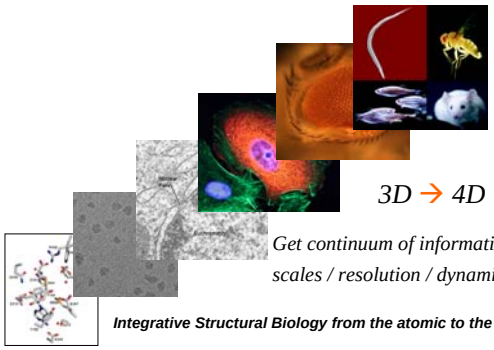
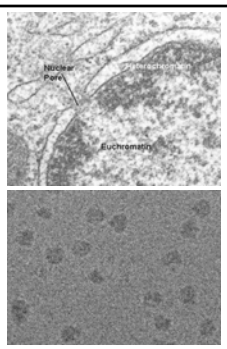
FRISBI: French Infrastructure for Integrated Structural Biology

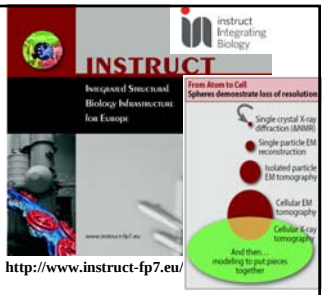


3D → 4D → 5D

Get continuum of information: scales / resolution / dynamics / function

Integrative Structural Biology from the atomic to the cellular level



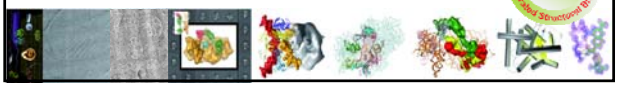


http://www.instruct-fp7.eu/

French Infrastructure for Integrated Structural Biology

FRISBI

Integrative Structural Biology from the atomic to the cellular level



Instruct

European hub of structural biology providing:

- **integrated infrastructure with cutting-edge technologies**
- **scientific expertise**
- **training**
- **peer review access for academia and industry**

Since 1rst of March 2012: Operational phase has started

16 distributed centres

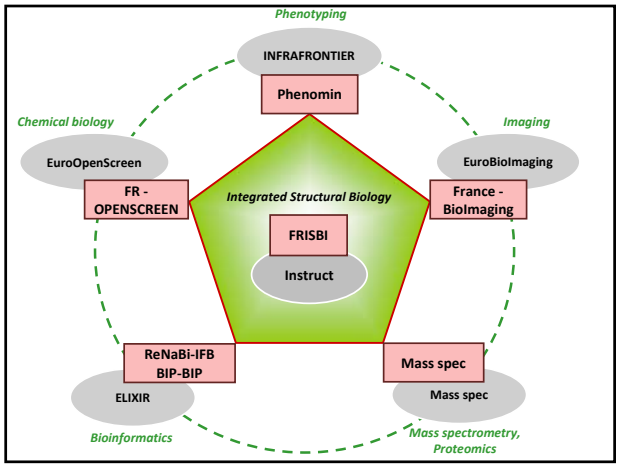
Online HUB in place:

www.structuralbiology.eu

(online proposal system, catalogue of technologies, description of Instruct centres, training, conferences…)

Instruct Access process

- Application and review process: efficient, transparent and quick (target turnaround time of 2 weeks).
- Evaluation on scientific merit; innovative approaches within integrative structural biology.
- Applications for individual platforms are possible



Infrastructures Françaises et Européennes de Biologie Structurale Intégrative

Instruct: Infrastructure Européenne de Biologie Structurale Intégrative
Démarrage phase opérationnelle Instruct: 1ier mars 2012

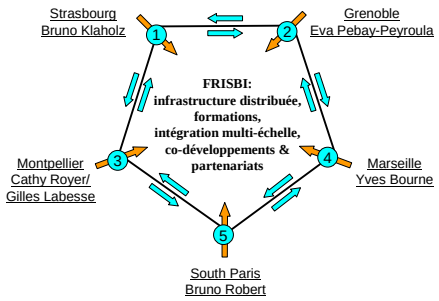
FRISBI: Infrastructure Française de Biologie Structurale Intégrative
Démarrage: 1ier mai 2011

French Infrastructure for **I**ntegrated **S**tructural **BI**ology

En lien avec Instruct: Infrastructure Européenne de Biologie Structurale Intégrative
Démarrage phase opérationnelle Instruct: 1ier mars 2012

French Infrastructure for **I**ntegrated **S**tructural **BI**ology

Organisation:



French Infrastructure for **I**ntegrated **S**tructural **BI**ology

Organisation:

- **Démarrage: 1ier mai 2011**
- **Signature de la convention ANR: avril 2012**
- **Ouverture à projets: depuis avril 2012 (annoncé lors du GTBio)**
- **Sélection de projet: via les comités des nœuds (national) ou Instruct (europ.)**
- **Executive committee: en place (1 représentant de chacun des 5 centres)**
- **Comité SAB et steering committee: en place**
- **Site web: http://www.frisbi.eu**

French Infrastructure for **I**ntegrated **S**tructural **BI**ology

Strategic aims of the infrastructure:

- **be at the forefront 3D analysis, imaging, bioinformatics & integrative cellular structural biology**
- **promote recruitment of new research teams for integrated structural biology**
- **provide access to state-of-the-art integrated structural biology infrastructures and expertise**
- **define & use data standards for storage and integrated analysis of structural information**
- **stimulate exchange and co-development with industrial partners**
- **organise training and dissemination of expertise**
- **develop innovations in the field of biomedical targets involved in human diseases**

French Infrastructure for **I**ntegrated **S**tructural **BI**ology

Benefits to the scientific community:

- **Project-based access & training**

  to state-of-the-art European structural biology infrastructures and expertise for the national and European scientific community http://www.structuralbiology.eu/

- **Development**

  of the next-generation structural biology technologies and procedures

- **Interactions**

  between structural, molecular and cellular biology communities

- **Industrial partnerships**

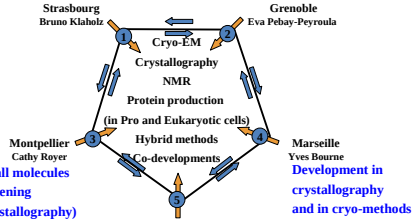
  co-developments in electron & optical microscopy, crystallography, computing (FEI, Leica, NatX-ray, Xenocs, Bruker,…)

French Infrastructure for **I**ntegrated **S**tructural **BI**ology

Shared know-how and developments:

Cryo-EM & tomography
Correlative microscopy
Crystallography development
Multi-resolution integration

NMR, crystallography developments and synchrotron (ESRF), Membrane proteins
Soluble fragment screening ESPRIT



Small molecules screening (crystallography)
In-cell NMR
High-pressure spectroscopy

Development in crystallography and in cryo-methods

Biophysics, Spectroscopies
Backscattering interference
Synchrotron (SOLEIL)

French Infrastructure for **I**ntegrated **S**tructural **BI**ology

Ouverture nationale et européenne des plateformes des 5 centres avec des technologies complémentaires de pointe:

- cristallographie, RMN, SAXS
- cryo-EM & tomographie
- microscopie corrélative et super résolutive
- systèmes d'expression pro- & eucaryotes
- production d'échantillons
- intégration multi-résolution
- interactions protéine-protéine
- caractérisation biophysique
- biophysique & molécules uniques
- interfaces avec imageries et bioinformatique

French Infrastructure for **I**ntegrated **S**tructural **BI**ology

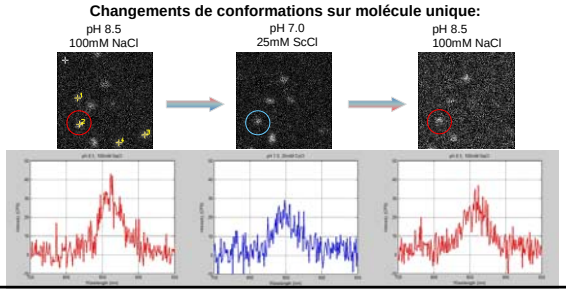
Examples where integrative approaches have allowed key advances

Examples where integrative approaches have allowed key advances

node 5, South-Paris:
(LEBS, SB2SM, BiochX, IBBMC, ICSN)

Crystallography, NMR, non-linear super-resolution microscopy (Raman STED)
Back Scattering Interferometry, PELDOR
***In vivo* difference FTIR spectroscopy**

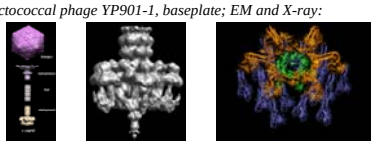
Changements de conformations sur molécule unique:



Examples where integrative approaches have allowed key advances

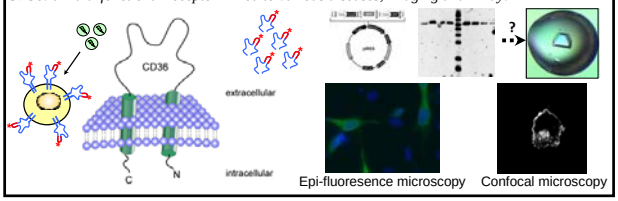
node 4, Marseille:

Lactococcal phage YP901-1, baseplate; EM and X-ray:



Veesler *et al.*, PNAS, *in press.*

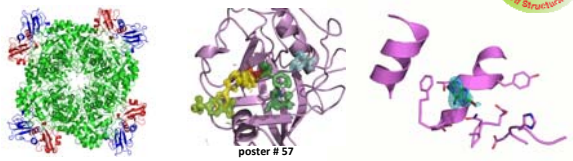
CD36: a multi-fonctional receptor linked to various diseases; imaging and X-ray:



Epi-fluoresence microscopy Confocal microscopy

Examples where integrative approaches have allowed key advances

node 3, Montpellier:



A structure ... some complexes ... a fine mapping ...

fragment screening

Towards automatic screening by X-ray crystallography:

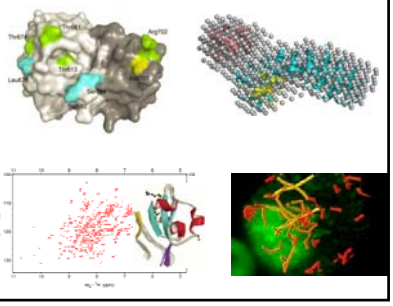
Collaboration CBS/IBS/FIP/NatXray
Le Maire *et al.*, *Acta D*, 2011.

Examples where integrative approaches have allowed key advances

node 2, Grenoble:

EMBL, IBS, ESRF & UVHCI **Influenza polymerase**

- Crystal structures of domains
- Fluorescence microscopy
- SAXS of complexes
- NMR – structure & dynamics
- EM of RNP
- Recombinant (green!) viruses

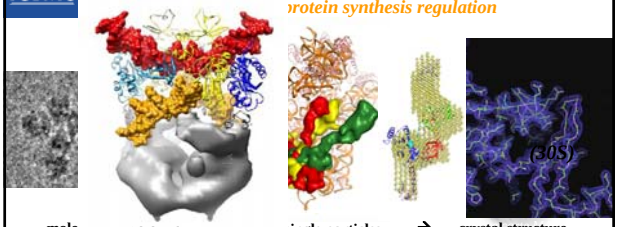


Examples where integrative approaches have allowed key advances

node 1, Strasbourg:

Multi-resolution integration

rotein synthesis regulation



mole Michel *et al.*, *EMBO J.* 2009 **ingle particles** → **crystal structure**

Myasnikov *et al.*, *in prep.* Simonetti *et al.*, *Nature* 2008. Simonetti *et al.*, *submitted.*

fluorescence microscopy *cryo electron tomography* *cryo-EM* *SAXS* *crystallography*

Description of the FRISBI node 1, Strasbourg):

Centre for Integrative Biology (CBI)

Key mission of the CBI:

Driving scientific projects:

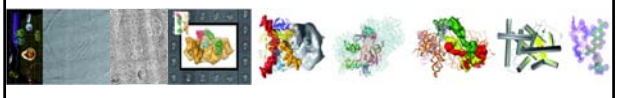
Integrative structural biology of gene expression regulation

- transcription
- translation
- RNA

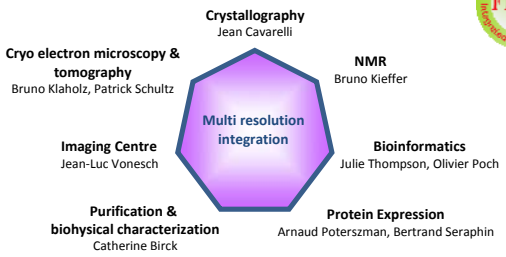
Will host French and European Infrastructures,

- allows strong investments into equipments and favours interdisciplinary developments

Integrative Structural Biology from the atomic to the cellular level



Specialities available within FRISBI node 1, Strasbourg):



major investmests

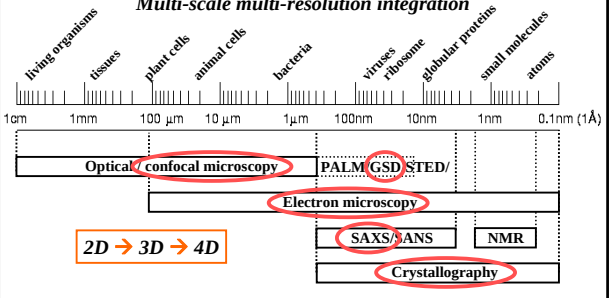
Developments:

Cryo-EM / tomography / CEMOVIS FIB
Super-resolution correlative microscopy
Pro- and eukaryotic (incl. mammalian) expression systems, stable cell lines

Crystallography, diffraction screening, in-house SAXS
In-vivo NMR

Multi-resolution Integration Bioinformatics

"From the atom to the cell":
Multi-scale multi-resolution integration



bio-informatics / multi-resolution integration
functional studies, sample preparation & characterisation
biological chemistry
structure-sequence-function
data storage and computing resources
mathematics/physics/informatics

FRISBI node 2

P S B

FRISBI
GRENOBLE

PSB
-The Partnership for Structural Biology –

350 Scientists within walking distances

4 Juin 2013: le PSB fête ses 10 ans

P S B

Les thématiques scientifiques du PSB

Host-Pathogen Interactions
- Bacterial pathogens
- Immunity
- Virology & viral infection

DNA/RNA & Gene Regulation
- Nucleic acid structure
- Gene regulation

Cell Division
- Eukaryotes
- Prokaryotes

Stress Responses in Prokaryotes
- Extremophilic bacteria
- Heavy atom homeostasis

TECHNOLOGY DEVELOPMENT

Methodologies for Structural Biology
- Protein Expression
- Crystallisation
- Functional Studies
- Structural Methods (NMR, EM, correlative microscopy…)
- Metalloproteins
- Membrane Proteins

Instrumentation
- Synchrotron
- Neutron scattering

Les enjeux futurs:
Du Nano vers le Micro et au delà…

GRENOBLE

FRISBI → Création d'une UMS
mise en commun plateformes IBS et UVHCI

Centre du réseau Eu Instruct (ESFRI)

Les défis scientifiques: Labex GRAL (UVHCI, IBS, iRTSV)

Création de l'UMS3518 - ISBG

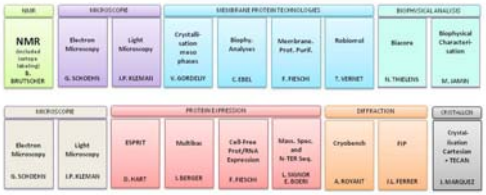
Directeur : Darren HART

Comité de Pilotage

Gestion : Yvette GAUDE

Qualité : Auriane DENIS-MEYERE

Plateaux techniques



User committees + common services group

Principes généraux de l'UMS

Écriture d'un texte basé sur les plateformes Européennes

Chaque utilisateur paie pour l'unité consommée
Le tarif de l'unité varie en fonction du type d'utilisateur

Tarification

1) Définir les unités d'accès pour chaque plateforme (temps, nbre manips,..)
2) Calculer l'unité de coût
3) Définir le type d'utilisateur
4) Définir le coût imputable par type d'utilisateur
5) Etablir une liste des tarifs

Au démarrage:
7 PF sont intégrées à l'UMS (UMS gère facturation, maintenance et fonctionnement)
Les autres entrent progressivement mais peuvent se faire assister par l'UMS pour la facturation

FRISBI - Grenoble

Investissements principaux à Grenoble (UMS-ISBG)

Upgrade et extension RMN: 3 nouveaux spectromètres 950, 800 et 700 MHz

RX Diffractomètre + détecteur

Microscopie électronique (upgrade)

Microscopie confocale + FACS

Caractérisations échantillons : Mass spec, upgrade AUC, SPR, SEC-MALS
Robotique pour production d'échantillons: production protéine et cristallisation

PSB

Un nouveau bâtiment pour l'IBS
Déménagement octobre 2013

Financement: CPER - Plan Campus
Région/Metro/Ville de Grenoble/Département Isère

SHON ~5000 m² ------> 9340 m²

INTEGRATED STRUCTURAL CELL BIOLOGY

SUMMER SCHOOL

July 7 - August 1 2014

Les Houches, France

Conférences et formations

Programme de 2012
- "Future challenges in integrative structural biology" (Strasbourg), 110 participants, 56 instituts, 16 pays
- "Production and characterization of macromolecular complexes" (Strasbourg), 84 participants, 48 instituts, 10 pays
- Formation: Production, purification and charact. of macromolecular complexes (Strasbourg), 16 participants., 16 instituts, 9 pays.
- Symposium on membrane protein crystallization (Grenoble)

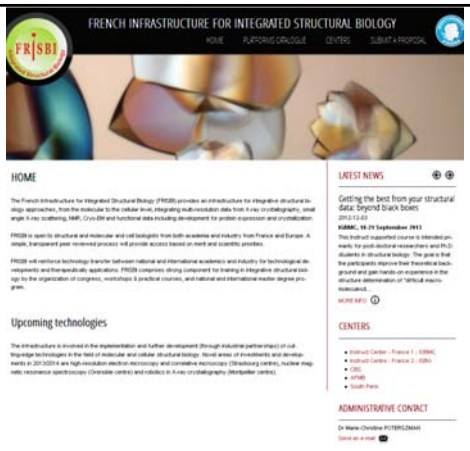
Programme de 2013 établi:
- Cryo-coupe et Immuno-marquage (Strasbourg), national
- Getting the best from your structural data: beyond black boxes (Strasbourg), européen
- RMN (Montpellier; UMS Biocampus), national
- Diffraction *in situ* sur G-rob (Montpellier), national

Programme de 2014 en cours d'établissement:
- Current challenges in integrative structural biology (Strasbourg), européen
- Ecole d'été: biologie structurale et cellulaire intégrée, Les Houches (Grenoble)
- Practical workshop: "High-throughput methods for Protein Production and Crystallization", Marseille, européen.

Formation doctorale: Projet avancé de Mise en place d'un Réseau National de Formation en Biologie Structurale Intégrative Bio3D (coord. J. Cavarelli)

http://frisbi.eu

http://frisbi.eu



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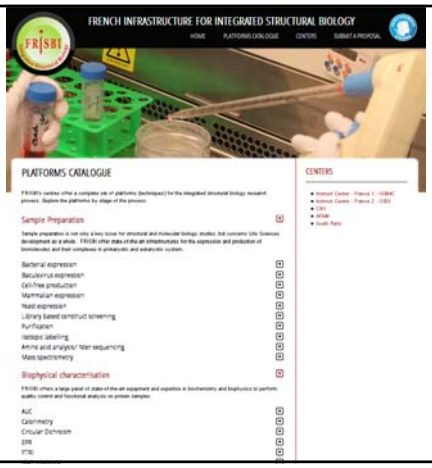

Soumission de projets sur FRISBI

Mode d'accès:
- sélection de projets par les comités des nœuds sur une base de faisabilité
- comité de sélection Instruct dans le cas de projet européens / intégrés

http://www.frisbi.eu

Accessible aussi depuis le site Instruct www.structuralbiology.eu
et les sites web des 5 nœuds de FRISBI