

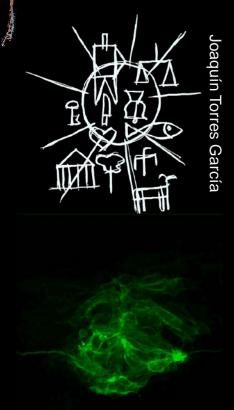
### From Microscopy, Imaging to Clinical Research: A Latin American Perspective



www.scian.cl

Laboratory of Scientific Image Analysis (SCIAN-Lab)
Biomedical Neuroscience Institute (BNI)
Institute of Biomedical Sciences (ICBM)
Anatomy and Developmental Biology Program,
ICBM, Faculty of Medicine,
University of Chile

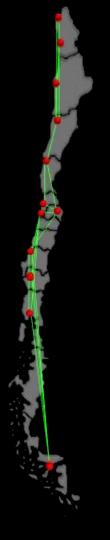
29<sup>th</sup> – 30<sup>th</sup> November 2013 | Hamamatsu TIGA Center BioQuant, Heidelberg University











# How to Survive in the Chilean Jungle

Steffen Härtel

www.scian.cl

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29<sup>th</sup> – 30<sup>th</sup> November 2013 | Hamamatsu TIGA Center BioQuant, Heidelberg University







### How to Survive in the <del>Chilean</del> Jungle Tissue

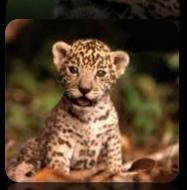
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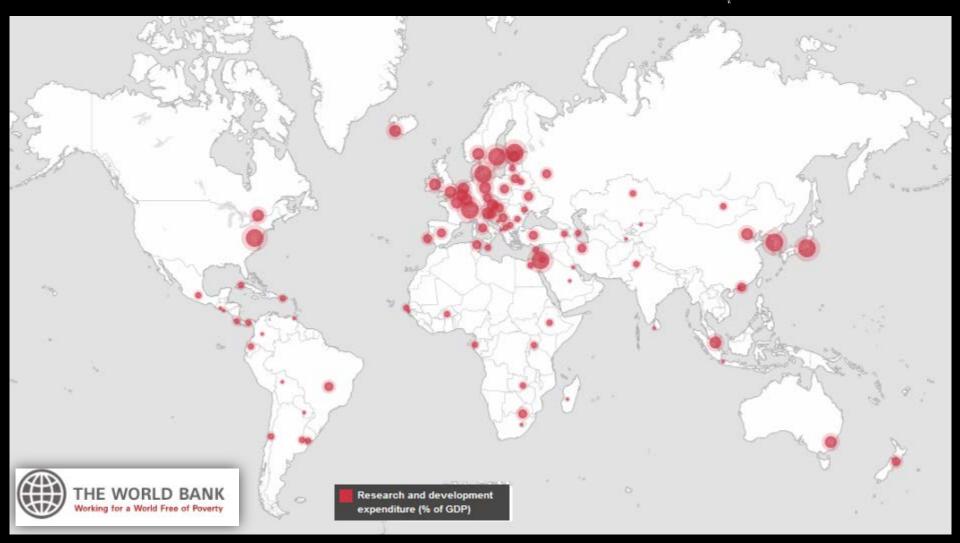








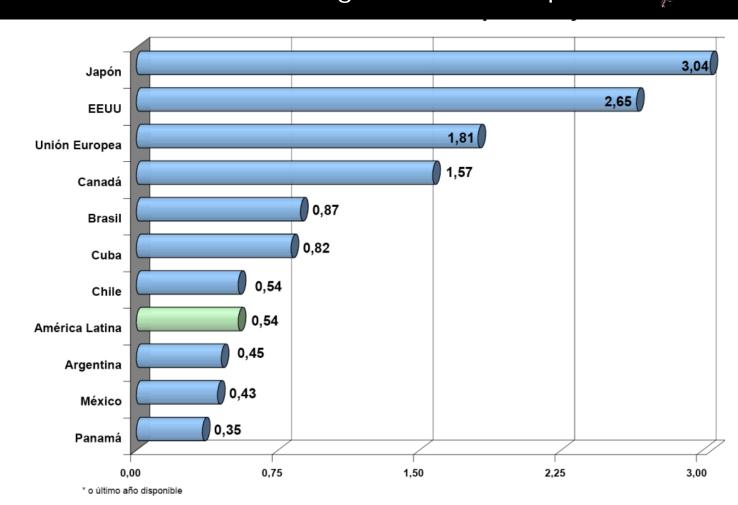
### Research & Development as % of Gross Domestic Product GDP







### R&D as % of gross domestic product &DP

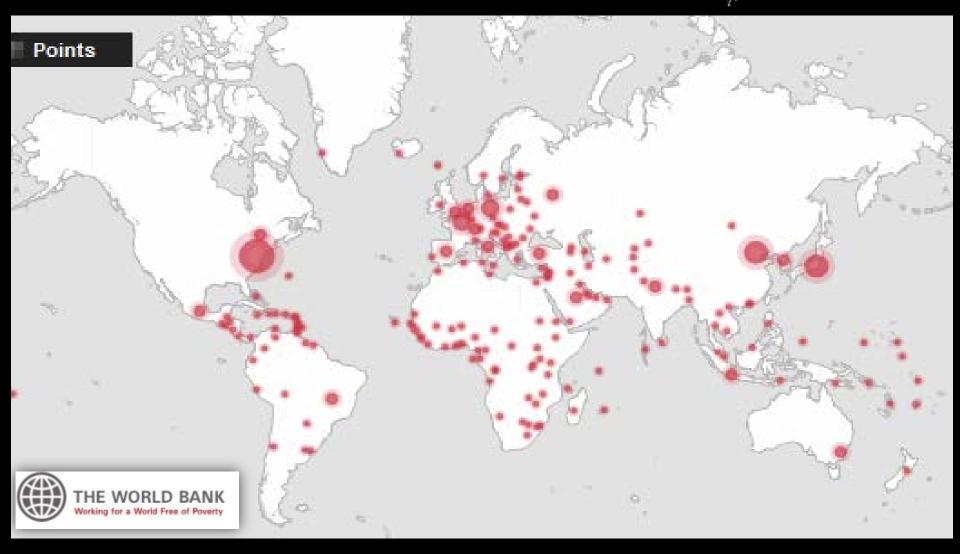


Ciencia y Tecnología en las Américas / Página 20





### **Gross Domestic Product GDP**

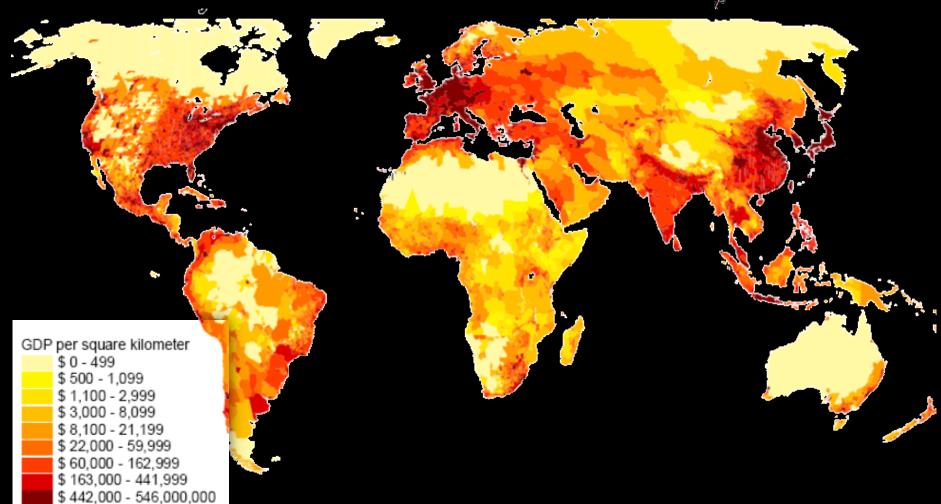


No Data





### **GDP** Density

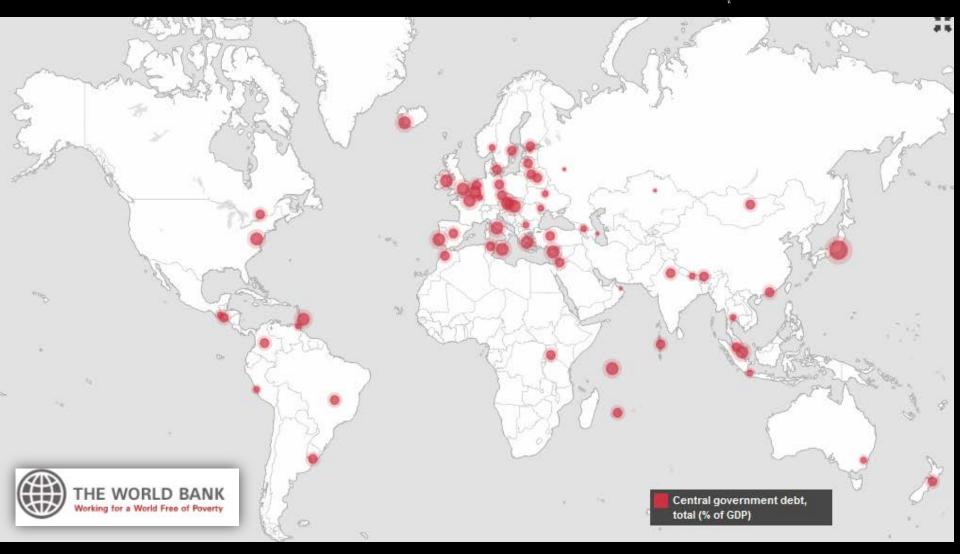


J Gallup, J Sachs and A Mellinger, 1999, International Regional Science Review ...
"GDP density": multiplying GDP per capita by the number of people per square km.





### Government Dept as % of Gross Domestic Product GDP









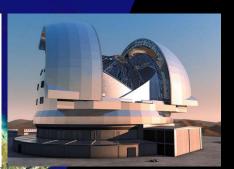


Very Large Telescope (VLT), 4 telescopes, 8m, 2600 m



Atacama Large Millimeter/submillimeter Array (ALMA), 66 antenna, 5000 m





E-ELT European Extremely Large Telescope, 39 m

NASA World Wind screenshot







Extraterrestrial Monster Science produces: TeraB, PetaB, ExaB, ZettaB, YottaB











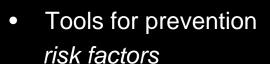


NEUROSC INSTITUTE MEDICINA UNIVERSIDAD DE CHILE



Data Quality and Quantity from Biomedical Sciences to Clinical Research:

Dr Bettina Müller, Medical Oncologist – National Caner Institute, Executive Director - GOCCHI

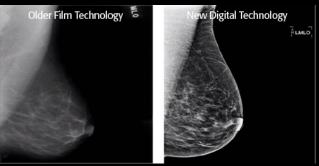


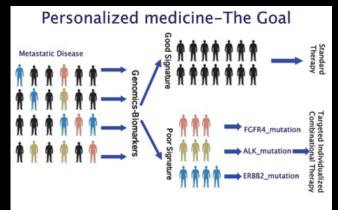




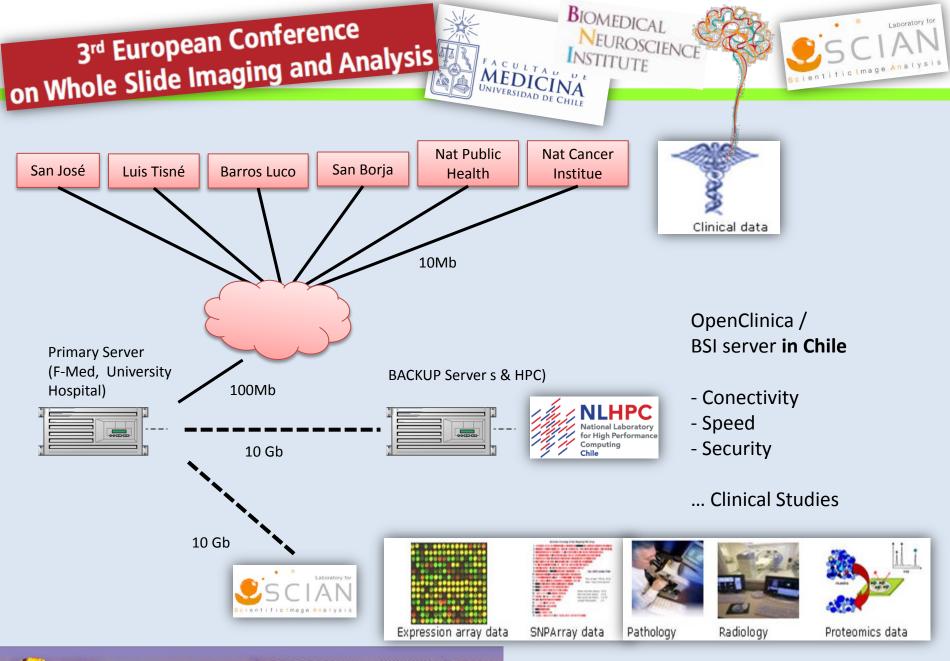
- Tools for early detection applicable - acceptable - efficient
- Personalized Treatments
   predictive and prognostic tools



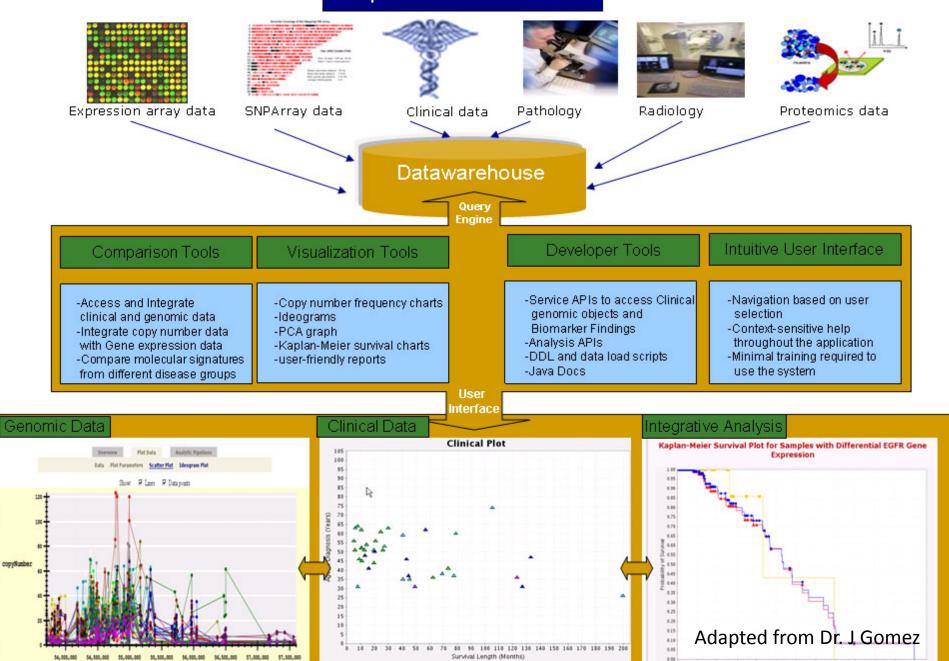








### Disparate Data Sources



ASTROCYTOMA C8M MIXED NON TUMOR OLICODENDROGLIOMA UNCLASSIFIED

CER 7 (80)













Basic Science R&D Human Capital Formation Basic Science

**Medical Informatics** 

FONDECYT FONDEF DAAD / DFG ICM

インインノイルトマルウルンインイン

#### SCIAN-Lab Members

CONICYT

PI Biophysics

CONICYT

PostDocs Biology / Computer Sc / Electric Engineer

PhD - students Computer Sc / Electric Engineer / Biology

Master - students • • Medical Technology / Electric Engineer

Undergraduate • Computer Sc

Research – Assistants Medicine / Computer Sc / Electrical Engineer / Biology

Technicians Biotechnology / Labtechnician / Administration













Basic Science R&D

Human Capital Formation

Basic Science

**Medical Informatics** 

FONDECYT CONICYT FONDEF

CONICYT

DAAD / DFG ICM



United States-Latin America Cancer Research Network, US-LA CRN

2013-2014: U-Redes BioMed-HPC: Network for High Performance Computing

2013-2014: Initiative for Big-Data-Management, Processing, and Distribution for Science and Education in R&D

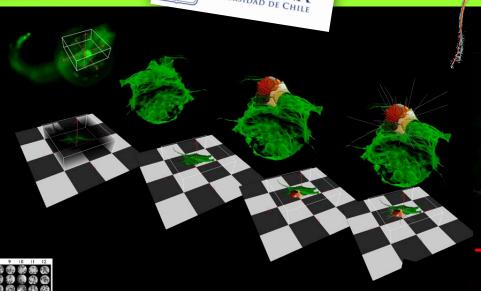
FONDEFS, U-Chile, BNI, F-Med, ICBM, REUNA, ...

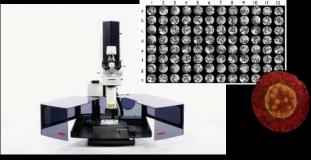






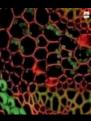
Perkin Elmer Spinning Disk













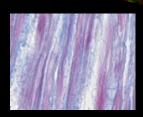
TB of Data per Experiment



NanoZoomer: Tissue Imaging











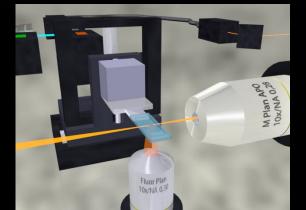
Pulgar, Concha, Keller 2012 unpublished

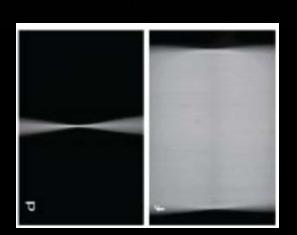
H2B-mCherry crestin::GFP









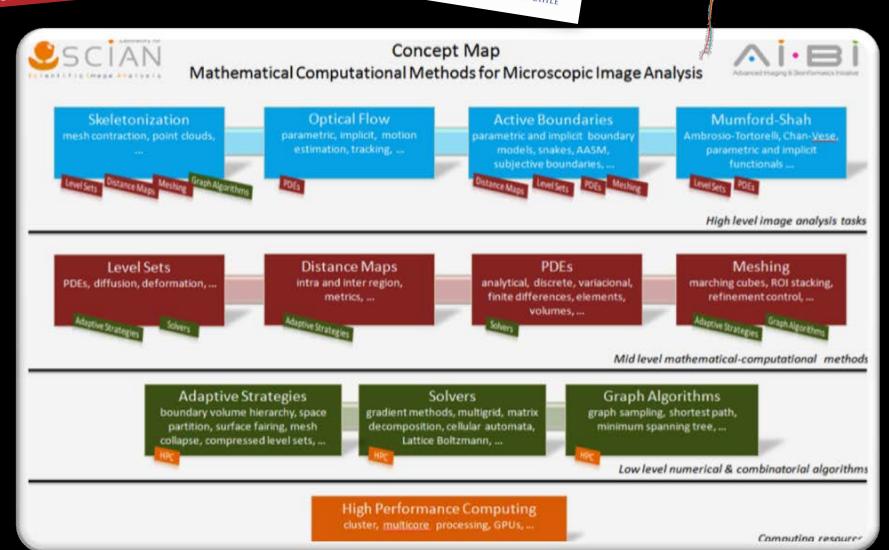


Tens of TB of Data

Keller et al, Science 322, 2008







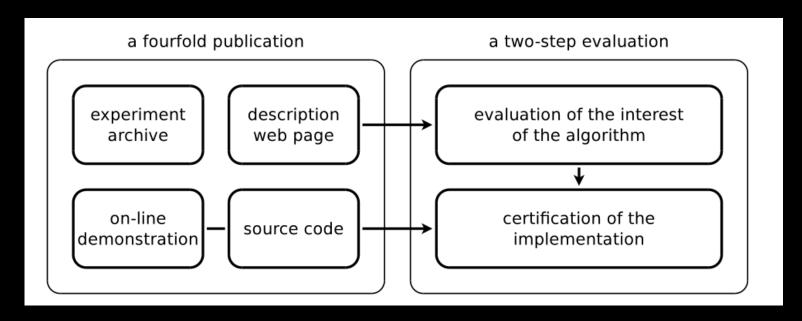


### ... Image Processing Online, iPol @ www.ipol.im





IPOL publishes image processing algorithms as precise and comprehensive as possible.



The publication of each algorithm includes:

- detailed description, bibliography, commented examples and a failure case analysis
- on line demo site for testing of user data
- downloadable program in C or C++
- discussion forum on the algorithm



# ... Image Processing Online: iPol @ www.ipol.im





iPol – Latin America (iPol – LA): financed by CLARA/REUNA from June 2011 – July 2012

Organisation and Coordination: Juan Cardelino / Haldo Spontón UdelaR (Uy)

Participation:

UBA (Arg) U-Chile (Ch)

Mission:

Diffusion of iPol philosophy ar



Published in Image Processing On Line on YYYY-MM-DD. ISSN 2105-1232 © YYYY IPOL & the authors CC-BY-NC-SA This article is available online with supplementary materials, software, datasets and online demo at http://www.ipol.im/pub/pre/44/

PREPRINT November 20, 2013

An Implementation of Multiscale Combined Local-Global Optical Flow

Jorge Jara<sup>1</sup>, Mauricio Cerda<sup>2</sup>, José Delpiano<sup>3</sup>, Steffen Härtel<sup>2</sup>

DCC, SCIAN-Lab, BNI, University of Chile, Chile (jjara@dcc.uchile.cl)
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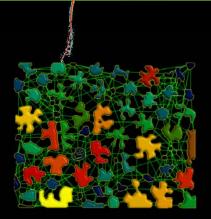


### Partial differential equations

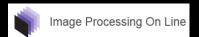
#### 2D/3D · Morpho-topology

2013 Development 2012 European Biophysics Journal 2011 J Microbiol Methods 2010 J of Struct Biol 2010 Development 2010 Biological research 2010 BBA

...

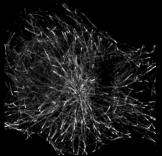


#### **IPOL**



#### Motion estimation and tracking

2014 Current Molecular Medicine 2013 IPOL 2013 IEEE Transactions on Pattern Analysis ... 2013 Biological Cybernetics 2013 Reproduction, Fertility and Development 2012 Machine Vision and Applications 2012 PLosOne



#### Cross correlation functions



#### Colocalization

2012 PLosOne 2011 JBC 2011 Arthritis & Rheumatism 2011 Biol Research 2011 Antioxid Redox Signal 2010 Journal of Microscopy

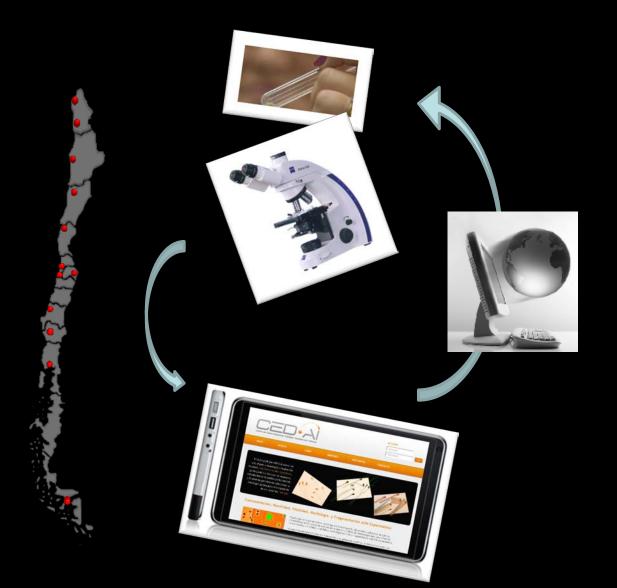
2011 Revista Médica de Chile





# Center for Internet Assisted Sperm Analysis





#### **CEDAI** cuantifies:

- i. concentration,
- ii. motility,
- iii. vitality,
- iv. DNA fragmentacion,
- v. morphology.

with mathematical algoritms calibrated and standardized by national experts.



# Gold Standards, M2M, and Expert Driven Calibrations



20 Muestras



20 Muestras











Digital CED·AI



Digital Supervisado CASA

Luis Sarabia (U-Chile)

Marcia Madariaga (IDIMI)

Adolfo Acosta (Clínica Las Condes)



Asistidos por Internet (CEDAI, F-Med, U-Chile)



SCA INFOBIC (U-Buenos Aires)



Motilidad (OMS 2010) Grupos: A Progresivo

B No progresivo C Inmóvil Concentración millones/ml Celulas redondas millones/ml

Vitalidad % Fragmentación ADN

C Inmóvil

D NO progresivo



\* Assisted

Usuario
Password
Acceder

İS



ACERC

SERVICIO

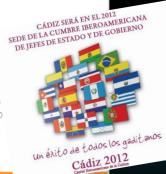
EQUIPO

EVENTOS

CONTACTO



Este proyecto permite el acce tecnología y diagnóstico de costos operativos, optimizar respuesta, estandarizando la cal y finalmente permitiendo selecci óptima para el tratamiento



### Premios Iberoamericanos a la Innovación y el Emprendimiento 2012



CHILE

#### Científicos chilenos desarrollan Centro de Espermiogramas Digitales



A través de modernos programas computacionales y desde Internet, se puede medir con mayor precisión la movilidad, concentración y vitalidad de espermatozoides en pacientes que consultan por infertilidad. El proyecto, liderado por el biofísico y académico de la Facultad de Medicina, profesor Steffen Hartel, está siendo testeado en el Instituto de Investigaciones Materno Infantil, Idimi, y en Clínica Las Condes. [Ver más]

#### Premios Iberoamericanos a la Innovación y el Emprendimiento 2012

La Secretaría General Iberoamericana tiene la satisfacción de anunciar que el Jurado de los Premios Iberoamericanos a la Innovación y el Emprendimiento, en su reunión del día 30 de Julio de 2012... [Ver Mas]

#### Premio Visión Emprendedora 100K Santander Universidades

La organización del certamen, en cuyo diseño y bases colaboraron distintas casas de estudios superiores, está a cargo de Universia, en su calidad de Red de Universidades Chilenas, con el apoyo... [Ver Mas]

#### Adjudicación Primer Concurso Programa Valorización de la Investigación en la Universidad

A través de su Programa Fondef, CONICYT adjudicará 54 propuestas seleccionadas del Primer Concurso de Valorización de Investigación en la Universidad, cuyo objetivo es promover la creación... [Ver más]



















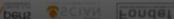














### Proyecto D11I1096

I+D precompetitivo



# CENTRO DE PATOLOGÍA DIGITAL ASISTIDA POR INTERNET

XIX Concurso de Proyectos FONDEF de I+D 2011

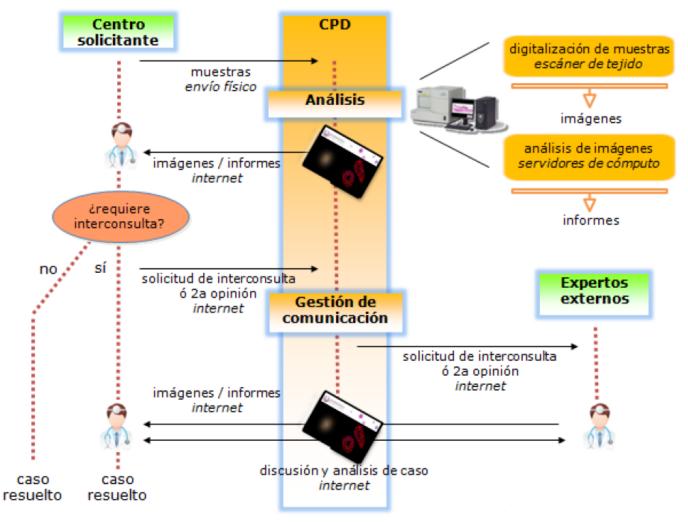




### CPD



### Center of Digital Pathology



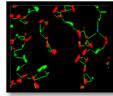


### Methodology I&D





Quantification of lymphosites in focal regions (**oral pathology**). I&D, clinical validation of image processing algorithms (HE).

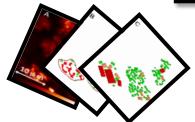


Quantification of estrogen **receptor in human mammalian tissue**. I&D, clinical validation of image processing algorithms (IHQ).

Quantification of **Cerb2 (IHQ) in human mammalian tissue**. I&D, clinical validation of image processing algorithms (IHQ).



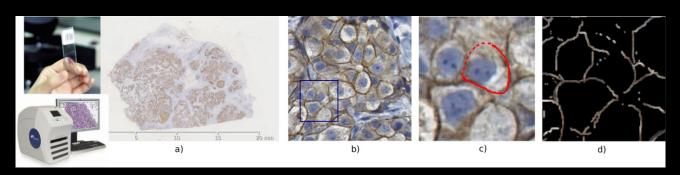




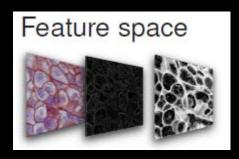


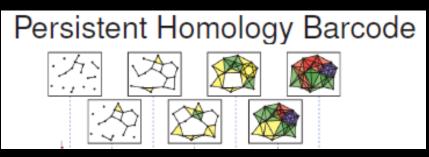


Raquel Pezoa (cand PhD): A segmentation method for images with subjective contours in the field of digital pathology



Poster Rodrigo Rojas (cand PhD): Topological Invariants for Segmentation of Nuclei and Membranes in Breast Cancer Analysis











Professional Development for High School Teachers

'Nervous Tissue: Interactive Practical Activity' Summer School for High School Students

'Basic Tissues of the Organism' First Year Medical School Students

'Interactive Histology'





Kothari S, et al. J Am Med Inform Assoc 2013;20:1099-1108

#### Review

Table 3 Summary of key methods in each component of a WSI-based clinical decision support system

Section	Subsection	Key methods
Quality control	Image artifacts Batch effects	Tissue folds, <sup>13–15</sup> blurred regions, <sup>16</sup> and chromatic aberration <sup>17</sup> Color normalization, <sup>18–20</sup> batch-invariant color space, <sup>21–23</sup> and scale normalization <sup>24</sup>
Image description	Pixel-level features  Object-level features Semantic-level features	Color, <sup>38</sup> gray-level intensity profiles, <sup>30</sup> Haralick features, <sup>23</sup> <sup>30</sup> <sup>35</sup> <sup>36</sup> wavelet and multiwavelet submatrices, <sup>30</sup> <sup>36</sup> <sup>37</sup> Gabor filter responses, <sup>23</sup> <sup>30</sup> <sup>36</sup> and Fractals <sup>30</sup> <sup>36</sup> Shape <sup>47</sup> <sup>48</sup> and graph-based topology <sup>52–56</sup> Bag-of-features <sup>60</sup> and spatial hidden Markov model <sup>61</sup>
Prediction modeling	ROI selection and tile-based WSI representation Informative feature selection and reduction Classification	ROI selection: supervised <sup>13 63-65</sup> and unsupervised <sup>66 67</sup> ; tile combination: feature <sup>49</sup> and prediction <sup>22</sup> ; multiscale analysis <sup>22 23 67 70</sup> Feature selection: filter, <sup>30 51 53 57</sup> sequential search (wrapper), <sup>22 36 91</sup> and random forest (embedded) <sup>65</sup> ; Feature reduction: PCA, <sup>32 39 91</sup> graph embedding, <sup>54</sup> ISOMAP, <sup>80</sup> and MDS <sup>92</sup> Multiple classifiers, <sup>22 29 36 39 80</sup> boosting, <sup>23 80 93</sup> ensemble methods, <sup>22</sup> and active learning <sup>3 94-96</sup>
Visualization and exploratory analysis	Unsupervised clustering and high-dimensional feature patterns Virtual microscope and spatial patterns	Hierarchal clustering, 49 68 72–74 Self-organizing maps, 75 76 k-means, 58 79 80 and expectation maximization <sup>22</sup> Image compression, 83 84 Google map interface, 82 85 86 highlight ROI, 56 64 65 67 70 87 annotation, 61 62 and spatial variation of features 13 71

MDS, ; PCA, ; ROI, region of interest; WSI, whole-slide image.

MDS, ; PCA, ; ROI, region of interest; WSI, whole-slide image.

unsupervised constering and high-dimensional feature patterns Virtual microscope and spatial patterns maximization<sup>22</sup>
Image compression, <sup>83</sup> <sup>84</sup> Google map interface, <sup>82</sup> <sup>85</sup> <sup>86</sup> highlight ROI, <sup>56</sup> <sup>64</sup> <sup>65</sup> <sup>67</sup> <sup>70</sup> <sup>87</sup> annotation, <sup>61</sup> <sup>62</sup> and spatial variation of features<sup>13</sup> <sup>71</sup>





- Human and Data Network? Ok!
- Instrument? Ok!
- ♦ Which software ... standards/quality? Black box ←→ development?
- What convinces the pathologist and the developer?
- How to integrate into the workflows?



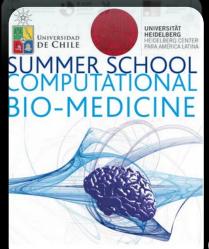
### 2013 ← Symposium & Curses → 2014





### **Physical Biology** of the Cell





### **Optics, Forces & Development**





SYMPOSIUM cellmorphodynamics.cl QuanTissue:

INTERNATIONAL SYMPOSIUM SANTIAGO / CHILE

nage Processing

manipulation of signals and forces in developing tissues



SANTIAGO / CHILE

**TEACHERS** 

**TOPICS** 

**Computational Bio-Medicine** 







# Thank you very much

— Muchas Gracias

Vielen Dank



# どうもありがとうございました





