						supervision					
Unit Label et site Web	**City**	**First Name and last Name of the Head of the team**	**Brief description of the research performed by the team (3 lines)**	**5 to 10 main publications related to the proposed thematic scope**	**proposed thematic scope**	**Number of PhD**	**profile, expertise, training (1)**	**Number of Post-docs**	**profile, expertise, training (1)**	Mail	Remarques/col passées ou en c Brésil
Inserm U1054 et CNRS UMR5048 http://www.cbs.cnrs.fr/	Montpellier	Catherine Royer	Our group is expert in the study of protein folding and conformational transitions using high pressure fluorescence and NMR. In particular, we are the only lab in France to have a high pressure NMR setup, and a dedicated 600 MHz spectormeter. Pressure is a particularly interesting approach as its action has its origin in the packing efficiency of the folded states oof proteins.	1. Kitahara, R., Hata, K., Maeno, A., Akasaka, K., Chimenti, M., Garcia-Moreno E., B., Schroer , M. A., Jeworrek, C., Tolan, M., Winter, R., Roche, J., Roumestand, C., Montet de Guillen, K. and Royer, C. A. Structural plasticity of staphylococcal nuclease probed by perturbation by pressure and pH, Proteins, 79, 1293-1305 (2011). 2. Rouget, J.-B., Aksel, T., Roche, J., Saldana, J.-L., Garcia, A. E., Barrick, D., and Royer, C. A. Size and sequence and the volume change of protein folding, JACS, 133(15):6020-7, (2011). 3. Rouget, J.B., Schroer, M.A., Jeworrek, C., Pühse, M., Saldana, J.L., Bessin, Y., Tolan, M., Barrick, D., Winter, R., Royer, C.A Unique features of the folding landscape of a repeat protein revealed by pressure perturbation, Biophys J., 98, 2712-2721. (2010). 4. Mitra, L., Hata, K., Kono, R., Maeno, A., Isom, D., Rouget, J.B., Winter, R., Akasaka, K.,Garcia-Moreno E., B. & Royer, C.A., Vi-Value Analysis: A Pressure-Based Method for Mapping the Folding Transition State Ensemble of Proteins, JACS, 129, 14108-14109, (2007). 5. Brun, L., Isom, D. Velu, P., Garcia-Moreno, B. & Royer, C.A. Hydration of the folding transition state ensemble of a protein, Biochemistry, 45, 3473-3480 (2006). 6. Kitahara, R., Royer, C.A., Yamada, H., Boyer, M., Saldana, J.-L., Akasaka, K. & Roumestand, C. Equilibrium and Pressure-jump Relaxation Studies of the Conformational Transitions of P13MTCP1, J. Mol. Biol. 320, 609-628 (2002). 7. Silva, J. L., Foguel, D. & Royer, C.A. New Insights into protein folding, dynamics and structure from high pressure studies, TiBS 26, 612-618. (2001). 8. Seeman, H., Winter, R. & Royer, C.A. Volume, expansivity and isothermal compressibility changes associated with temperature and pressure unfolding of staphylococcal nuclease, J. Mol. Biol 307, 1091-102 (2001). 9. Panick, G., Vidugiris, GJA, Mallessa, R., Rapp, G., Winter R. & Royer C.A. Exploring the Temperature-Pressure Phase Diagram of staphylococcal Nuclease, Biochemistry 38, 4157-4164 (1999). 10. Vidugiris, G. A. J., Truckses, D., Markley, J. L. & Royer, C. A. Proline Isomerization and the High Pressure Denaturation of Staphylococcal Nuclease, Biochemistry 35, 3857-3864 (1996).	Molecular biophysics, portein structure and dynamics	3	Biophycisist, Biophysical Chemist	3	Biophysics, Physics, biology, biochemistry, physical chemistry	catherine.royer@cbs.cnrs.fr	Déjà eu un étu "sandwich" très Jerson Silva : "C me the informa the high pressu system? I talke jerson@bioqm to my PhD stud Guilherme, and interested in sp months in your
Inserm U998 CNRS UMR7284 http://ircan.org/index.php?option=com_content&view=article&id=1&Itemid=1	Nice	Gianni Liti	We use the budding yeast for population genomics and quantitative genetics studies to dissect complex phenotypic variation	1. Liti G and Schacherer J. 2011. The rise of yeast population genomics. Comptes Rendus Biologies. 334 (8-9), 612-619. 2. Warringer J, et al. 2011. Trait variation in yeast is defined by population history. PLoS Genetics. 7(6), e1002111. 3. Parts L, et al. 2011. Revealing the genetic structure of a trait by sequencing a population under selection. Genome Research. 21(7), 1131-8. 4. Nieduszynski CA and Liti G. 2011. From sequence to function: insights from natural variation in budding yeasts. Biochemical Biophysical Acta. 1810 (10), 959-66. 5. Cubillos FA et al. 2011. Assessing the complex architecture of polygenic traits in yeast. Molecular Ecology. 20 (7), 1401-13. 6. Cubillos F et al. 2009. Generation of a Large Set of Genetically Tractable Haploid and Diploid Saccharomyces Strains. FEMS Yeast Research. 9, 1217-1225. 7. Liti G, et al. 2009. Segregating YKU80 and TLC1 Alleles Underlying Natural Variation in Telomere Properties in Wild Yeast. PLoS Genetics. 5 (9); e1000659. 8. Liti G, et al. 2009. Population genomics of domestic and wild yeasts. Nature. 19; 458(7236), 337-41.	Most human traits, including many diseases, are regulated by multiple interacting quantitative trait loci (QTLs). Although human association studies have already identified hundreds of common risk variants, they fail to explain much of the heritability and we are unable to make predictions from the genetic and environmental interactions characterised thus far. Dissecting the genetic mechanisms underlying this phenotypic variation is a major challenge. This is due to the complex genetic architecture with many loci contributing to phenotypic effects, low penetrance, gene-gene, and gene-environment interactions. In order to advance our understanding of complex traits there is a need for a suitable genetic system that can be used in high-throughput studies. We use the budding yeast, Saccharomyces cerevisiae, to dissect the genetic architecture of multiple medically and biotechnological relevant complex traits and to determine how they vary across natural populations. The objectives are relevant for human health in two ways: the first consists of modelling complex traits in a simple eukaryotic genetic system; the second aims to dissect medically relevant traits. The PhD/Post-doc candidate will work on four closely interlinked objectives with each utilizing data from others: A. Generating an artificial outbred *S. cerevisiae* population as a resource for linkage and association studies. To generate a resource of recombinants from four founder strains representative of the major diverged lineages. The recombinants will be obtained after twelve rounds of random intercross (F12) to allow an expansion of the genetic map and resulting in high resolution QTL mapping. These segregants will be analysed as a pool (B) or individually (C). Two sets of 96 segregants of opposite mating type and with complementary auxotrophic markers will be sequenced (1-2X coverage) and used to produce 9216 hybrid heterozygous combinations. B. Massively parallel sequencing of bulk segregants to map QTLs. We have pioneered a novel method for rapid QTL mapping by combining a step that selects segregants with specific phenotypes with massively parallel sequencing. This approach uses large pools of million of segregants and will provide a sensitive and high resolution strategy for QTL mapping. Loci responsible for a fitness effect will be under selection and beneficial alleles will be strongly enriched in the pool whereas the neutral portion of the genome will remain unchanged. Selective conditions are described in section (D). C. Dissect the architecture of complex traits. The 192 segregants isolated in (1) will be subjected to high-throughput phenotyping (quantitative growth at 100 environmental conditions) as well as phenotyped for the trait described in section (D). Analysis of individual segregants will help to dissect epistatic interaction (a current limit of the bulk segregant analysis) and to establish yeast as a model for GWAS. The 9216 diploid heterozygous will be used as a model for GWAS and phenotyped for growth at high temperature. D. Identify ageing, virulence and senescence QTLs. To fully dissect and validate QTLs responsible for natural variation in medically relevant traits. I will focus my research on ageing (replicative life span) given that longevity pathways are conserved from yeast to humans, virulence (ability to grow at high temperature), and cell senescence in the absence of telomerase (using telomerase inhibitors) with a link to genome stability. Conclusions and Outlook. This project aims to elucidate essential aspects of individual variation among Saccharomyces strains with the major goal of understanding the genetic mechanisms underlying complex traits and human diseases.			2	Microbiologist, molecular biology, genetics, yeast system biology, bioinformatics	Laurence.Genet@unice.fr - Eric.GILSON@unice.fr	
INSERM U998 - CNRS UMR 7284 (Institute of Research on Cancer and Ageing of Nice - IRCAN - from 01/2012) http://ircan.org/index.php?option=com_content&view=article&id=1&Itemid=1	Nice	Gael CRISTOFARI	Impact of repetitive DNA and cellular reverse transcriptases (telomerase, retrotransposons) on the stability and the plasticity of mammalian genomes. Expertise of the lab: molecular and cellular biology, genomics, cytogenetics, next-generation sequencing, bioinformatics	Cristofari, G. et al. EMBO J. 21, 4368-79 (2002). Cristofari, G. et al. Cell. 25, 565-574 (2003). Cristofari, G. et al. EMBO J. 25, 565-574 (2006). De Cian, A. et al. Proc Natl Acad Sci USA. 104, 17347-17352 (2007). Cristofari, G. et al. Nat Methods. 4, 851-853 (2007). Cristofari, G. et al. Mol Cell. 27, 882-889 (2007). Abreu, E. et al. Mol Cell Biol. 30, 2971-2982 (2010). Chaurasiya, K. R. et al. Nucleic Acids Res. (2011), doi:10.1093/nar/gkr726	- Role of retrotransposons in the genomic instability of tumors - Links between the DNA damage machinery and retrotransposons - Genetic screens based on transposable elements and retroviruses	1	molecular and cellular biology	1	molecular and cellular biology		
UMR7284 INSERM998 http://ircan.org/index.php?option=com_content&view=article&id=1&Itemid=1	NICE	Thierry MAGNALDO	role of XPC in carcinoma microenvironnment and genetic stability in the human	Preclinical corrective gene transfer in xeroderma pigmentosum human skin stem cells. Warrick, E., Garcia, M., Chagnoleau, C., Chevallier, O., Bergoglio, V., Sartori, D., Mavilio, F., Angulo, J.F., Avril, M.F., Sarasin, A.,Larcher, F., Del Rio, M., Bernerd, F., Magnaldo, T. Molecular Therapy, (2011) in press.ACL-E8- 15 Valin, A., Barnay-Verdier, S., Robert, T., Ripoche, H., Brellier, F., Chevallier-Lagente, O., Avril, M. F., Magnaldo, T. (2008). PTCH +/- dermal fibroblasts isolated from healthy skin biopsy of Gorlin syndrome patients exhibit features of carcinoma associated fibroblasts. Plos One. (4) 3 e4818 (2009). Fréchet, M., Warrick, E., Vioux, C., Benhamou, S., Spatz, A., Sarasin, A., Bernerd, F., Magnaldo, T. Over expression of matrix metalloproteinase 1 in dermal fibroblasts from DNA repair deficient / cancer prone xeroderma pigmentosum group C patients, Oncogene, 27, 5223 – 5232 (2008). Brellier, F., Bergoglio, V., Valin, A., Barnay, S., Chevallier-Lagente, O., Viel, P., Spatz, A., Gorry, P., Avril, M., Magnaldo, T. Heterozygous mutations in the tumor suppressor gene PATCHED provoke basal cell carcinoma-like features in human organotypic skin cultures Oncogene, 27, 6601-6606 (2008a). Brellier, F., Marionnet, C., Chevallier-Lagente, O., Toftgard, R., Mauviel, A., Sarasin, A. and Magnaldo, T. (2004). Ultraviolet radiation represses PATCHED transcription in human epidermal keratinocytes through an AP1-depedent process. Cancer Res 64, 2699-2704. Bernerd, F., Asselineau, D., Vioux, C., Chevallier-Lagente, O., Bouadjar, B., Sarasin, A. and Magnaldo, T. (2001). Clues to epidermal cancer proneness revealed by reconstruction of DNA repair-deficient xeroderma pigmentosum skin in vitro. Proc Natl Acad Sci U S A 98, 7817-7822.	role of XPC in genome maintenance and expression in human cells	1	Molecular and cellular biology DNA repair	2	Molecular and cellular biology , genomics, bioinformatics		
Inserm U1054 et CNRS UMR5048 http://www.cbs.cnrs.fr/	Montpellier	Pierre-E. MILHIET	Single molecule analysis using fluorescence and atomic force microscopy	D.N. Krementsov, P. Rassam, E. Margeat, N. Roy, J. Schneider-Schaulies, P.E. Milhiet and M. Thali (2010) HIV-1 assembly differentially alters dynamics and partitioning of tetraspanins and raft components**Traffic** 11, 1401-1414. Corresponding author.	Structure and dynamics of tetraspanin-enriched microdomains during infection using single molecule fluorescence microscopy	1	cell biologist, biophysicist	1	Biophysicist, physicist	pem@cbs.cnrs.fr	
				Espenel C, Margeat E, Dosset P, Arduise C, Le Grimellec C, Royer CA, Boucheix C, Rubinstein E, Milhiet PE. (2008) Single-molecule analysis of CD9 dynamics and partitioning reveals multiple modes of interaction in the tetraspanin web.**J Cell Biol.** 2008 182(4):765-76. Faculty of 1000.							
				Charrin, S., Le Naour, F., Silvie, O., Milhiet, P.E., Boucheix, C., Rubinstein, E. (2009) Lateral organization of membrane proteins: tetraspanins spin their web. **Biochem. J.** 420, 133-154.							
				O. Barreiro, F. Sanchez-Madrid, P.E. Milhiet. Dynamic partitioning of tetraspanins within plasma membrane in "Tetraspanins", **Pan Stanford Publishing**, Singapore, sous presse.							
				Kapanidis, A. N., Laurence, T. A., Lee, N. K., Margeat, E., Kong, X., and Weiss, S. (2005) Alternating-laser excitation of single molecules. **Acc Chem Res** 38, 523-33.							
UMR7104 Institut de génétique et de biologie moléculaire et cellulaire (IGBMC) / Inserm U 964 Web : http://www-ulp.u-strasbg.fr/unite_recherche.php?u=14	Illkirch	Bruno Klaholz	integrative structural analysis of transcription and translation complexes	1) I. Orlov, N. Rochel, D. Moras & B. P. Klaholz. Cryo-electron microscopy structure of the 100kDa full nuclear receptor RXR/VDR heterodimer complex with its target DNA. Submitted. 2) B. P. Klaholz. Molecular recognition and catalysis in translation termination complexes. Trends Biochem. Sci., 2011, 36, 282-292; invited review. 3) A. Simonetti, S. Marzi, A. G. Myasnikov, A. Fabbretti, G. Yusupova, M. Yusupov, C. O. Gualerzi & B. P. Klaholz. Structure of the 30S translation initiation complex. Nature, 2008, 455, 416-420. 4) S. Marzi, A. G. Myasnikov, A. Serganov, C. Ehresmann, P. Romby, M. Yusupov & B. P. Klaholz. Structured mRNAs regulate translation initiation by binding to the platform of the ribosome. Cell, 2007, 130, 1019–1031. 5) A. G. Myasnikov, S. Marzi, A. Simonetti, A. M. Giuliodori, C. O. Gualerzi, G. Yusupova, M. Yusupov & B. P. Klaholz. Conformational transition of initiation factor 2 from the GTP- to GDP-bound state visualized on the ribosome. Nat. Struct. Mol. Biol., 2005, 12, 1145-1149. 6) B. P. Klaholz, A. G. Myasnikov & M. van Heel. Visualisation of release factor 3 on the ribosome during termination of protein synthesis. Nature, 2004, 427, 862-865. 7) B. P. Klaholz, T. Pape, A. V. Zavialov, A. G. Myasnikov, B. Vestergaard, E. Orlova, M. Ehrenberg & M. van Heel. Structure of the Escherichia coli ribosomal termination complex with release factor 2. Nature 2003, 421, 90-94. 8) B. P. Klaholz & D. Moras. CH…O hydrogen bonds in the nuclear receptor RAR – a potential tool for drug selectivity. Structure 2002, 10, 1197-1204. 9) N. Rochel, J.-M. Wurtz, A. Mitschler, B. Klaholz & D. Moras. The crystal structure of the nuclear receptor for vitamin D bound to its natural ligand. Mol. Cell 2000, 5, 173-179. 10) B. P. Klaholz, A. Mitschler, M. Belema, C. Zusi & D. Moras. Enantiomer discrimination illustrated by high resolution crystal structures of the human nuclear receptor hRAR. Proc. Nat. Acad. Sci. 2000, 97, 6322-6327.	nuclear receptor complexes, structure-function of chromatin complexes	2	biochemist, chemical biologist	6	physics, biology, mathematics, biochemistry, molecular biology, crystallography, electron microscopy	klaholz@igbmc.fr	
UMR7104 Institut de génétique et de biologie moléculaire et cellulaire (IGBMC) / Inserm U 964 Web : http://www-ulp.u-strasbg.fr/unite_recherche.php?u=14	Strasbourg/Illkirch	Patrick SCHULTZ	Structure/function studies of transcription complexes by cryo electron microscopy.	Papai G et al., 2011, Curr Opin Genet Dev. (2):219-24. Kizilyaprak C et al., 2010, PLoS One 5(6): e11039 Papai G et al.,2010 Nature 465(7300):956-60. Papai G et al., 2009, Structure, 17(3), 363-373. Michel F et al., 2009, EMBO J 28(7), 980-991. Eberlin A et al., 2008 Mol Cell Biol. (5):1739-54. Kurshakova MM et al., 2007, EMBO J. 26 : 4956-65. Jawhari A et al., 2006, EMBO Rep. 5:500-505 Wu et al., 2004, Mol. Cell. 15, 199-208. Leurent et al., 2004, EMBO J. 23(4), 719-27	In vivo chromatin structure	1	cell biologist			patrick.schultz@igbmc.fr	

UMR7104 Institut de génétique et de biologie moléculaire et cellulaire (IGBMC) / Inserm U 964 Web : http://www-ulp.u-strasbg.fr/unite_recherche.php?u=14	Strasbourg/Illkirch	Patrick SCHULTZ	Structure/function studies of transcription complexes by cryo electron microscopy.	Papai G et al., 2011, Curr Opin Genet Dev. (2):219-24. Kizilyaprak C et al., 2010, PLoS One 5(6): e11039 Papai G et al.,2010 Nature 465(7300):956-60. Papai G et al., 2009, Structure, 17(3), 363-373. Michel F et al., 2009, EMBO J 28(7), 980-991. Eberlin A et al., 2008 Mol Cell Biol. (5):1739-54. Kurshakova MM et al., 2007, EMBO J. 26 : 4956-65. Jawhari A et al., 2006, EMBO Rep. 5:500-505 Wu et al., 2004, Mol. Cell. 15, 199-208. Leurent et al., 2004, EMBO J. 23(4), 719-27	human DNA topoisomerases II and cellular cofactors			1	biophyics, Structural biologist	patrick.schultz@igbmc.fr	
UMR7104 Institut de génétique et de biologie moléculaire et cellulaire (IGBMC) / Inserm U 964 Web : http://www-ulp.u-strasbg.fr/unite_recherche.php?u=14	Strasbourg-Illkirch	Annick Dejaegere	We use molecular dynamicsl simulations with other computational methods to study macromolecular complexes. Biological applications focus on molecular mechanisms of transcription regulation.	1 J. Fidelak, S. Ferrer, M. Oberlin, D. Moras, A. Dejaegere, R.H. Stote, « Dynamic correlation networks in human peroxisome proliferator-activated receptor-gamma nuclear receptor protein », Eur. Biophys. J. 2010, 39 1503-1512. 2 E. Samarut, I. Amal, G.V. Markov, R. Stote, A. Dejaegere, V. Laudet, C. Rochette-Egly, Evolution of nuclear retinoic acid receptor alpha (RAR(alpha)) phosphorylation sites. Serine gain provides fine-tuned regulation, Mol Biol Evol. 28(7) 2125-37 (2011). 3 C. Grauffel, R. H. Stote and A. Dejaegere, A molecular mechanics force field for covalently modified lysine side-chains and its validation by molecular docking and molecular dynamics simulations of histone tail peptide – protein complexes, J. Comp. Chem., 31:2434–2451 (2010) 4 G. Moroy, E. Martin, A. Dejaegere, R.H. Stote, Molecular basis for Bcl-2 homology 3 domain recognition in the Bcl-2 protein family: identification of conserved hot spot interactions, J Biol Chem. 284:17499- 511 (2009) 5 Browning C, Martin E, Loch C, Wurtz JM, Moras D, Stote RH, Dejaegere AP, Billas IM (2007) Critical Role of Desolvation in the Binding of 20-Hydroxyecdysone to the Ecdysone Receptor. J Biol Chem 282(45): 32924-32934 6 A. Eberlin, C. Grauffel, M. Oulad-Abdelghani, F. Robert, D. Spehner, L. Ponce-Perez, J.M. Würtz, R.H. Stote, P. Schultz, A. Dejaegere, L. Tora, Histone H3 tails containing dimethylated lysine and adjacent phosphorylated serine modifications adopt a specific conformation during mitosis and meiosis, Mol Cell Biol. 28(5):1739-54 (2008).	Molecular dynamics simulations of protein complexes	1	theoretical/ physical chemist, or structural biologist	1	theoretical/physical chemist, or structural biologist		
UMR7104 Institut de génétique et de biologie moléculaire et cellulaire (IGBMC) / Inserm U 964 Web : http://www-ulp.u-strasbg.fr/unite_recherche.php?u=14	Strasbourg	Laszlo TORA	Our main research interest is to study how specific protein coding genes are turned on and off in the nucleus of a given cell, during growth, differentiation and development. By using new genomic and imaging technologies we aim to better understand the role of histone acetyltransferase complexes in the dynamic regulation of chromatin structure.	1 Krebs AR, Karmodiya K, Lindahl-Allen M., Struhl K and TORA L. (2011) SAGA and ATAC histone acetyl transferase complexes regulate distinct sets of genes and ATAC defines a novel class of p300-independent enhancers. Mol. Cell, in press. 2 Lang G, Bonnet J, Umlauf D, Karmodiya K, Koffler J, Stierle M, Devys D, Tora L (2011) The Tightly Controlled Deubiquitination Activity of the Human SAGA Complex Differentially Modifies Distinct Gene Regulatory Elements. Mol Cell Biol 31(18): 3734-3744 3 Krebs AR, Demmers J, Karmodiya K, Chang NC, Chang AC, TORA L (2010) ATAC and Mediator coactivators form a stable complex and regulate a set of non-coding RNA genes. EMBO Rep 11(7): 541-547 4 Nagy Z, Riss A, Fujiyama S, Krebs A, Orpinell M, Jansen P, Cohen A, Stunnenberg HG, Kato S, TORA L (2010) The metazoan ATAC and SAGA coactivator HAT complexes regulate different sets of inducible target genes. Cell Mol Life Sci 67(4): 611-628 5 Bonnet J, Wang YH, Spedale G, Atkinson RA, Romier C, Hamiche A, Pijnappel WW, Timmers HT, TORA L, Devys D, Kieffer B (2010) The structural plasticity of SCA7 domains defines their differential nucleosome-binding properties. EMBO Rep 11(8): 612-618. 6 Orpinell M, Fournier M, Riss A, Nagy Z, Krebs AR, Frontini M, TORA L (2010) The ATAC acetyl transferase complex controls mitotic progression by targeting non-histone substrates. EMBO J 29(14): 2381-2394 7 Gazdag E, Santenard A, Ziegler-Birling C, Altobelli G, Poch O, TORA L, Torres-Padilla ME (2009) TBP2 is essential for germ cell development by regulating transcription and chromatin condensation in the oocyte. Genes Dev 23(18): 2210-2223. 8 Jobert L, Pinzon N, Van Herreweghe E, Jady BE, Guialis A, Kiss T, TORA L (2009) Human U1 snRNA forms a new chromatin-associated snRNP with TAF15. EMBO Rep 10(5): 494-500 9 Nagy Z, Riss A, Romier C, le Guezennec X, Dongre AR, Orpinell M, Han J, Stunnenberg H, TORA L (2009) The Human SPT20-Containing SAGA Complex Plays a Direct Role in the Regulation of Endoplasmic Reticulum Stress-Induced Genes. Mol Cell Biol 29(6): 1649-1660. 10 Zhao Y, Lang G, Ito S, Bonnet J, Metzger E, Sawatsubashi S, Suzuki E, le Guezennec X, Stunnenberg HG, Krasnov A, Georgieva SG, Schule R, Takeyama K, Kato S, TORA L, Devys D (2008) A TFTC/STAGA module mediates histone H2A and H2B deubiquitination, coactivates nuclear receptors, and counteracts heterochromatin silencing. Mol Cell 29(1): 92-101	Imaging HAT complexes in vivo / Dynamics of SAGA recruitment and activity	1	Molecular and cell biologist.	1	Molecular and cell biologist.		
UMR7104 Institut de génétique et de biologie moléculaire et cellulaire (IGBMC) / Inserm U 964 Web : http://www-ulp.u-strasbg.fr/unite_recherche.php?u=14	Illkirch	Bruno Kieffer	Recent topics which have been addressed by the group include the study of several structural domains of transcription factors such as TFIIH and SAGA. The group is also involved in the study of the Human Papilloma Virus E6 protein and its interaction with host PDZ domains. Often, the molecular plasticity of proteins is crucial for their function, as illustrated by the self-association properties of p8, the smallest subunit of TFIIH or by the role of flanking regions of PDZ domains in protein- peptide interactions. Recently, novel experimental and theoretical tools have been developed to study the disordered states of proteins that are involved in signaling mechanisms. These tools are currently used to study AB domains of nuclear receptors such as RARγ and to describe their modification upon phosphorylation.	(1) Charbonnier S, Nominé Y, Ramirez J, Luck K, Chapelle A, Stote RH, Travé G, Kieffer B, Atkinson RA (**2011**) The structural and dynamic response of MAGI-1 PDZ1 with noncanonical domain boundaries to the binding of human papillomavirus E6. ***J Mol Biol*** **.406**: 745-63 (2) Bonnet J, Wang YH, Spedale G, Atkinson RA, Romier C, Hamiche A, Pijnappel WW, Timmers HT, Tora L, Devys D, Kieffer B (**2010**) The structural plasticity of SCA7 domains defines their differential nucleosome-binding properties. ***EMBO Rep*** **11**(8): 612-618 (3) Lebars I, Martinez-Zapien D, Durand A, Coutant J, Kieffer B, Dock-Bregeon AC (**2010**) HEXIM1 targets a repeated GAUC motif in the riboregulator of transcription 7SK and promotes base pair rearrangements. ***Nucleic Acids Res*** **38**(**21**)**:** 7749-7763 (4) O. assemat, M.-A. Coutouly, R. hajjar, and M.-A. Delsuc (**2010**) Validation of molecular mass measurements by means of diffusion-ordered nmr spectroscopy; application to oligosaccharides. ***CRChimie*** **13**:412–415 (5) C. Pascal, F. Paté, V. Cheynier, and M.-A. Delsuc (**2009**) Study of the interactions between a proline-rich protein and a flavan-3-ol by nmr: Residual structures in the natively unfolded protein provides anchorage points for the ligands ***Biopolymer*** **91**:745–756 (6) S. Augé, P. Schmit, C. A. Crutchfield, M. T. Islam, D. J. Harris, E. Durand, M. Clemancey, A. Quoineaud, J. Lancelin, Y. Prigent, F. Taulelle, and M.-A. Delsuc (**2009**) Nmr measure of translational diffusion and fractal dimension. application to molecular mass measurement *J Phys Chem B* **113**:1914–1918	The project consists in describing the rôle of disordered parts of nuclear receptors in their binding functions using heteronuclear NMR. For this purpose, novel approaches will be developped such as the use of fluorinated residues , Residual dipolar couplings and translational diffusion experiments.	1	Physical chemistry, NMR				
Inserm U565 / UMR7196 Acides nucléiques : dynamique, ciblage, et fonctions biologiques (M.N.H.N) http://www.mnhn.fr/usm503/spip.php?rubrique1	Paris	Jean-François RIOU	Biophysical characterisation of DNA G-quadruplex structures with specific ligands. Biological roles of G-quadruplex structures at telomeres and the involvement of telomeric proteins and RPA in the mechanism of action of G4 ligands. Biochemical and biological functions of Topoisomerase III in telomere recombination mechanisms. Evolution of telomere maintenance mechanisms in rodents and in primates and their contribution to longevity.	Arnoult, N., Saintome, C., Ourliac-Garnier, I., Riou, J.F. and Londono-Vallejo, A. (**2009**) Human POT1 is required for efficient telomere C-rich strand replication in the absence of WRN. *Genes & Development* , 23, 2915-2924.	Characterise new G-quadruplex ligands targeting telomere: biophysical interactions, pharmacological activity of cell lines and synthetic lethality using specific inhibitors of the DNA repair pathways.	3	Cell biology, pharmacology, biophysic	1	Cell Biology, molecular biology	riou@mnhn.fr	
				Temime-Smaali, N., Guittat, L., Sidibe, A., Shin-Ya, K., Trentesaux, C., and Riou, J.F. (**2009**) The G-quadruplex ligand telomestatin impairs binding of Topoisomerase III to G-quadruplex-forming oligonucleotides and uncaps telomeres in ALT cells. *PLoS One* , *4:* e6919.							
				Temime-Smaali, N., Guittat, L., Wenner, T., Bayart, E., Douarre, C., Gomez, D., Giraud-Panis, M.J., Londono-Vallejo, A., Gilson, E., Amor-Guéret, M. and Riou J.F. (**2008**) Topoisomerase III is required for normal proliferation and telomere stability in alternative lengthening of telomeres. *EMBO J* . 27, 1513-1524.							
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Inserm U565 / UMR7196 Acides nucléiques : dynamique, ciblage, et fonctions biologiques (M.N.H.N) http://www.mnhn.fr/usm503/spip.php?rubrique1	Paris	Carine GIOVANNANGELI/ Erika BRUNET	Our team is interested in (1) the development of novel chemical and protein-based nucleases with sequence-specific activity, as original tools for DNA repair studies. This work also includes the optimization and the design of sequence-specific DNA agents. (2) the characterization of molecular mechanisms of chromosomal translocation rearrangements and their role in oncogenesis (http://www.mnhn.fr/usm503/spip.php?rubrique58)	Simsek, D.*, Brunet, E.*, Wong, S. Y., Katyal, S., Gao, Y., McKinnon, P. J., Lou, J., Zhang, L., Li, J., Rebar, E. J., Gregory, P. D., Holmes, M. C., and Jasin, M. (2011) DNA Ligase III Promotes Alternative Nonhomologous End-Joining during Chromosomal Translocation Formation, PLoS Genet 7, e1002080. Nakanishi, K., Cavallo, F., Perrouault, L., Giovannangeli, C., Moynahan, M. E., Barchi, M., Brunet, E., and JasinM. (2011) Homology-directed Fanconi anemia pathway cross-link repair is dependent on DNA replication, Nat Struct Mol Biol 18, 500-503. Concordet, J. P., and Giovannangeli, C. (2011) Engineered nucleases for targeted genome modification, Curr Gene Ther 11, 1. Marlin, F., Simon, P., Saison-Behmoaras, T., and Giovannangeli, C. (2010) Delivery of oligonucleotides and analogues: the oligonucleotide conjugate-based approach, ChemBioChem 11, 1493-1500. Brunet, E., Simsek, D., Tomishima, M., DeKelver, R., Choi, V. M., Gregory, P., Urnov, F., Weinstock, D. M., and Jasin, M. (2009) Chromosomal translocations induced at specified loci in human stem cells, Proc Natl Acad Sci U S A 106, 10620-10625. Simon, P., Cannata, F., Perrouault, L., Halby, L., Concordet, J. P., Boutorine, A., Ryabinin, V., Sinyakov, A., and Giovannangeli, C. (2008) Sequence-specific DNA cleavage mediated by bipyridineNucleic Acids Res 36, 3531-3538.	DNA repair, tailor-made nucleases		biochemistry , cell and molecular biology			giovannna@mnhn.fr	
INSERM U869 Laboratoire ARNA http://www.iecb.u-bordeaux.fr/arna_u869/contactus.php	Bordeaux	Martin Teichmann	Regulation of RNA polymerase III transcription during tumoral transformation of human cells.	Orioli, A., Pascali, C., Quartararo, J., Diebel, K.W., Praz, V., Romascano, D., Percudani, R., van Dyk, L.F., Hernandez, N., Teichmann, M. and Dieci, G. (2011). Widespread occurrence of non-canonical transcription termination by human RNA polymerase III. Nucleic Acids Res. Mar 17.	Regulation of RNA polymerase III transcription	1	cell and molecular biologist	1	cell and molecular biologist	martin.teichmann@inserm.fr	
				Lefèvre, S., Dumay-Odelot, H., Budd, A., Legran, P., Pinaud, N., Teichmann, M. and Fribourg, S. (2011). Structure - function analysis of hRPC62 provides insights into RNA polymerase III transcription initiation. Nature Structural & Molecular Biology, Mar;18(3):352-8. Epub 2011 Feb 27.							
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				Haurie, V., Durrieu-Gaillard, S., Dumay-Odelot, H., Da Silva, D., Rey, C., Prochazkova, M., Roeder, R.G., Besser, D. and Teichmann, M. (2010). Two isoforms of human RNA polymerase III with specific functions in cell growth and transformation. Proc. Natl. Acad. Sci. USA, 107:4176-4181. Epub 2010 Feb 12.							
				Woiwode, A., Johnson, S.A., Zhong, S., Zhang, C., Roeder, R.G., Teichmann, M. and Johnson, D.L (2008). PTEN represses RNA polymerase III-dependent transcription by targeting the TFIIIB complex. Mol. Cell. Biol. 28 (12): 4204-4214.							
INSERM U869 Laboratoire ARNA http://www.iecb.u-bordeaux.fr/arna_u869/contactus.php	Bordeaux	Fabien Darfeuille	Functionnal studies of riboregulation in Helicobacter pylori	1. Sharma CM, Hoffmann S, Darfeuille F, Reignier J, Findeiss S, Sittka A, Chabas S, Reiche K, Hackermüller J, Reinhardt R, Stadler PF, Vogel J.The primary transcriptome of the major human pathogen Helicobacter pylori. Nature. 2010 Mar 11;464(7286):250-5. 2, Belair C, Darfeuille F, Staedel C. Helicobacter pylori and gastric cancer: possible role of microRNAs in this intimate relationship. Clin Microbiol Infect. 2009 Sep;15(9):806-12. Review. 3, Repoila F, Darfeuille F. Small regulatory non-coding RNAs in bacteria: physiology and mechanistic aspects. Biol Cell. 2009 Feb;101(2):117-31. Review. 4, Sharma CM, Darfeuille F, Plantinga TH, Vogel J. A small RNA regulates multiple ABC transporter mRNAs by targeting C/A-rich elements inside and upstream of ribosome-binding sites. Genes Dev. 2007 Nov 1;21(21):2804-17. 5, Darfeuille F, Unoson C, Vogel J, Wagner EG.An antisense RNA inhibits translation by competing with standby ribosomes. Mol Cell. 2007 May 11;26(3):381-92. 6, Udekwu KI, Darfeuille F, Vogel J, Reimegård J, Holmqvist E, Wagner EG. Hfq-dependent regulation of OmpA synthesis is mediated by an antisense RNA. Genes Dev. 2005 Oct 1;19(19):2355-66.	We proposed to characterize several families of small RNA that have been identified recently in this organism by using cutting-edge technologies such as deep sequencing and in vivo expression studies. We also need to complete two stories concerning their biogenesis and control of stability.	1	microbiologist	1	bioinfomaticiian		fabien.darfeuille@u-bordeaux.fr
INSERM U869 Laboratoire ARNA http://www.iecb.u-bordeaux.fr/arna_u869/contactus.php	Bordeaux	Sébastien Fribourg	We are interested in gaining functional input from a structural biology approach of RNA maturation processes (Pol III transcription, mRNA maturation, rRNA maturation)	Lefevre S, Dumay-Odelot H, El Ayoubi L, Budd A, Legrand P, Pinaud N, Teichmann M, Fribourg S (2011) Structure-function analysis of hRPC62 provides insights into RNA polymerase III transcription initiation. Nat. Struct. Mol. Biol., 18(3), 352-358., Moreno-Morcillo M, Mackereth CD, Minvielle-Sébastia L, Fribourg S (2011) Hexameric architecture of CstF supported by CstF-50 homodimerization domain structure. RNA,17, 412-418., Moreno-Morcillo M, Minvielle-Sebastia L, Fribourg S, Mackereth CD (2011) Locked tether formation by cooperative folding of Rna14p monkeytail and Rna15p hinge domains in the yeast CF IA complex. Structure, 19, 534-545., Lebars I, Legrand P, Aimé A, Pinaud N, Fribourg S, Di Primo C. (2008) Exploring TAR-RNA aptamer loop-loop interaction by X-ray crystallography, UV spectroscopy and surface plasmon resonance. Nucleic Acids Res., 36, 7146-56., Choesmel V, Fribourg S, Aguissa-Touré AH, Pinaud N, Legrand P, Gazda HT & Gleizes PE. (2008) Mutation of ribosomal protein RPS24 in Diamond-Blackfan anemia results in a ribosome biogenesis disorder. Hum Mol Genet.,17, 1253-1263 ., Gregory L.A., Aguissa-Touré A.H., Legrand P., Pinaud N., Gleizes P.E. & Fribourg S. (2007) Molecular basis of Diamond-Blackfan anemia: structure and function analysis of RPS19. Nucleic Acids Res., 35, 5913-5921., Legrand P., Pinaud N., Minvielle-Sebastia L. & Fribourg S. (2007) The structure of CstF-77 provides insights into CstF assembly. Nucleic Acids Res., 35, 4515-4522.	Pol III transcription, rRNA maturation or 3' end mRNA maturation	1	Biochemistry, Molecular Biology, Structural Biology or Yeast Genetics	2	Biochemistry, Molecular Biology, Structural Biology or Yeast Genetics		
INSERM U869 Laboratoire ARNA http://www.iecb.u-bordeaux.fr/arna_u869/contactus.php	Pessac	Jean-Louis Mergny	Analysis of nucleic acid structures and drug-DNA/RNA interactions	De Cian, A., Cristofari, G., Reichenbach, P., Delemos, E., Monchaud, D., Teulade-Fichou, M.P., Shin-ya, K., Lacroix, L., Lingner, J. & Mergny, J.L. Reevaluation of telomerase inhibition by quadruplex ligands and their mechanisms of action (2007) Proc. Natl. Acad. Sci. USA. Vol. 104, pp 17347-17352. Rosu, F., Gabelica V., De Pauw, E., Mailliet, P. & Mergny, J.L. Interaction of a phenothiazine derivative with double-stranded DNA in a novel 2:1 minor groove binding mode. (2008) ChemBioChem Vol. 9, pp 849-852. Amrane, S., De Cian, A., Rosu, F., Kaiser, M., Gabelica, V., Teulade-Fichou, M.P. & Mergny, J.L. Identification of trinucleotide repeat ligands with a FRET melting assay (2008) ChemBioChem Vol. 9, pp 1229-1234. Monchaud, D., Yang, P., Lacroix, L.,Teulade-Fichou, M.P. & Mergny, J.L. A Metal-Mediated Conformational Switch That Controls G-Quadruplex Binding Affinity (2008) Angew. Chem. Int Ed. Vol. 47, pp 4858-4861. Yang, P., De Cian, A., Teulade-Fichou, M.P., Mergny, J.L. & Monchaud, D., Engineering Bisquinolinium/Thiazole Orange Conjugates for Fluorescent Sensing of G-Quadruplex DNA (2009) Angew. Chem. Int. Ed. Vol. 48, pp 2188-2191. Ribeyre, C. Lopes, J., Boulé, J.B., Piazza, A., Guédin, A., Zakian, V., Mergny, J.L. & Nicolas, A. The yeast Pif1 helicase prevents genomic instability caused by G-quadruplex forming sequences in vivo (2009) PLoS Genetics, Vol. 5, pp e1000475. Guédin, A., Alberti, P. & Mergny, J.L. Stability of intramolecular quadruplexes: sequence effects in the central loop (2009) Nucleic Acids Res. Vol. 37, pp 5559-5567. Reinhold, W.C., Mergny, J.L., Liu, H., Ryan, M., Pfister, T.D., Kinders, R., Parchment, R., Doroshow, J., Weinstein, J.N., & Pommier, Y. Exon Array Analyses across the NCI-60 Reveal Potential Regulation of TOP1 by Transcription Pausing at Guanosine Quartets in the First Intron (2010) Cancer Res. Vol. 60, 2191-2203. Guédin, A., Gros, J. & Mergny, J.L. How long is too long ? Effect of loop size on G-quadruplex stability (2010) Nucleic Acids Res. Vol. 38, 7858-7868. Lacroix, L., Séosse, A. & Mergny, J.L. Fluorescence based duplex-quadruplex competition screen for telomerase RNA quadruplex ligands (2011) Nucleic Acids Res. Vol. 39, e21.	Design of new real-time in vitro assay to follow nucleic acids i) unfolding by helicases ii) ligand/chaperone associated folding. Application to single molecule measurements	1	Biochemist, Biophysicist	1	Biochemist or structural biologist		
U1022 (Daniel Scherman)	Paris	Michel Bessodes (head of team 2)	***Design, synthesis and study of new molecular, particulate or vesicular vectors and their targeting for therapy and imaging(anatomy, functional, diagnosis). Study of membrane destabilisation initiated by chemical agents (amphiphilic polymers) or by physical methods (electric fields, ultrasounds).***	Maldiney, T., Richard, C., Seguin, J., Wattier, N., Bessodes, M., and Scherman, D. Effect of core diameter, surface coating, and PEG chain length on the biodistribution of persistent luminescence nanoparticles in mice. *ACS Nano* (**2011**) *5* , 854-62.	Our team is multidisciplinary, aimed at the preparation, characterization and validation of new imaging systems for anatomy, functional evaluation and diagnosis purposes. We can offer projects in the domains of chemistry, physical chemistry, cell biology, small animal imaging.	1	chemist, physical chemist, cell biologist, imaging	1	chemist, physical chemist, cell biologist, imaging	michel.bessodes@bbox.fr	
				Safi, M., Sarrouj, H., Sandre, O., Mignet, N., and Berret, J. F. Interactions between sub-10-nm iron and cerium oxide nanoparticles and 3T3 fibroblasts: the role of the coating and aggregation state. *Nanotechnology* (**2010**) *21* , 145103.							
				Mignet, N., and Scherman, D. Liposome biodistribution via europium complexes. *Methods Mol Biol* (**2010**) *606* , 509-18.							
				Chaumet-Riffaud, P., Martinez-Duncker, I., Marty, A. L., Richard, C., Prigent, A., Moati, F., Sarda-Mantel, L., Scherman, D., Bessodes, M., and Mignet, N. Synthesis and application of lactosylated, 99mTc chelating albumin for measurement of liver function. *Bioconjug Chem* (**2010**) *21* , 589-96.							
				Richard, C., Chaumet-Riffaud, P., Belland, A., Parat, A., Contino-Pepin, C., Bessodes, M., Scherman, D., Pucci, B., and Mignet, N. Amphiphilic perfluoroalkyl carbohydrates as new tools for liver imaging. *Int J Pharm* (**2009**) *379* , 301-8.							
				Richard, C., Doan, B. T., Beloeil, J. C., Bessodes, M., Toth, E., and Scherman, D. Noncovalent functionalization of carbon nanotubes with amphiphilic gd3+ chelates: toward powerful t1 and t2 MRI contrast agents. *Nano Lett* (**2008**) *8* , 232-6.							
				le Masne de Chermont, Q., Chaneac, C., Seguin, J., Pelle, F., Maitrejean, S., Jolivet, J. P., Gourier, D., Bessodes, M., and Scherman, D. Nanoprobes with near-infrared persistent luminescence for in vivo imaging. *Proc Natl Acad Sci U S A* (**2007**) *104* , 9266-71.							
marseille (ex : U1006 curie paris : Microscopie à force atomique de protéines membranaires en membranes natives - Institut Curie / Inserm U1006)	Marseille	Simon SCHEURING	We perform high-resolution atomic force microscopy (AFM) imaging and force spectroscopy of membrane proteins. We are interested in "the structure and assembly of membrane proteins in native membranes studied by atomic force microscopy". Information concerning structure, function related conformational changes, and supramolecular assemblies, crucial for a complete understanding of a membrane protein, can be contributed by AFM. AFM experiments are performed in physiological buffer at room temperature and under normal pressure. The AFM features an outstanding signal-to-noise ratio allowing membrane proteins to be directly visualized in their native environment, the native membrane. We also perform technical developments trying to improve resolution, image acquisition rate, and reproducibility of AFM.	Forces guiding assembly of LH2 complexes in native membranes PNAS, 2011, 108 (23): 9455-9459 Lu-Ning Liu, Katia Duquesne, Filipp Oesterhelt, James N Sturgis & Simon Scheuring* Experimental evidence for membrane-mediated protein-protein interaction Biophys J, 2010, 99 (7): 47-49 Ignacio Casuso, Pierre Sens, Felix Rico & Simon Scheuring* The supramolecular architecture of junctional microdomains in native lens membranes EMBO R, 2007, 8 (1): 51-55 Nikolay Buzhynskyy, Richard K Hite, Thomas Walz, & Simon Scheuring* 2-Chamber-AFM: Probing membrane proteins separating two aqueous compartments Nature Methods, 2006, 3 (12): 1007-1012 Rui Pedro Gonçalves, Guillaume Agnus, Pierre Sens, Christine Houssin, Bernard Bartenlian, & Simon Scheuring* Chromatic adaptation of photosynthetic membranes Science, 2005, 309 (5733): 484-487 Simon Scheuring*, & James Sturgis	Imaging and force spectroscopy of membrane proteins using high-speed atomic force microscopy (HS-AFM)	1 (à partir de 2012)	biochemist, biophysicist, biotechnologist	4	biochemist, biophysicist, biotechnologist	simon.scheuring@curie.fr	
U759 Imagerie intégrative : de la molécule à l'organisme - Institut Curie / Inserm U759 http://curie.fr/fr/la-recherche/recherche-fondamentale/unites-de-recherche/imagerie-integrative-de-la-molecule-lorganisme-002371	Orsay	MARCO GARRIDO, Sergio (MOUAWAD, Liliane responsible of the proposed project)	We recently focused on the study of a part of a microtubule by molecular modeling and more specifically normal mode analysis approach. To this purpose we have introduced some developments allowing us to work with such a large number of atoms (> 350,000). In addition to the technological challenge, this study shed new light on the mechanism of stabilization of microtubules.	O. Sperandio, **L. Mouawad,** E. Pinto, B.O. Villoutreix, D. Perahia & M.A. Miteva J. How to choose relevant multiple receptor conformations for virtual screening: a test case of Cdk2 and normal mode analysis. *Eur. Biophys. J.* (2010) **39**(9):1365-72 //// L. Mouawad, & D. Perahia All-atom normal mode calculations of large molecular systems using iterative methods. In "Normal mode analysis: theory and applications to biological and chemical systems" C&H/CRC Mathematical & computational biology series, Vol. 9, CRC Press (2006) //// **L. Mouawad**, & D. Perahia Motions in hemoglobin studied by normal mode analysis and energy minimization: Evidence for the existence of tertiary T-like, quaternary R-like intermediate structures *J. Mol. Biol.* (1996) **258**, 393-410 //// D. Perahia, **L. Mouawad** Computation of low frequency normal modes in macromolecules: improvements to the method of diagonalization in a mixed basis and application to hemoglobin. *Comp. Chem.* (1995) **19**, 241-246 //// **L. Mouawad** & D. Perahia Diagonalization in a mixed basis: A method to compute low frequency normal modes for large macromolecules *Biopolymers* (1993) **33**, 599-611	**Title: Development of new methods to calculate large amplitude motions for huge macromolecular assemblies. Application to microtubules with molecular motors**.//// Project: The functional units in cells are often assemblies of macromolecules, like the Microtubule (MT)-Kinesin traffic system. MT filaments extend throughout the cytoplasm of eukaryotic cells and form the scaffolds to maintain cell shape and compartmentalization. Kinesins are motor proteins that interact with MT filaments, regulating their dynamics and using their framework as highways for the transport of vesicles, organelles, chromosomes, protein complexes, by converting the energy from ATP hydrolysis into mechanical energy. Perturbation of this traffic leads to multiple genetic diseases, some of which are currently under investigation in the host laboratory. Despite the aggregated experimental and theoretical information, the walking mechanism of the kinesin on the microtubule remains an open question. Molecular simulations have the potential to reveal the missing structural and dynamical link between the ATP hydrolysis of kinesin and its motion along MT. The Normal Mode Analysis (NMA) is the appropriate method to obtain large amplitude conformational rearrangements, which are responsible for the protein function. However, the use of NMA is limited because this method is based on the diagonalization of the Hessian matrix, whose number of elements increase as the square of the number of atoms (1012 elements in the case of MT). The Diagonalization In a Mixed Basis (DIMB) and Elastic Network Model (ENM) methods address this limitation in two different ways. The first is an iterative process, which allows the calculation of exact NM, considering all atoms of the system, without any limitation of dimension, but is too time consuming. The second is a coarse-grained method based on a reduced representation of the protein, where each residue is represented only by its Cα atom. However simulations studies of huge macromolecular systems such as MT-kinesin, with reasonable atomic details, are far beyond practical computational costs and timescales for both methods. In this context we propose the development of new methods to overcome these limitations by: i. implementing DIMB to be able to diagonalize ENM matrices expanding by orders of magnitude its applicability; ii. Develop a hybrid method for NMA combining ENM/DIMB and all-atom/DIMB, for an overall coarse-grain picture with a detailed description of MT-kinesin interfaces. The knowledge of structure and dynamics of macromolecular complexes have a high impact in the mechanistic description of biochemical and cellular processes. These developments are of general interest and applicable to any macromolecular systems, opening new horizons for simulations of collective motions and the relation of dynamics and function of proteins.	0		1	molecular modelling and dynamics as well as knowledge in computer programming	Sergio.Marco@curie.fr	