European Cooperation in the field of Scientific and Technical Research

- COST -

Brussels, 15 May 2014

COST 024/14

MEMORANDUM OF UNDERSTANDING

Subject :	Memorandum of Understanding for the implementation of a European Concerted Research Action designated as COST Action BM1403: Native Mass Spectrometry and Related Methods for Structural Biology

Delegations will find attached the Memorandum of Understanding for COST Action BM1403 as approved by the COST Committee of Senior Officials (CSO) at its 190th meeting on 14 May 2014.

MEMORANDUM OF UNDERSTANDING
For the implementation of a European Concerted Research Action designated as

COST Action BM1403
NATIVE MASS SPECTROMETRY AND RELATED METHODS FOR STRUCTURAL BIOLOGY

The Parties to this Memorandum of Understanding, declaring their common intention to participate in the concerted Action referred to above and described in the technical Annex to the Memorandum, have reached the following understanding:

1. The Action will be carried out in accordance with the provisions of document COST 4114/13 "COST Action Management" and document COST 4112/13 "Rules for Participation in and Implementation of COST Activities" , or in any new document amending or replacing them, the contents of which the Parties are fully aware of.

2. The main objective of the Action is to create a lasting expertise infrastructure in novel mass-spectrometry based approaches for the determination of protein structure and interactions, to enable better cures against disease.

3. The economic dimension of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at EUR 32 million in 2014 prices.

4. The Memorandum of Understanding will take effect on being accepted by at least five Parties.

5. The Memorandum of Understanding will remain in force for a period of 4 years, calculated from the date of the first meeting of the Management Committee, unless the duration of the Action is modified according to the provisions of section *2. Changes to a COST Action* in the document COST 4114/13.

A. ABSTRACT AND KEYWORDS

The aim of this Action is to nucleate a group of researchers with a common interest, namely developing and applying new biomolecular Mass Spectrometry (MS) methods in order to make the characterisation of protein structure and dynamics more rapid and routine. Methods include non-denaturing MS approaches in combination with ion mobility, as well as hydrogen-deuterium exchange, chemical crosslinking and other labelling techniques together with computational approaches. This toolbox will be made available to the broader scientific community, and will greatly enhance our ability to design new drugs and ensure the quality and efficacy of biopharmaceuticals, thereby benefiting human health.
Keywords: Native mass spectrometry, ion mobility, structural proteomics, computational methods, protein structure and interactions

B. BACKGROUND

B.1 General background

Novel biophysical and analytical methods are crucial for our understanding of the structures and dynamical interactions of the molecules which make up the complex networks that characterize biological systems. Proteins in particular are involved in all key cellular processes – they have a structural role, control the transport of other molecules, store and turn over energy, and manage the flow of information from generation to generation. Our knowledge of the different roles of proteins has so far relied heavily on the application of traditional biophysical or analytical approaches which originate in the Physical Sciences, such as X-ray crystallography, electron microscopy and fluorescence labelling. While very powerful, these methods usually only give a static view of the molecular structure or fail in some cases. We propose to integrate and further develop alternative methods base on mass spectrometry which target dynamic and heterogenic phenomena in molecular structures, such as conformational change of biomolecules, association equilibria and aggregation processes; and provide snapshots of dynamical change and higher-order structure in biological systems.

The elucidation of biomolecular structures, and the way in which they function and malfunction, have always been at the heart of our effort to understand molecular processes in nature, and enable us to design drug molecules cure disease. Historically Europe has been at the forefront of development of the structural biology techniques used today, and the field of "native" MS which

originated in the U.K. is still at its strongest here. Collaboration is a crucial element, not only between academics with a physical or instrumentation background and bio-scientists who study complex molecular systems, but also with senior development scientists at SMEs (instrument manufacturers) which even though often U.S.-owned, design and build the majority of their scientific equipment in Europe, in close collaboration with academic laboratories. The techniques which are developed in this context are at the forefront of our efforts to understand molecular processes which e.g. control cell development, viral infections or cause protein misfolding diseases. Efforts in combating disease and improving health require collaboration on a very wide scale, across regions and countries as well as spanning from academic laboratories to equipment manufacturers and biotech and pharmaceutical industries. As "cultures" in the different areas of science and industry differ, a common language has to be found in order to aid dissemination of novel methodology and knowledge, and to avoid duplication of efforts. While the scientific community might well have established platforms for such exchange, e.g. conferences and publications, the wider community particularly including SMEs and industry cannot easily participate in these. Our progress as a society as well as the competitiveness of European biotech and pharmaceutical industries relies on the transformative power of scientific knowledge, i.e. the dissemination and implementation of novel methods and instruments in the industrial context. Frameworks such as COST are ideally suited to train the next generation of scientists in a multidisciplinary context, and to provide access to crucial knowhow to the broader research community in Europe.

Whereas the applicants have their own research funding, often in interdisciplinary collaborations with other scientists worldwide (e.g. biologists, medical doctors, physicists, engineers, computer modellers etc), they are engaged in applying novel tools which they developed individually to relevant problems from biology and medicine. What is completely lacking is a concerted effort in developing these tools (instrumentation, experimental and computational approaches etc.), a platform on which to share and propose ideas for new methods and developments, compare and standardize their approaches, develop new research proposals, and train the next generation of scientists in this field (PhD students and postdoctoral scientists).

B.2 Current state of knowledge

A concerted effort in method development and integration has been hampered by a lack of dedicated structures and funding, as well as by the novelty of many of the tools described here. One particularly striking example for the need of a concerted approach is the design and production of

new biotherapeutics, i.e. antibody- and peptide-based drugs. These "drugs of the future" are already now one of the fastest growing fields in the biotech and pharmaceutical industries. Until recently, the vast majority of drugs have been based on small molecules which are synthetically made and often derived from plant ingredients. In comparison, biotherapeutics have superior biophysical, pharmacokinetic and pharmacodynamic properties, and the potential for the design of “tailor-made” drugs is vastly greater than that with chemical structures. Monoclonal antibodies and antibody fragments in particular are fast becoming an important class of biotherapeutics, and over 200 therapeutic proteins have been approved for clinical use in the EU and USA already, with annual sales exceeding 100 billion U.S. dollars (2010). There is an urgent need for a well-defined set of analytical and computational methods to provide input into the design of such drugs, but also for the quality control of such protein products.

The proposed collaboration will bundle a range of currently individual efforts and enable new technologies and applications in the field of biomolecular MS, by bringing experts from varying physical and life science disciplines as well as from bioinformatics together and integrating research groups, institutes and SMEs who are active in the native MS field. These technologies are very important but not readily available yet in a routine setting, e.g. at most universities, biotech or pharma companies. The Action will act as a mediator and platform for different partners to keep ahead in this fast-developing field. The analytical know-how and infrastructure catalyzed by COST will be available for research collaborations with academic partners and crucially also aid biomedical investigations, e.g. by giving early access to the bio-/pharma industries engaged in drug development. It will therefore also strengthen European competitiveness in this key research area.

B.3 Reasons for the Action

This Action is aimed at both scientific/technological advance and at economic/societal needs. The technology platform which the Action intends to develop and disseminate will benefit efforts to combat disease and improve health in collaboration with equipment manufacturers, biotechs and the pharma industry. It also aims to further our understanding of biomolecular structure and interactions, and further approaches in structural biology which try to capture snapshots of proteins and protein complexes in action.

As the capabilities of the technology in this field are ahead of the expertise of the user community, the current focus of activity needs to be on the consolidation of expertise and methodology as well as training of the next generation of users. There is also an urgent need for improved data analysis and integration approaches and molecular modelling software solutions that can generate structural

models of proteins and protein complexes based on different types of native MS data. A key objective is to provide a common platform for collaborations with scientists in other fields, for instance structural bioinformatics and computational modelling.
The combination of expertise will speed up the development of methodology and instrumentation, and provide a unique opportunity for academia to work with industry. The research area targeted by this proposed Action is of common interest for the whole research community with considerable potential for improvements of the applied methodology.

B.4 Complementarity with other research programmes

While the native MS research itself is funded at the national level, there is a clear identifiable demand for alignment and coordination of the various activities across Europe, with particular emphasis on knowledge dissemination and training (student/staff exchange). We think that COST provides the ideal platform to further integrate and "incubate" new approaches in this multidisciplinary field. The groups which are active in this research are dispersed throughout Europe and lack a platform for collaboration. In the first instance, a range of leading groups (ca. 15-20) from up to ca. 10 different European countries will identify the precise structure and operation of this COST action. This COST will also be the nucleation point for an ITN (Marie Curie action).
The proposed Action will be - to some extent - complementary to the ESFRI INSTRUCT (Integrated Structural Biology), which builds a European infrastructure of facilities and instruments, by adding an infrastructure of experts and knowledge in a specific sub-field of the methodology covered by INSTRUCT. Other relevant activities are the future European XFEL research facility, as well as efforts to collect large-scale data on the structures and interactions of proteins (e.g. PDB, Pride).
The Proposer and other colleagues contributing to this initial effort to create a COST Action are individually engaged in various different FP7 programmes, which aim at the utilization of some aspects of this technology rather than a concerted effort in creating a platform for its development, which was identified as a highly desirable goal. Efforts in two other structural biology areas, x-ray crystallography and NMR spectroscopy, have been bundled by the CCP4 and CCPN networks which are funded form a variety of sources. In the case of the novel MS-based technology proposed here, no such current network exists between key innovators.

C. OBJECTIVES AND BENEFITS

C.1 Aim

The aim of the Action is to create a lasting expertise infrastructure in novel mass-spectrometry based approaches for the determination of protein structure and interactions, to enable better cures against disease.

C.2 Objectives

i. to define and develop better tools for Structural Biology and Structural Proteomics, in particular for dynamic and heterogeneous systems, as well as intrinsically disordered and integral membrane proteins.

This will have a high impact on our understanding of structure and function of otherwise difficult to study proteins which are prime targets for drug development. For example large efforts are underway in the biotech and pharmaceutical industries, as well as publicly funded initiatives, to find cures for age-related diseases such as Parkinson's and Alzheimer's, which require a thorough understanding of how proteins fold and misfold and how drugs can prevent the detrimental effects linked to this molecular behaviour. Novel approaches proposed in this action will help to (re-)gain European competitiveness in the Health sector.

ii. to integrate existing approaches and methodologies, and also enhance data interpretation by means of bioinformatics tools and modelling approaches (merging activities in experimental and computational sciences)

This will enable experimental and computational scientists to fully utilize the capabilities of current state-of-the-art equipment and maximise the knowledge generated. It will also allow instrument manufacturers and bioinformatics companies (many of which are based in Europe or conduct key R&D there) to acquire a leading competitive edge by adopting these approaches. Databases which benefit from standardization of reported results can be used by the wider community to mine information. We expect that at least 5 new software tools (programs) will be made publicly available from within this COST consortium.

iii. to develop new equipment and instrumental approaches, including collaboration with research scientists at instrument manufacturers

One of the crucial high-tech industries in which Europe is leading is the (bio-)analytical equipment manufacturing industry. Even though largely U.S.-owned, many of the leading companies (e.g. Waters, Thermo, Agilent and Bruker) conduct key research into new instrumentation and propose applications in the European research and manufacturing centres. These activities have a high added value and feed directly into the technology base of industries which rely on advanced

instrumentation for the characterization of their products, in particular biotech and pharmaceutical industries. We expect that close collaboration with at least 3 of the major instrument manufacturers will result from this.

iv. to train students and staff from all branches of the life sciences in the use of these methods, which are currently not well established yet in academia and industry

In knowledge-based economies, the efficiency of know-how transfer within the community (laterally) and also "downstream" (vertically) into the commercial sector is crucial. To a large extent, such knowledge transfer occurs via recent, highly trained graduates who switch from academia to industry and innovate processes and products. We expect that at least 50 students and staff will benefit from this exchange and be trained in novel methodology.

v. to apply them in a biological context together with collaborating groups in academia and biotech-/pharma industry

We expect that close collaboration with biotech and pharmaceutical companies which will want to adopt this novel technology will result in at least 8 new tech transfer agreements/and or spinoffs. A single production batch of biotherapeutic agent (e.g. antibody) is worth 100 million USD, and if it cannot be used because of poorly characterized properties or inconsistent quality of the product, the need for better characterization tools becomes apparent.

C.3 How networking within the Action will yield the objectives?

This will be the first time such issues have been addressed as a community, with combined input from academics, instrument designers, and biopharmaceutical industries working towards the same goals. The results could lead to improved techniques for future research, a better understanding of biological systems, new and improved therapeutics to combat disease, improved instrument design and manufacture, and improved biopharmaceutical manufacturing processes.

C.4 Potential impact of the Action

The impact of this Action will be twofold. It will provide a novel and cutting-edge technology platform in Europe which builds on the considerable expertise and lead in the field of native MS. It will also boost existing research activities in Structural Biology both in academia and industry, thanks to the novel possibilities which this approach enables. We estimate that between the participating academic groups, ca. 30-60 PhD students will be awarded doctorates in this novel field, and a total grant volume of ca. 50 million Euros directly related to the aims of the COST

Action will be managed. Further to these benefits which will accrue within the academic community, the novel methodology will greatly benefit our understanding of the structure and interactions of proteins, which are at the heart of the process of designing and manufacturing new drugs.

C.5 Target groups/end users

a) the academic community which needs access to such advanced tools to investigate biomolecular structure,
b) instrument manufacturers and software companies which will commercialize tools and solutions,
c) the biotech and pharmaceutical industries which rely on such technology to understand disease and design new drugs, in particular biopharmaceuticals, and
d) society with benefit from novel insights into molecular processes of life and enhanced therapeutic design.
The academic community as well as instrument manufacturers have been involved in the preparation of the proposal, by providing vital input and by organizing and hosting meetings which led to the advances made recently. As the technology is ahead of the know-how of the user group, there is now an urgent need to coordinate efforts in fully utilizing it. Instrument manufacturers have also recognised this and are keen to join such efforts, which in turn will increase their competitiveness in a fast-growing international market.

D. SCIENTIFIC PROGRAMME

D.1 Scientific focus

Over the last two decades, mass spectrometry has become a powerful tool for investigating biomolecules and their interactions. Traditional proteomics approaches have included the study of intact proteins under denaturing conditions (acidic solution and/or high concentration of organic solvent) to determine accurate protein masses or map post-translational modifications (PTMs) using MS/MS fragmentation of protein digests.
Recently, interest has grown rapidly in the use of “native” approaches, where conformations of individual proteins and noncovalent complexes are preserved throughout the ionization process and analysis inside the mass spectrometer. The formation of biologically active protein structures is

mediated by numerous noncovalent contacts. It is therefore very desirable to study these systems under conditions that preserve these interactions, in order to gain information about their function. Native Ion Mobility (IM)-MS is one route that is being increasingly used in the field of structural biology as a complimentary tool to NMR spectroscopy and X-ray crystallography, as well as electron microscopy and other biophysical and spectroscopic approaches. This new MS technology has opened up numerous possibilities for the characterization of protein complexes, and information on protein-protein, protein-DNA, protein-RNA, protein-metal ion and protein-drug interactions are now readily accessible.

In addition to these native MS approaches, a plethora of novel labelling and "footprinting" techniques as well as top-down fragmentation methods are being introduced to the Structural Proteomics toolbox which do not require the preservation of the native structure inside the mass spectrometer. With these methods (e.g. H/D exchange, chemical crosslinking, radical footprinting, covalent surface labelling, top-down ETD, SID or laser induced fragmentation) a more detailed picture of the native fold of proteins and complexes can be generated. Diagnostic fragments preserve information on the exposed surface or the contact points between protein subunits, but are detected and analysed using standard (bottom-up) proteomics instrumentation and methodology. Taken together, these techniques form a powerful set of tools for the elucidation of protein structure, dynamics and interactions. Current efforts in this field are rather fragmented though, being funded mainly by individual research grants and focusing on specific aspects only. Elements of this work are included in various different FP7 grants, but are mainly aimed at utilizing a particular technique for the benefit of understanding a specific protein or disease better. What is also completely lacking is an effort to better utilize the data generated, by advanced data interpretation tools and integration of data from various sources, in order to enable data mining and the formulation of novel hypotheses.

During the period of four years of the Action, the efforts of the consortium will focus on the development of new integrated methods in Structural Proteomics, within a highly collaborative context which includes computer scientists, instrument manufacturers and the large community of users. The Action has a clear vision towards improving methods in Structural Biology and enabling better understanding of molecular processes in biological systems, with the ultimate aim to improve drug design and human health. The bioanalytical programme proposed here will rely on recombinant or isolated protein complexes from a biological context, which are readily available from suppliers or being produced in our labs or those of collaborators. The methods included in the scope of this Action are

i. Ionization/desorption techniques: Predominantly nano-electrospray ionization (nanoESI), but also

alternative approaches such as MALDI, LILBID, LAESI etc. will be investigated for non-denaturing ionization.
ii. Mass spectrometric approaches: Native MS in combination with ion mobility, top-down sequencing; radical footprinting and other labelling approaches, crosslinking, hydrogen-deuterium exchange (HDX) etc.
iii. Bioinformatics approaches: Develop data standards for native MS data, open access data combined with bioinformatics tools for spectral interpretation and structural modelling approaches
iv. Dissemination and knowledge sharing, training

D.2 Scientific work plan methods and means

- Establish application areas of importance:

1. Intact proteins/biomolecular complexes (subunit composition, thermodynamics and kinetics of assembly, size and shape, regulation by post-translational modifications)
2. Protein folding, unfolding, aggregation (conformational studies, including intrinsically disordered proteins and amyloid protein, identification of intermediates and developing models for aggregation processes)
3. Protein-ligand interactions (drug screening, metal binding, determination of binding affinities; specificity, stoichiometry and co-operativity)

Despite the advances in both mass spectrometry and ion mobility instrumentation, advances in the software to process native and IM data has been limited. Software supplied by the manufacturers is not designed with these applications in mind and is therefore limited in scope. A number of programs to process intact protein, protein complex MS and IM data have been or are being developed by proposers of this Action. It is therefore timely that as a community we establish a) standards for the easy dissemination of the data (like mzML used for proteomics) and b) incorporate the best functionalities from existing programs into one program that the entire community uses and further develops. The goal of the Action is to provide an MS-based method platform for structural analysis of proteins. The existing methods have to be evaluated in order to generate optimum experimental procedures. COST will provide generally accessible tools for scientists who have access to mass spectrometry.
What do we want to achieve? Robust methodology incl. steps towards high-throughput, better and

faster spectral interpretation tools, an internationally accepted gold standard for experimental procedures as well as structural interpretation. Synergies between groups focused on method development and groups focused on biological applications; and possible new methods, new instrumentation and new collaborations.

- Decide what methodology is required:

1. Current issues, shortcomings, strengths (increased sensitivity, improved ion source design etc.)
2. Future requirements: data processing and interpretation, instrumentation, high throughput protein-ligand screening, biopharmaceuticals characterization
3. Method development: HDX, footprinting, IMS, top-down sequencing, in-vivo and in-vitro crosslinking, novel top-down fragmentation techniques (ETD, SID, laser dissociation), coupling of native MS to free electron laser crystallography

What equipment, methodologies and expertise do we have between us? The laboratories involved in this initial phase of the application provide a wide range of know-how in structural proteomics/native MS as well as sophisticated equipment to conduct these experiments. A range of software tools is also being developed by the proposers, which will be shared among all participants and will also be made publicly available on the internet.
What do we need to achieve our goals? We need a set of open source software to help for native MS and IM MS data interpretation, modelling, etc. The Action will also schedule regular meetings to discuss progress and compare protocols. Training courses will be offered to both experts in the methodology as well as the user community.

- How can we go forward as a community?

1. What do we expect to achieve from our own funded, on-going research (co-ordinate activities; Achieve more collaboration)? Identified needs: pool resources, facilitate exchange within our community, exchange of knowledge by short stays of students/members in other labs.
   Current research topics include protein folding studies, amyloid aggregation/inhibition, virus assembly, membrane proteins, oligonucleotides etc. – identify need for other important applications

2. We need to widen participation in this research effort beyond the mass spectrometry community, by closer interaction with computational scientists (data analysis and interpretation, protein structure modelling) and industrial partners (selected instrument design companies and manufacturers)

While we welcome that the characterization of biotherpautics poses an urgent demand on the methodology, , we want to maintain the focus of our efforts on the further development of the analytical toolbox. We have many different contacts to most leading players in the biotech-/pharmaceutical industry in Europe between us. The focus of this Action will be on analytical method development though, rather than specific applications.

- How do we monitor and disseminate our achievements?

1. Publish data (many of us are on the editorial board of journals and may be able to request a “Special Edition”)
2. Publish protocols for methods (SOP, standard operating procedure), internet resources (internal and external website including a 'wiki' type page and discussion board)
3. Organise seminars/workshops.
4. Target industry (many of us have links with (bio-)pharmaceutical companies, see above)
5. Target the press (most universities have Press Offices)

- Who would benefit?

1. PhD students, post-doctoral scientists, from training in other laboratories
2. Academic supervisors from enhanced research, possible new methods and new instrumentation
3. Instrument manufacturing industry
4. Improved therapeutics design and manufacture

E. ORGANISATION

E.1 Coordination and organisation

The Action will be organised according to the structures set out for this purpose, which will not be

repeated here. The focus on the Action is on the co-ordination of ongoing efforts in ~~Member~~ Europe, which are already funded individually but not coordinated at the moment. It is very important that this Action is open to all Researchers as well as colleagues in industry, i.e. they can become Action Participants with the same access to shared resources and active participation as everybody else involved in the proposal or management of the Action.

Next to the Management Committee (MC), we propose a Steering Group to be formed from the original proposers, but open to other members (not more than 10 in total though). This Steering Group will catalyze the process of identifying new areas to highlight, propose changes to the work programme and facilitate exchange with industry and the wider public..

The major tools used for monitoring progress of this Action will be Milestones, which refer to checkpoints for the implementation of certain structures and tools (see Part F). Next to the Steering Group, the organisation will also rely on Working Groups which cover important areas within the wider topic of the Action (see below). Researchers and MC members can be members of several Working Groups.

An important aspect of this Action will be the organisation of frequent workshops or conferences, both for the Action participants (experts in the methodology; ca. 8 during the 4-year period) and also for the broader scientific community (at least 2 during the 4-year period). Next to that, training schools (at least 2) and scientific exchanges of students and staff (as required, but estimated at least 20 exchanges of up to 1 week each) are essential elements of the Action.

A regularly updated website (with a nominated website administrator or team) will be implemented both for COST-internal purposes as well as a public, external portal which will serve as a depository for tools, software, SOPs, publications, conference announcements, scientific contacts and services offered, as well as providing a forum for scientific debate and a "breeding ground" for new research proposals. A similar concerted effort (Consortium for Top-Down Proteomics) initiated by colleagues in the USA and Europe has been taken up well, and we will take up some ideas from this example.

E.2 Working Groups

This Action will make use of Working Groups, to cover specific sub-areas in depth and make coordination of such more focused efforts simpler. The Working Groups will be able to propose their own conferences, training and outreach activities (to be approved by the MC of the Action), and we expect that the targeted activities of these Working Groups will be a major factor for the expected high outputs of this Action. The proposed topics for the Working Groups are:

1) Native MS/Ion mobility, experimental methods (incl. collaboration with instrument manufacturers, possible new equipment and methods, generation of SOPs, comparative studies, standardisation of methods, collaboration with biotech/pharma)
2) Crosslinking, HDX and other labelling techniques (incl. development of novel experimental approaches, comparison of methodologies, SOPs, collaboration with biotech/pharma)
3) New fragmentation techniques (incl. collaboration with instrument manufacturers, research into fundamentals, possible sharing of equipment)
4) Computational methods (incl. data collection and interpretation, protein structure modelling and development of novel integrated approaches for structure interpretation, sharing of software tools)
5) Data standards, access and dissemination (incl. standardisation of data from various sources, SOPs, data and software repositories, organisation of training activities)

E.3 Liaison and interaction with other research programmes

The Proposer of this Action is also member of the MC of COST Action CM1004, and colleagues of the Proposer are MC members of COST BM1104. A close collaboration (where appropriate) is planned with these and other COST Actions, possibly aiming at joint conferences and student/staff exchange. As several members of the team proposing this Action are already involved in ongoing FP7 programmes, ample opportunity will present itself for linking up efforts and exchanging information, and most crucially for testing novel approaches developed within the framework of this Action in the wider research context.
The team behind this proposed Action is also closely involved in the ESFRI INSTRUCT, with several members of the proposing team involved either in the INSTRUCT Centres or Platforms, or in the organisation of INSTRUCT. Because of the complementarity between the ESFRI-funded infrastructure and the knowledge base assembled in this Action, we will strive whenever possible to co-organise and co-locate dissemination and training events with INSTRUCT facilities and colleagues.

E.4 Gender balance and involvement of early-stage researchers

As in the composition of the team of applicants, we believe in including as many appropriate people, regardless of gender or nationality, as is necessary for the success of this project. We each have zero tolerance to discrimination of any form or nature.

F. TIMETABLE

Activity	y1				y2				y3				y4			
	q1	q2	q3	q4	q1	q2	q3	q4	q1	q2	q3	q4	q1	q2	q3	q4
Annual meetings (MC)	x		M 1		x				x				x			
Progess/ Working Group meetings			x				x		M 4a		x		M 4b		x	
Update of website			o	o	o	o	o	o	o	o	o	o	o	o	o	o
Dissem. of knowledge at non-COST conf.	o	o	o	o	o	o	M 2a	o	o	o	o	o	o	o	M 2b	o
Publications of collaborative papers				o	o	o	o	o	o	o	o	o	o	o	o	o
Exchange of students/staff between labs			o	o	o	M 3a	o	o	o	o	o	o	o	M 3b	o	o
Comparative studies in native MS/IMS			o	o	o	o	o	o	o	o	o	o	M 5	o	o	o
Generation of novel computational tools					o	o	o	o	o	o	o	o	o	o	o	o
Comparative studies in labeling techniques							o	o	o	o	o	o	M 5	o	o	o
Collab. with instrument manufact.; SOPs							o	o	o	o	o	o	o	o	o	o

x (event), o (ongoing)

M1: Management Committee and Working Groups established, Steering Group membership confirmed, Website established
M2: Conference (or specific session at a conference) for the dissemination of Action know-how to the broader scientific community
M3: Training schools for the wider scientific community
M4: Application for further collaborative grants between Researchers participating in the Action
M5: Checkpoint for dissemination of know-how to biotech and pharma industries

G. ECONOMIC DIMENSION

The following COST countries have actively participated in the preparation of the Action or otherwise indicated their interest: BE, CH, DE, DK, ES, FR, IT, UK. On the basis of national estimates, the economic dimension of the activities to be carried out under the Action has been estimated at 32 Million € for the total duration of the Action. This estimate is valid under the assumption that all the countries mentioned above but no other countries will participate in the Action. Any departure from this will change the total cost accordingly.

H. DISSEMINATION PLAN

H.1 Who?

The target audiences are the following:
Other experts working in the fields of native MS and ion mobility, structural proteomics, computational methods (determination of biomolecular structure by use of molecular dynamics, spatial restraints and protein folding simulations).
The technology is aimed at scientist working in the fields of molecular biochemistry and biomedicine, with particular emphasis on efforts in structural biology (protein structure determination, interaction networks, ligand binding studies etc.) and in molecular biophysics.
The technology will be made available to instrument manufacturers and software providers which are often themselves engaged in the research community, as well as pharmaceutical and biotechnology companies which are interested in adopting these novel analytical strategies for their own research.
Policy makers and planners as well as the general public will benefit from deeper insights into the molecular structure and interactions of molecules which are involved in the key processes of life, and in the possibility to develop better cures for disease.

H.2 What?

The dissemination methods of this Action will include a web portal which will integrate contents and highlight the specific efforts of the COST, and in turn link to the individual websites of the participants which host publicly available software tools as well as recent results of our research

efforts. We will also make internal documents available within the group of COST participants on a password-protected website.
The main channels of sharing the knowledge and technology with the research community will be via the publication of articles in peer-reviewed journals, as well as contributions in international scientific meetings. We will also organise regular scientific meetings ourselves to benefit the community engaged in the development of these techniques, as well as workshops aimed at the uptake of this technology by colleagues in the biotech and pharmaceutical industries, and training activities (short courses and lab placements) hosted in the various participating groups an collaborating Actions and activities (e.g. INSTRUCT). Various members of the consortium are already engaged in activities aimed at schools and the broad public, as well as in the use of social media to disseminate key findings.
The possibility of protecting IP or creating start-up business from within the community of Action participants to catalyze commercial activity based on the results of this research will also be considered.

H.3 How?

The dissemination activity will offer a tool to monitor work progress, both in terms of scientific results and technology transfer.
The effectiveness of the dissemination plan will be critically evaluated on a half-yearly basis, by the number and quality of publications, reports and external contacts, and possibly intensified by goal-directed strategies that will be discussed in internal meetings and in discussions with the major stakeholders of the Action.
The major milestones will be reviewed and if necessary re-assigned every semester.
A key element of the planned Action is to host students from other labs as well as colleagues from industry, to enable efficient knowledge transfer. General public including school children will have regular opportunities to visit laboratories and members of the consortium give frequent general access talks.