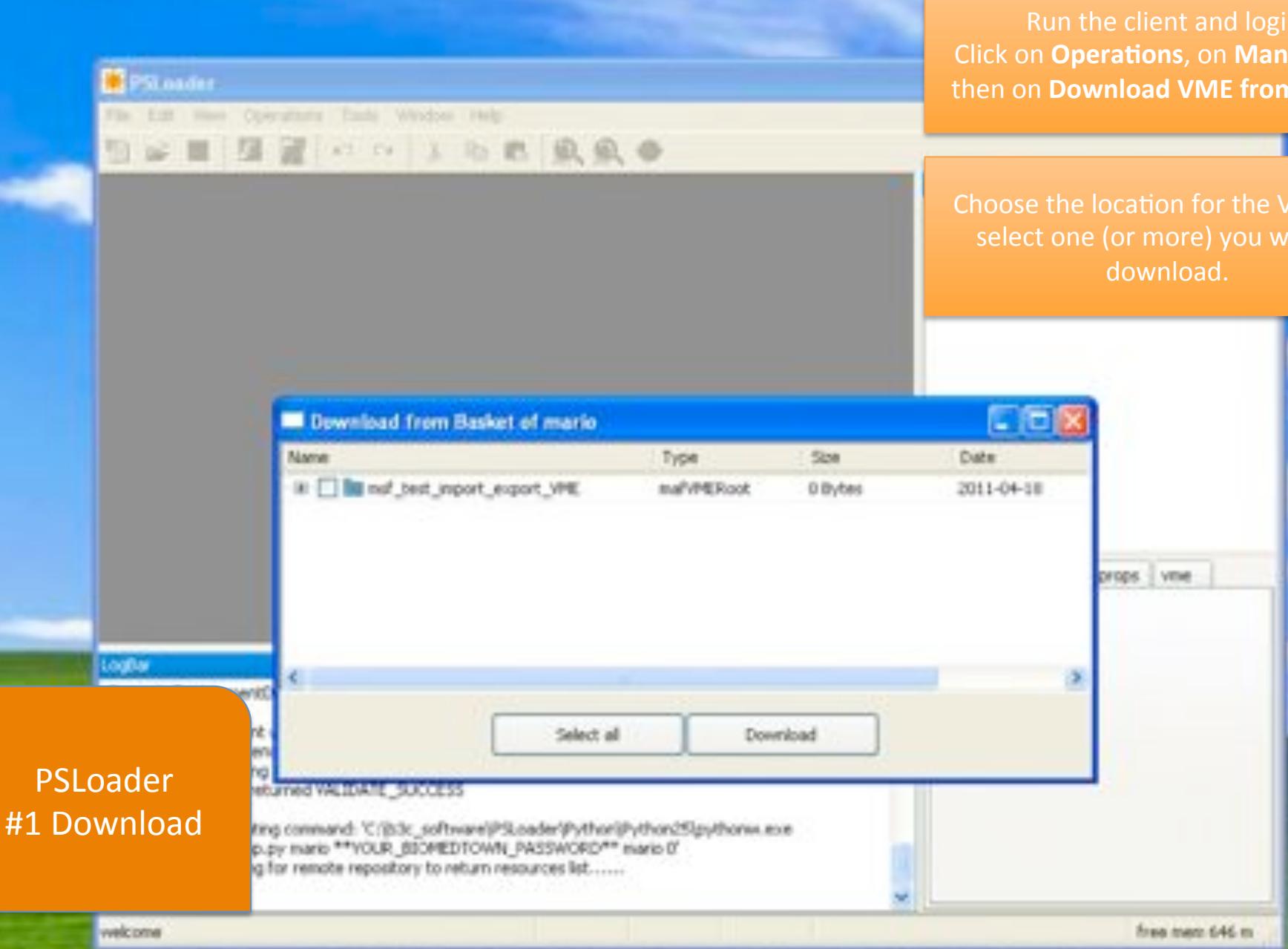
[mat\\_test\\_import\\_export\\_VHD](#)



Now you have the DataResource in  
your basket.

You can download it  
(you must run the client)

4 datasets



PSLoader  
#1 Download

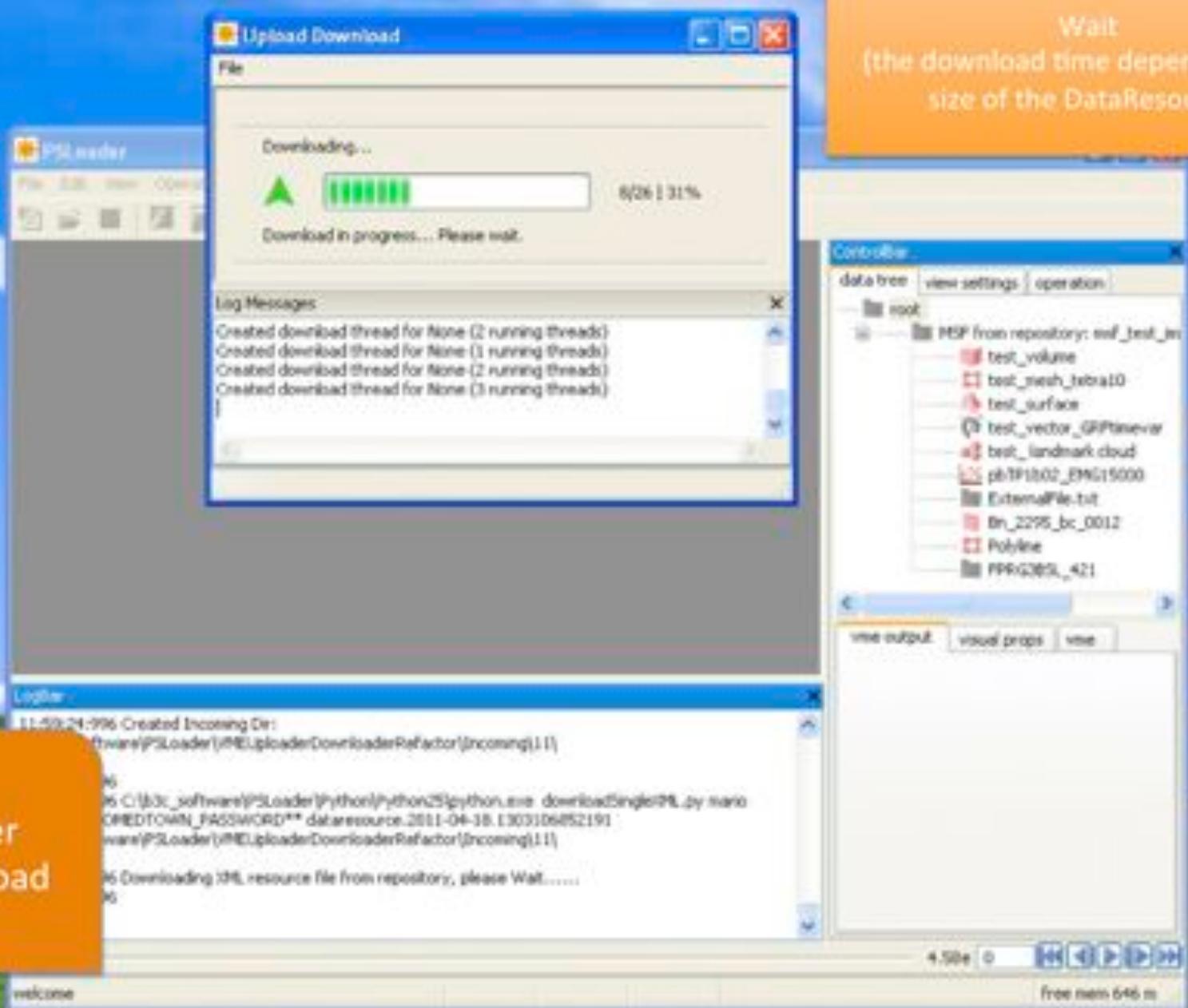
Run the client and login.  
Click on **Operations**, on **Manage** and  
then on **Download VME from Basket**

Choose the location for the VME and  
select one (or more) you want to  
download.

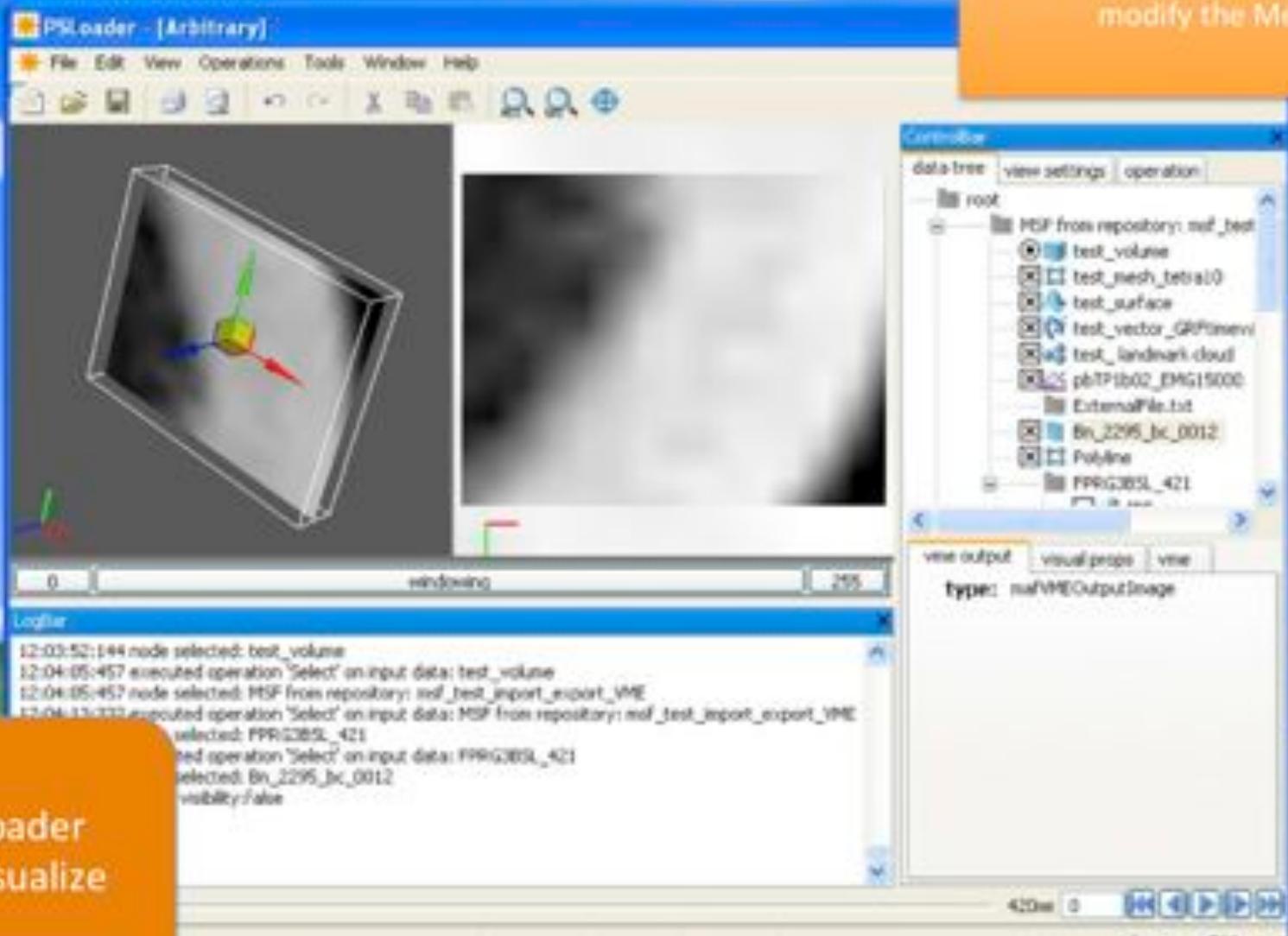
## PSLoader #2 Download

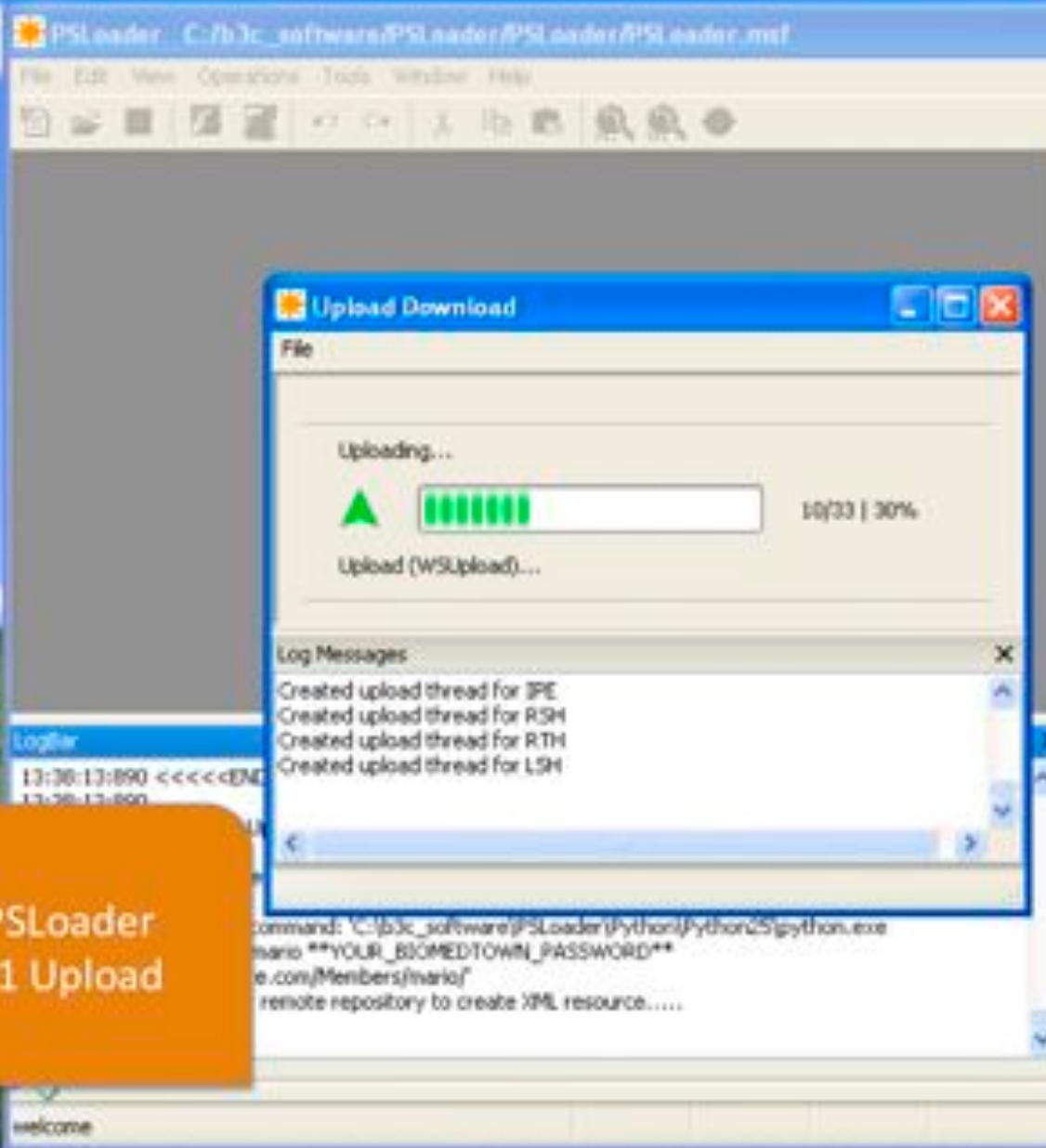
welcome

Wait  
(the download time depends on the  
size of the DataResource)



Now you can visualize the VME and  
modify the Metadata





To able to upload a new DataResource (the one you have modified, or a new one) open it, and click on **Operation**, **Manage** and then on **Upload Multi-VME**

test\_mesh\_tetra10

Wait  
(the upload time depends on the size  
of the DataResource)





The DataResource is now in your  
Sandbox

home users news events public

## Mario's repository

You are here: home → users → mario rossi

### Shares

View shares & DataResources

Paper 11  
Jan 13, 2011

Complete human 3D  
human skeleton model  
available on  
PhysiomeSpace

June 28, 2010

Share share

### DATA

Download

### Tools

Add citation information

SANDBOX

## Mario Rossi's Sandbox

Maximum items per page: 5 10 20 50 100

Quality index: Default Quality Index

Sort by: Order by

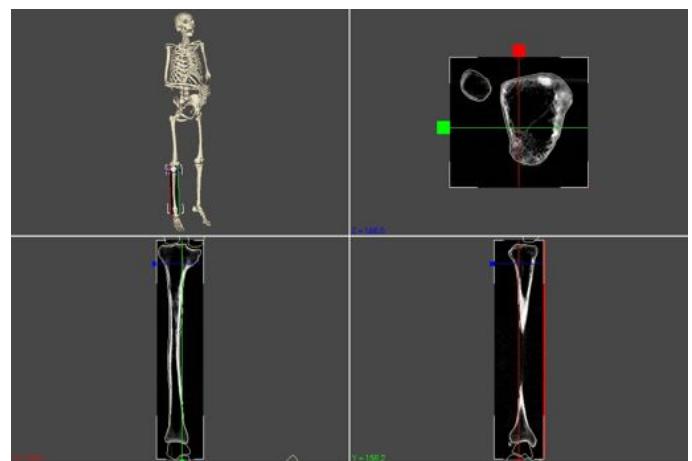
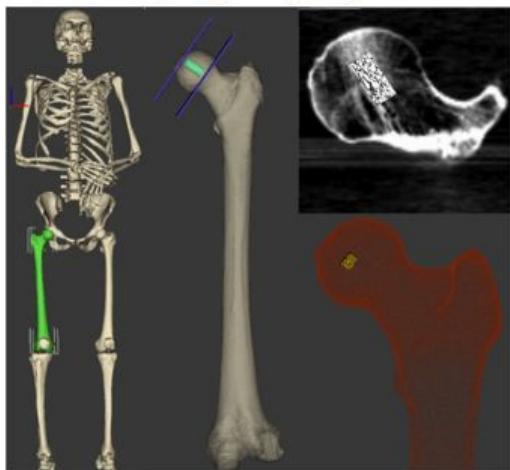
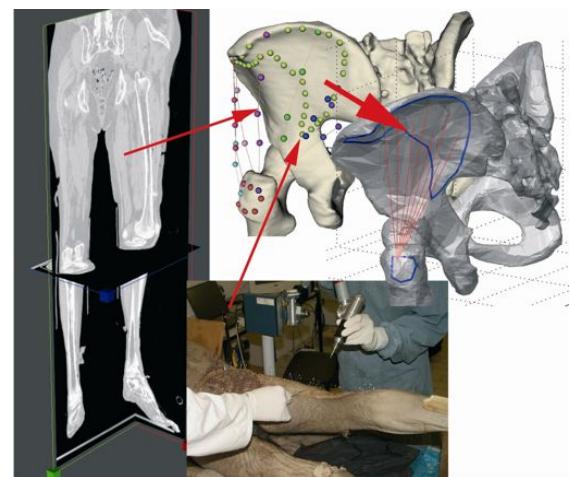
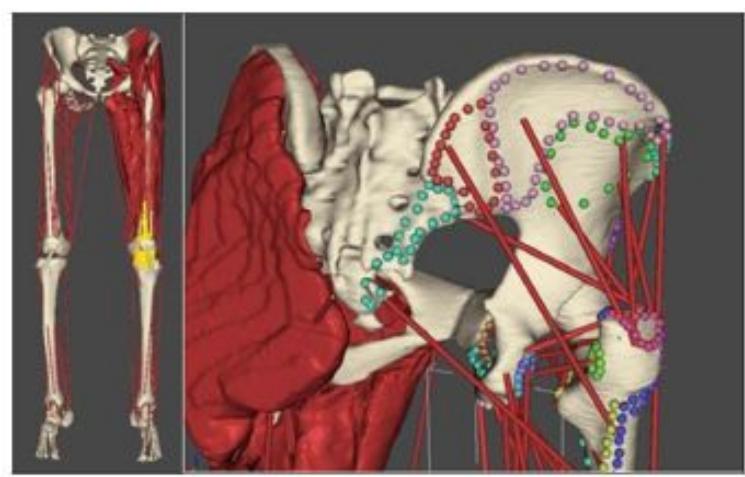
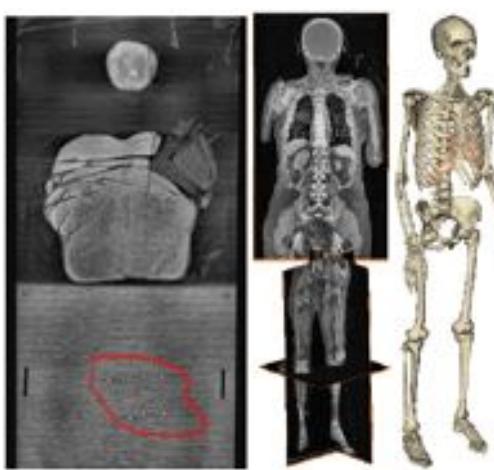
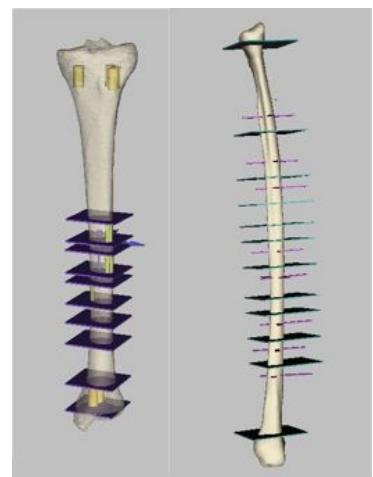
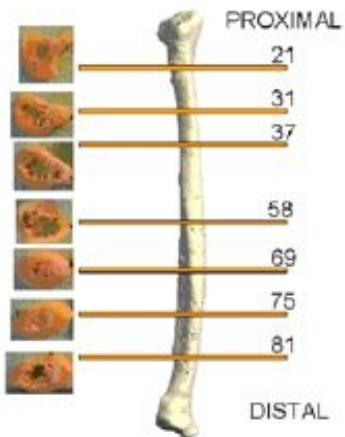
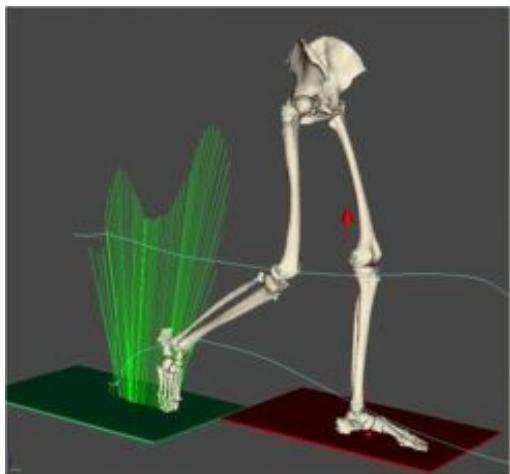
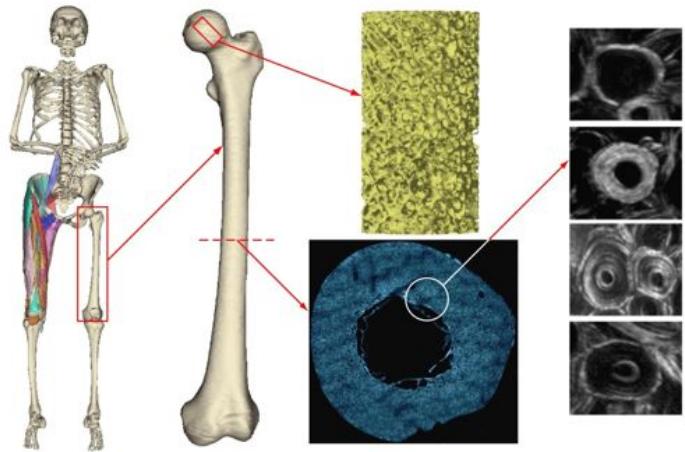
← prev 1 next →

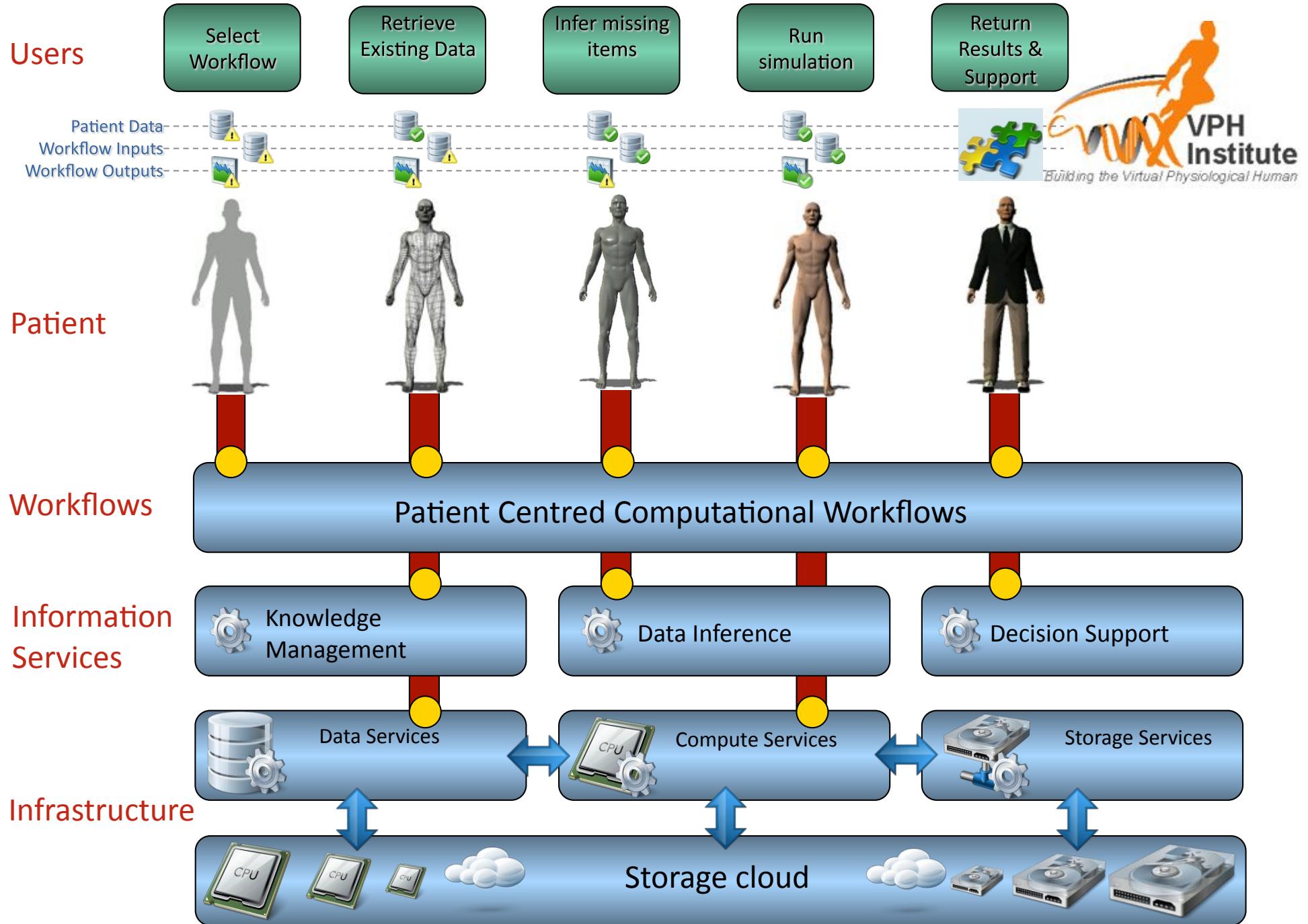
PSI Loader



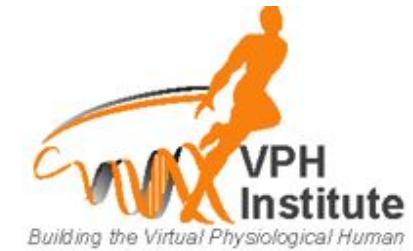
Here you can:

- Edit the metadata
- Share the DataResource with others users
- Delete the DataResource
- Add a licence

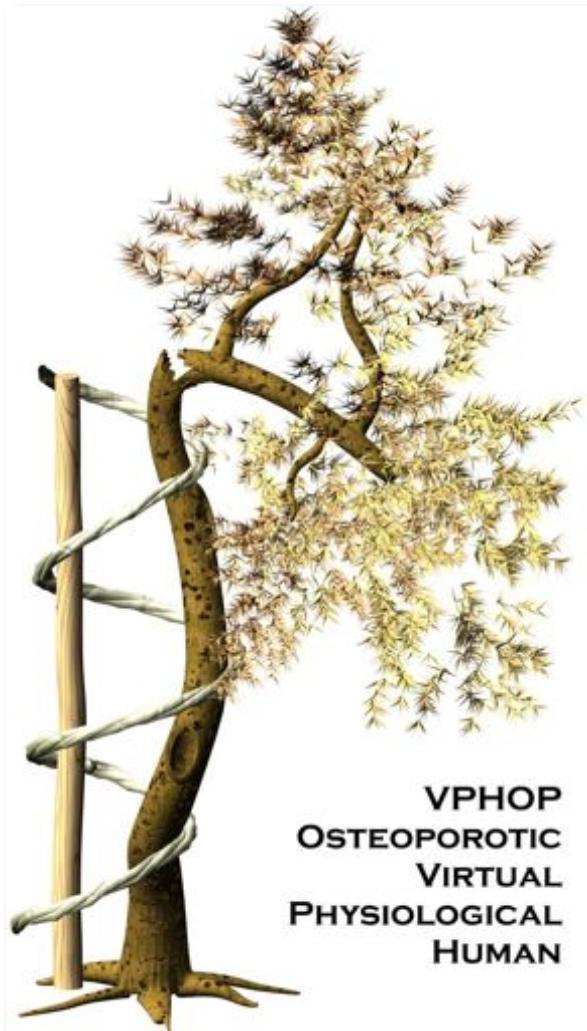




# What's next?



- Live linked data
  - Based on the linked data metaphor:
    - Use URIs as names for things
    - Use HTTP URIs so that people can look up those names.
    - When someone looks up a URI, provide useful information
    - Include links to other URIs, so that they can discover more things.
  - Add a new type of linked data, that is the result of the calculation of a predictive model, which uses as input other linked data



# VPHOP: multiscale modelling to fight osteoporotic fractures

By Marco Viceconti  
Project Coordinator

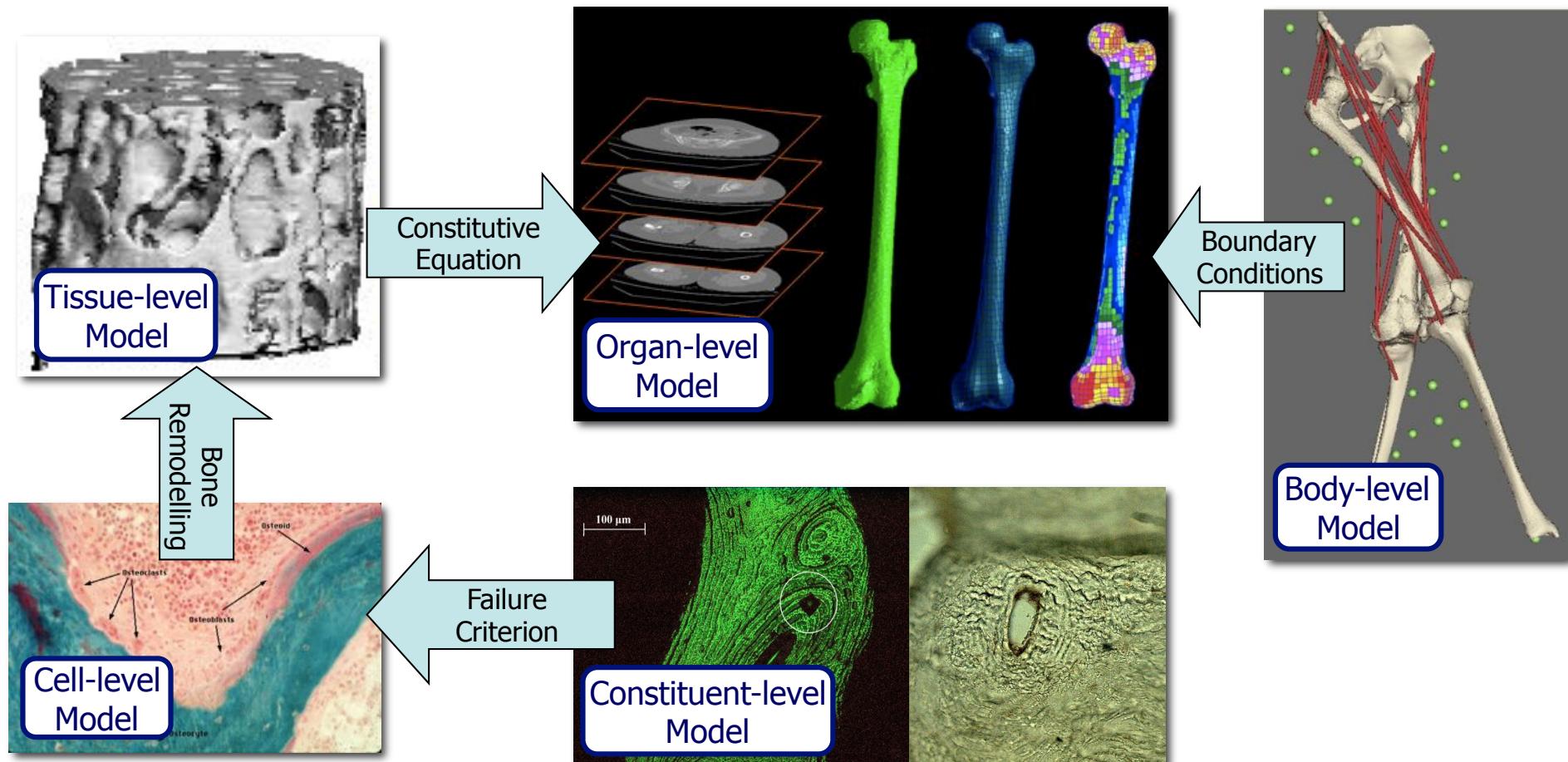






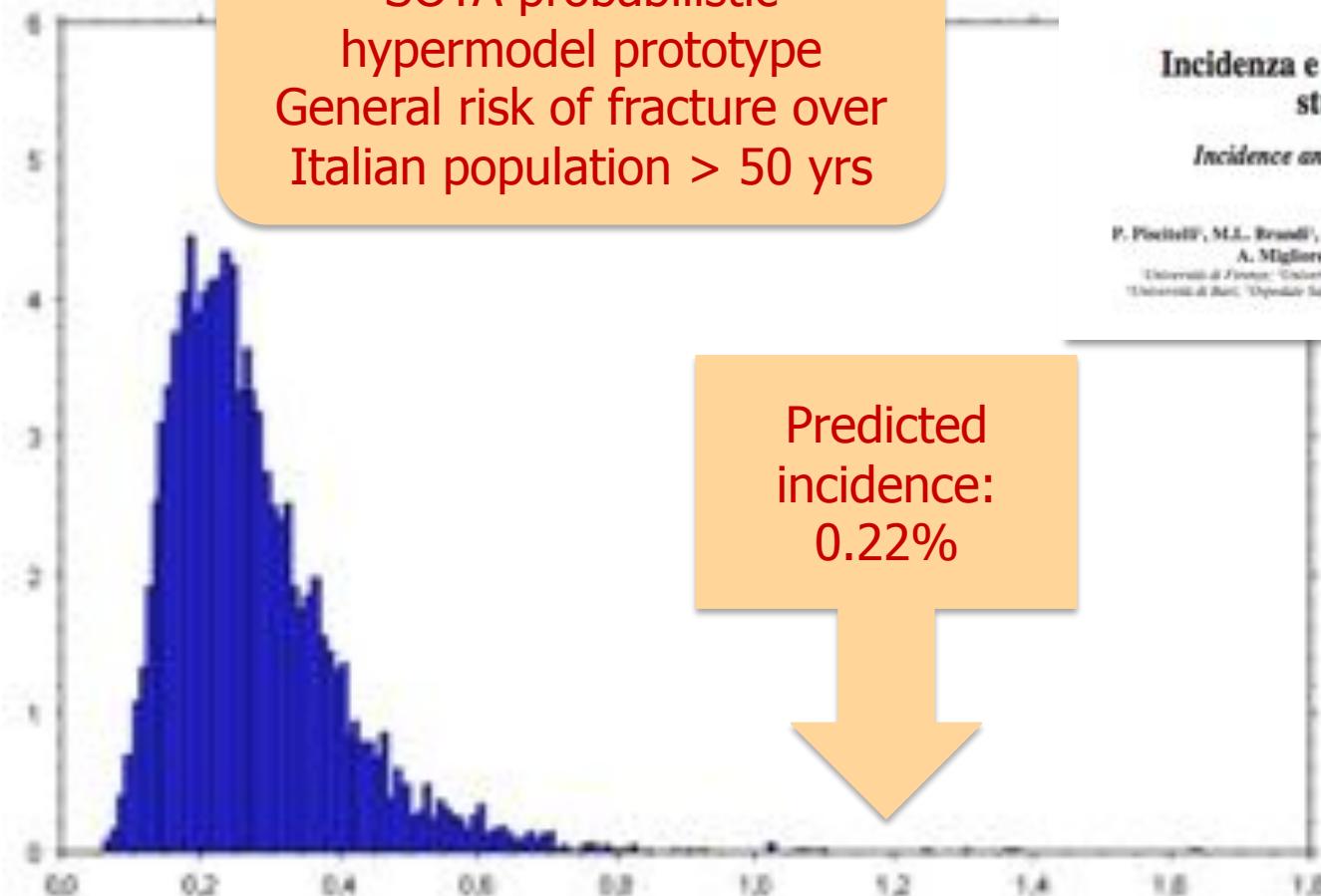
# VPHOP Technology to fight osteoporosis

Osteoporotic  
Virtual Physiological Human





# Integrative modelling works!



Franzini A, 2009; 4(2):113-119

LAVORO ORIGINALE

**Incidenza e costi delle fratture di femore in Italia: studio di estensione 2003-2005**

*Incidence and socioeconomic burden of hip fractures in Italy: extension study 2003-2005*

P. Piscitelli<sup>1</sup>, M.L. Brandi<sup>1</sup>, U. Tarantini<sup>1</sup>, A. Baggianni<sup>2</sup>, A. Distante<sup>3</sup>, M. Marzocchi<sup>4</sup>, V. Grattaglione<sup>5</sup>, A. Migliore<sup>6</sup>, M. Granata<sup>7</sup>, G. Guglielmi<sup>8</sup>, R. Gimigliano<sup>9</sup>, G. Innamorato<sup>10</sup>

<sup>1</sup>Università di Firenze, <sup>2</sup>Università di Roma Tor Vergata, <sup>3</sup>Università di Pisa, <sup>4</sup>VPHOP, <sup>5</sup>Pisa, <sup>6</sup>Osp. San Giacomo, <sup>7</sup>ASL Lazio, <sup>8</sup>Università di Bari, <sup>9</sup>Ospedale San Pietro-Panthonianum, <sup>10</sup>IRCCS Casa Sollievo della Sofferenza, <sup>11</sup>Università Roma3, <sup>12</sup>Seconda Università di Napoli



# Clinician interface

**VOP**

EOS/QT

CT

XperCT

XtremeCT

ActiBelt long

If needed, you may change the study's role or request access to a new study with a different role.

Info

Study: VPHOP baseline  
Start Date: 01-Nov-2009  
End Date: 31-Dec-2012  
PI: Debora Rizzoli

Protocol Activation/IRB Approval Date: 07-Sep-2009

Statuses

Not Started  
Scheduled  
Data Entry Started

Welcome to VPHOP baseline

You are logged in as a Data Manager.

Notes & Discrepancies Assigned to Me.

Site Enrolled Expected Enrollment Percentage

CHARITE	100	100	100%
GEN	30	100	30%
INGERM	23	100	23%
IOR	32	100	32%

Study Enrolled Expected Enrollment Percentage

VPHOP baseline	223	500	45%
----------------	-----	-----	-----

Event Status # of Events Percentage

scheduled	5	5%
data entry started	366	98%
completed	1	0%
signed	1	0%
locked	0	0%
skipped	0	0%
stopped	0	0%

Study Subject Status # of Study Subjects Percentage

available	173	78%
signed	1	0%
removed	49	22%

Request Personalised Risk assessment

```
graph TD; EOS[EOS/QT] --> VOP[VOP]; CT[CT] --> VOP; XperCT[XperCT] --> VOP; XtremeCT[XtremeCT] --> VOP; ActiBelt[ActiBelt long] --> VOP; VOP --> RPRA[Request Personalised Risk assessment]
```



# UC C5: upload patient data

repository view | edit | sharing | search | sandbox | basket | dashboard | statistics | management

## PhysiomeSpace

maximum items per page: 5 8 update

order by title owner quality - date

<< first < prev 1 2 3 4 5 next > last (10) >>

<a href="#">LHDL_Donor2_Femora_LowerLimbs</a>	IOR LTM	2011-03-21	0.0 %
<a href="#">LHDL_Donor2_Femora_OrganLevelCT</a>	IOR LTM	2011-03-10	0.0 %
<a href="#">LHDL_Donor_1_Femora_OrganLevelCT</a>	IOR LTM	2011-03-10	0.0 %
<a href="#">LHDL_Donor1_Femora_LowerLimbs</a>	IOR LTM	2011-03-10	0.0 %
<a href="#">Cadaver1_LowerLimbsCT_femoral_surfaces</a>	IOR LTM	2011-03-01	66.67 %

[DataSource available for request](#)  
 [DataSource already requested](#)  
 [DataSource can be added to your basket](#)  
 [DataSource description](#)

[DataSource owner](#)  
 [DataSource upload date](#)  
 [DataSource metadata quality](#)  
 [DataSource binary size](#)

[Run an execution webservice with the selected DataSource](#)  
 [Add the DataSource to your basket](#)  
 [The DataSource is already into your basket](#)  
 [Send a request to the DataSource owner](#)



# Service UC: HyperMonitor

## Workflow Editor

- 1 Initialise workflow #1123
- 2 Load 112, \*
- 3 Send 112, morph → LoadingDB
- 4 Send output → OrganLevel
- 5 Send 112,iMV → LargeVOIdb
- 6 Send output → OrganLevel
- 7 Run OrganLevel
- 8
- 9

## Services Status

- |   |  |
|---|--|
| <span style="color: green;">●</span> ParFE        | <span style="color: green;">●</span> SIBA plus   |
| <span style="color: yellow;">●</span> ParFEnl     | <span style="color: green;">●</span> EOSppMT     |
| <span style="color: red;">●</span> Ansys v12      | <span style="color: green;">●</span> CTppMT      |
| <span style="color: yellow;">●</span> Organ-level | <span style="color: red;">●</span> Probab engine |
| <span style="color: green;">●</span> Loading DB   | <span style="color: green;">●</span> Octave      |
| <span style="color: green;">●</span> Large VOI DB | <span style="color: red;">●</span> Open SIM      |

## Command line

```
>Vice: help all  
Start stop kill warn hold query elapsed  
load download erase test help  
>Vice: help load  
Load <patID>, <VmeID>  
This command load a given VME at the  
node closest to the next module in  
execution.  
>  
>Load 112, VmeVolume112a
```

## Log

```
◊ Workflow #1123 executing ....  
◊ Patient ID#112 data loaded  
◊ Querying loading DB ....  
◊ Load spectrum stored  
◊ EOSppMT started  
◊ EOSppMT finished on  
14:44-2012-04-04  
◊ Organ-level started  
◊ Querying Large VOI ....  
◊ CE for patient ID #112 computed  
◊ Organ-level finished on  
19:45-2012-04-04
```



# Mechanical Turks

ORACLE® BPM Worklist  
Welcome, jcooper [jzm.com]

My Tasks Initiated Tasks

My Tasks (Inbox)

Work Queues

- Inbox
- My Work Queues
- Standard Views
  - High Priority Tasks
  - Tasks Due Soon
  - New Tasks
- My Views
  - None
- Proxy Work Queues
  - Delegated Views
  - None

Search: Keyword Category Priority Status Advanced Search

Task Number	Title	Priority	Assigned Users	Assigned Groups	State	Created Date	Expiration Date	Actions
No tasks to display.								

ORACLE® Mobility Worklist

Accession #	Patient ID	Patient Name	Birthdate	Gender	Study Date	Modality	Body Part
00001	Z.Murakami	Joseph	1/10/1900	M	5/23/2006	US	Neck
00004	5	Laliberte, Steve	3/10/1979	F	5/23/2006	US	Neck
00005	6	Malville, Jack	4/15/1900	M	5/23/2006	US	Neck
00006	7	Beaven, Dan	3/9/1962	M	5/23/2006	US	Neck
00007	8	Smith, Valerie	3/15/1964	F	5/23/2006	US	Neck
00008	9	Martin, Jane	11/18/1972	F	5/23/2006	US	Neck
00009	10	Deneen, Joseph	1/30/1961	M	5/23/2006	US	Neck
00010	11	Mulligan, Joseph	5/5/1966	M	5/23/2006	US	Neck
00011	12	Louis, Joe	3/16/1960	M	5/23/2006	US	Neck
00012	13	Jones, Anne	9/21/1945	F	5/23/2006	US	Neck
00013	14	Odebo, Brian	3/22/1967	M	5/23/2006	US	Neck
00014	15	Amen, Francisco	3/27/1962	M	5/23/2006	US	Spine

Create Study Cancel

Oracle BPM Worklist - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Address: http://localhost:9700/integration/worklist/app/TaskList?startRow=1&endRow=11

ORACLE® BPM Worklist

Search: My & Group Any Assigned Advanced Search

Home (My & Group Tasks)

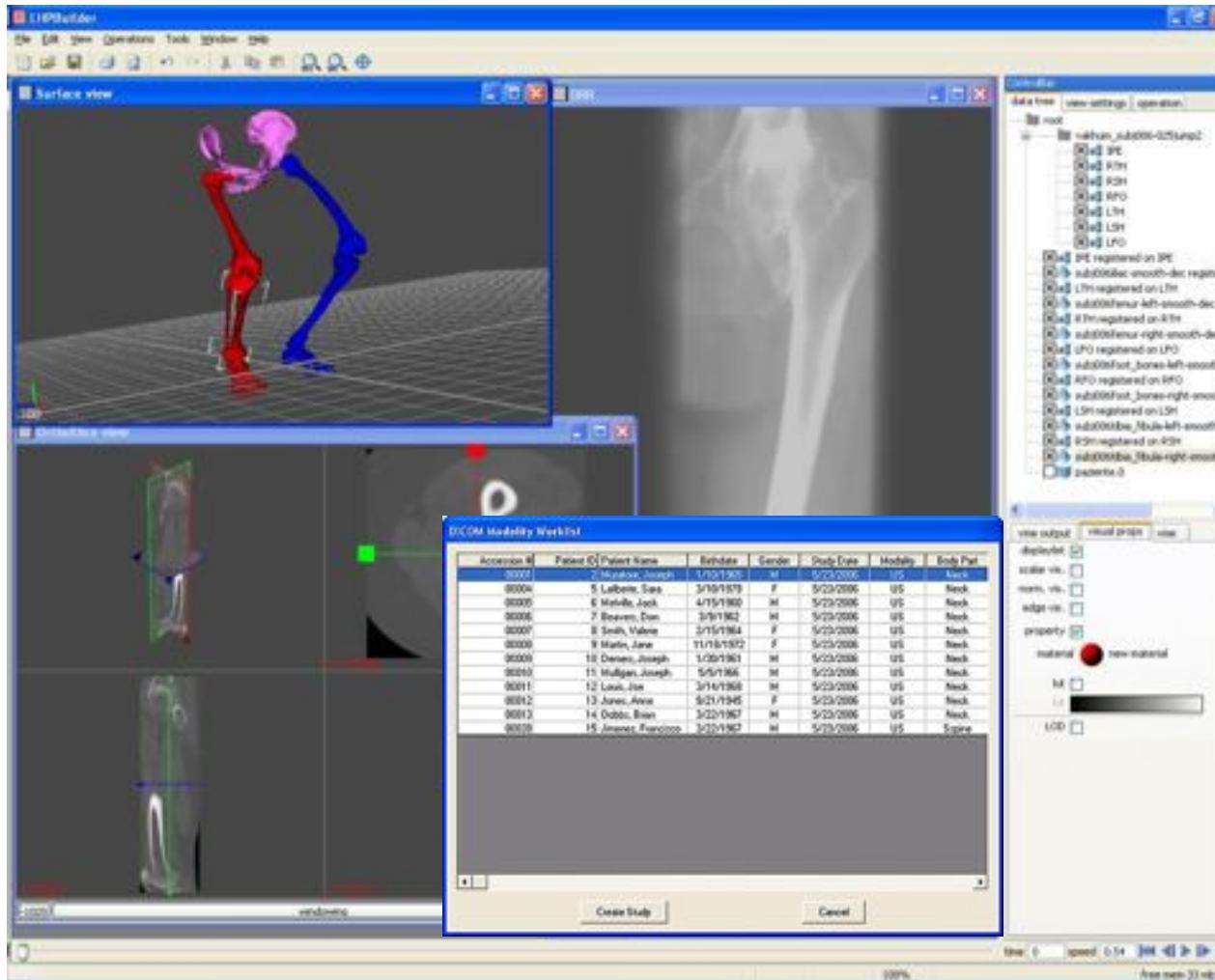
Number	Title	Priority	Males	Assigned	Expiration Date	Modified Date	Actions
10060	Vacation request for scooter	3	Assigned	steve (U)	Mar 29, 2005 4:05 PM	Mar 26, 2005 4:05 PM	-- Select an Action --
10061	Expense Approval for James	3	Assigned	steve (U)	Mar 28, 2005 8:23 PM	Mar 26, 2005 4:23 PM	-- Select an Action --
10062	Expense Approval for Anne	3	Assigned	steve (U)	Mar 28, 2005 8:28 PM	Mar 26, 2005 4:28 PM	-- Select an Action --
10063	PQ Approval for Roberts	3	Assigned	steve (U)	Mar 28, 2005 8:28 PM	Mar 26, 2005 4:28 PM	-- Select an Action --
10064	Vote for hiring QA Engineer	3	Assigned	steve (U)	Mar 28, 2005 10:28 PM	Mar 26, 2005 4:28 PM	-- Select an Action --
10065	Vacation request for mireya	3	Assigned	steve (U)	Mar 29, 2005 4:30 PM	Mar 26, 2005 4:30 PM	-- Select an Action --
10066	Expense Approval for Kathy	3	Assigned	steve (U)	Mar 28, 2005 8:31 PM	Mar 26, 2005 4:31 PM	-- Select an Action --
10070	PQ Approval for Luis	3	Assigned	steve (U)	Mar 28, 2005 8:32 PM	Mar 26, 2005 4:32 PM	-- Select an Action --
10071	Vote for hiring Product Manager	3	Assigned	steve (U)	Mar 28, 2005 10:32 PM	Mar 26, 2005 4:36 PM	-- Select an Action --
10075	Expense Approval for David	3	Assigned	steve (U)	Mar 28, 2005 8:33 PM	Mar 26, 2005 4:33 PM	-- Select an Action --

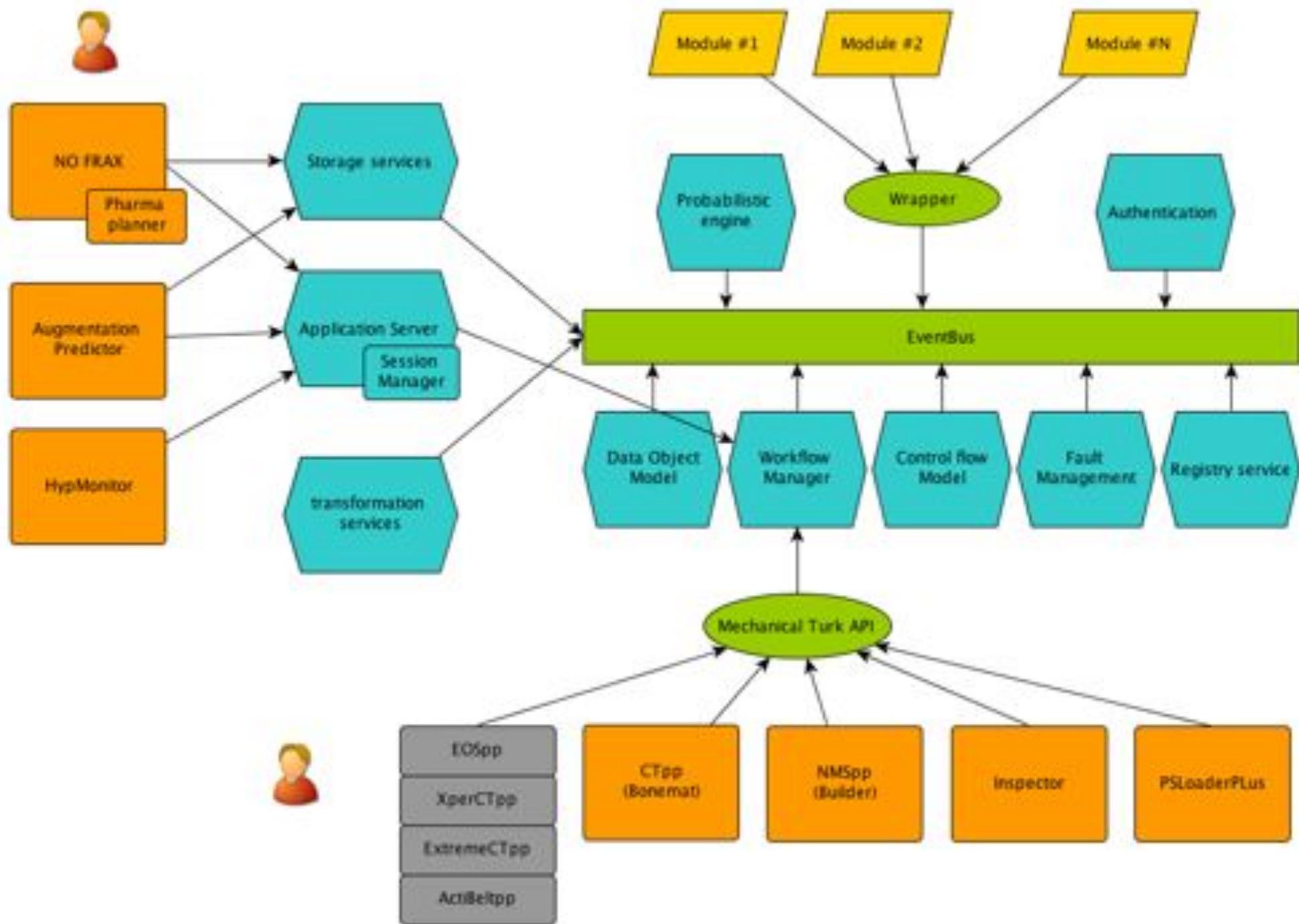
[ 1 - 10 ] Best





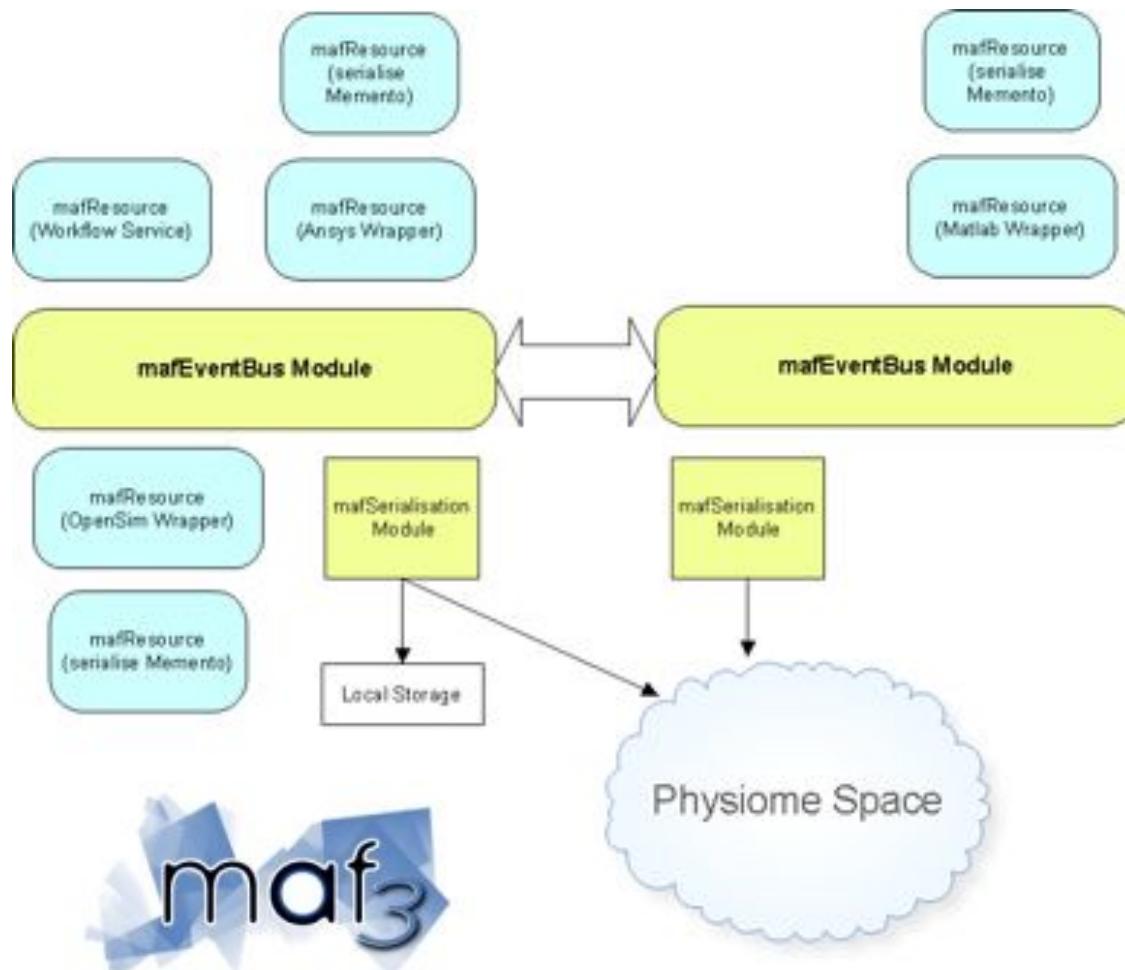
# Mechanical Turks (MAF)







# MAF3 – hypermodel scenario



- Multimod Application Framework version 3 (MAF3)
- Distributed execution on heterogeneous architectures
- Serialisation to and from Physiome Space
- Wrappers for modelling environments



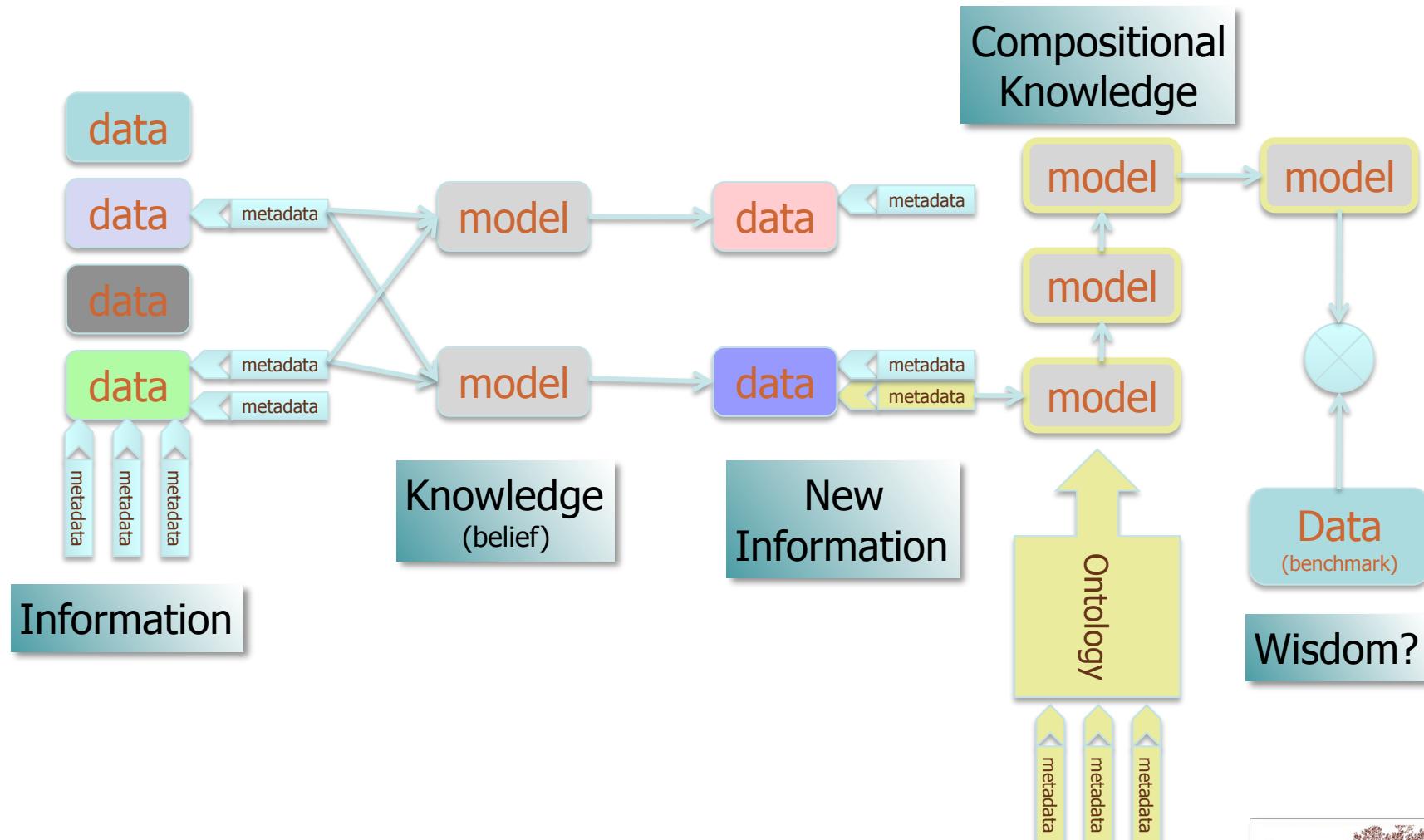
# MAF3 outperforms competitors



	Jade	maf3	ESB
Resources allocation	✗	✓	✗
Execution time	-	-	✗
Easy development of workflow	✓	✓	✓
Debug tools	✓	-	-
Cross-platform	✓	✓	✓
Maintenance	✓	✓	✓
Documentation	✓	✗	✓
Extensibility	✓	✓	✓
Re-usability	✓	✓	✓
Modules availability	✓	✗	✓

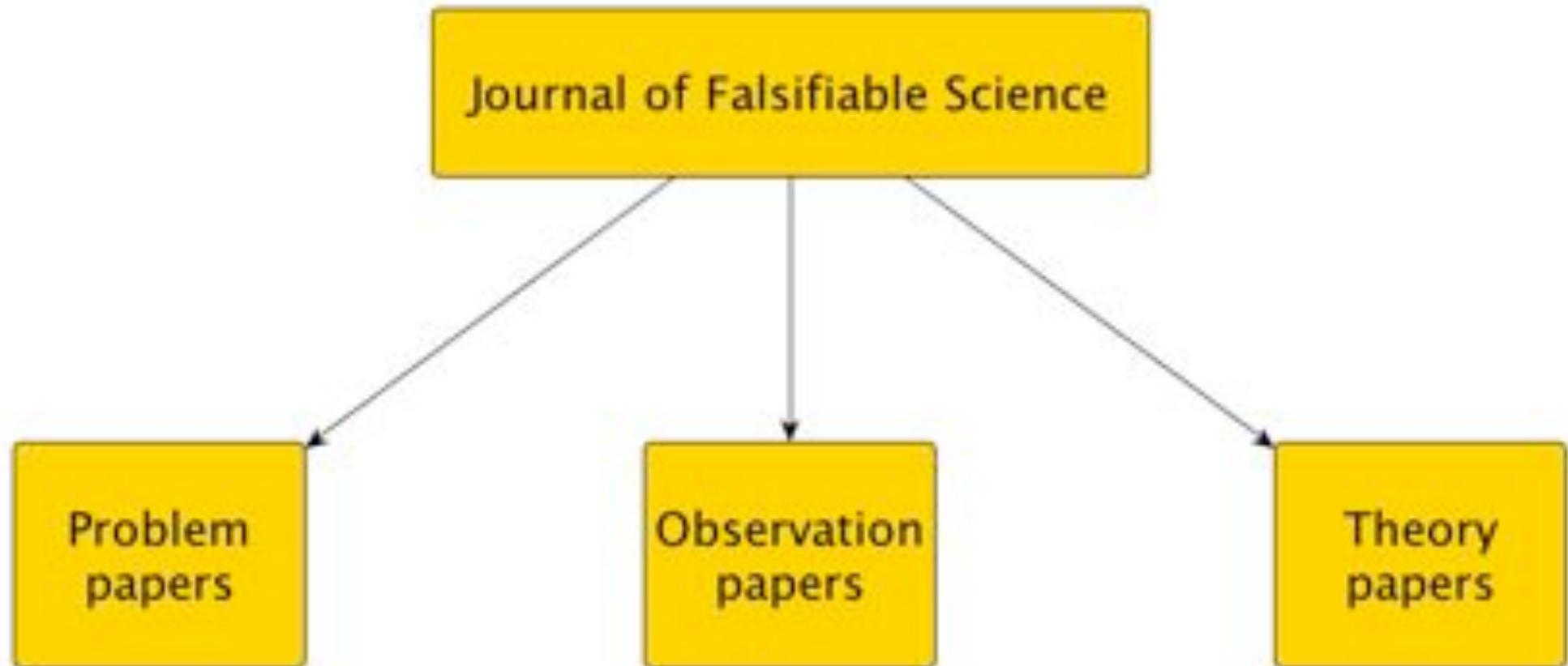


# Vision: “Web of models”



## Topic # 28: Benchmark-based editorial model for computational modelling research

Marco Viceconti  
Steven Niederer



# Problem papers

- Define the research question in term of:
  - Semantics (problem ontology)
  - Observable quantities & predictable quantities
  - Falsification metrics, falsification thresholds
- As soon as a problem paper is accepted, a new stub is automatically created that links inputs and outputs, observables and predictions.
- Typically multiple observation papers and multiple theory papers are connected to a problem paper.
- Problem papers can also re-organise existing observation and theories into an alternative research question. In such case semantic mediation may be required.

# Observation papers

- Experimental papers that provide the necessary causation framework required to falsify theories (validate models)
- As soon as an observation paper is accepted, all theories on that problem are automatically tested against this new set of experimental results.
- Problem papers suggest experimentalists news research directions for their observational studies
- In theory, observations could refuse the problem itself (i.e. A do not cause B); in practice in our class of problems the theories are rarely falsified at this level, but rather at the mechanistic level, where we try to explain **why** A cause B

# Theory paper

- These are the modeller papers, where an explanatory theory is proposed for the problem statement, and this explanation is challenged against all available observation sets.
- The paper includes the model (or the access to the model), so to let the system automatically run the model to predict all available observations sets, according to the falsification metrics.
- As soon as a theory paper is accepted, it is automatically tested against all available observations, according to the problem statement.

# Citations

- Every time new observation or theory papers are linked to a problem paper, that problem paper gets cited.
- Every time an observation is used to test a theory that observation paper is cited. In addition, when the observation falsifies a theory it gets a heavy citation.
- Every time a theory is tested against some new observation it gets a citation. In addition, when the theory resists the falsification attempt against an observation, it gets a heavy citation.



“Per aspera ad astra”

*Seneca, Hercules furens, act II, . 437*

Thank You!