ISTITUTO NAZIONALE DI FISICA NUCLEARE

Preventivo per l'anno **2001**

Nuovo Esperimento	Gruppo
MODA2	5

Struttura
ROMA II

Ricercatore responsabile locale: Morante S.

Rappresentante Nazionale: S. MORANTE

Struttura di appartenenza: ROMA II

Posizione nell'I.N.F.N.: P.A. Associata

PROGRAMMA DI RICERCA

A) INFORMAZIONI GENERALI

Linea di ricerca	Dinamica Molecolare di Biosistemi (Membrane Cellulari) con Supercomputers della famiglia APE
Laboratorio ove si raccolgono i dati	RM1, RM2, LNGS e Casaccia (Enea)
Acceleratore usato	
Fascio (sigla e caratteristiche)	
Processo fisico studiato	
Apparato strumentale utilizzato	
Sezioni partecipanti all'esperimento	RM2
Istituzioni esterne all'Ente partecipanti	CNR Genova
Durata esperimento	2

B) SCALA DEI TEMPI: piano di svolgimento

PERIODO	ATTIVITA' PREVISTA
2001	vedi proposal allegato
2002	vedi proposal allegato

Mod. EN. 1

(a cura del rappresentante nazionale)

ISTITUTO NAZIONALE DI FISICA NUCLEARE

Preventivo per l'anno **2001**

Nuovo Esperimento	Gruppo
MODA2	5

Struttura
ROMA II

PREVENTIVO LOCALE DI SPESA PER L'ANNO 2001

In ML

VOCI DI SPESA		DESCRIZIONE DELLA SPESA	IMPORTI Parziali	IMPORTI Totale Compet.	A cura della Comm.ne Scientifica Nazionale
Viaggi e missioni	Interno	Missioni Genova 1 mese uomo	5	**5**	
	Estero	Contatti con M.L. Klein (Università di Philadelphia) 1 viaggi di una settimana 1 congresso internazionale 1 workshop internazionale	3 3 2	**8**	
Materiale Consumo					
Trasp.e facch.					
Spese Calcolo		Consorzio | Ore CPU | Spazio Disco | Cassette | Altro			
Affitti e manutenz. apparecchiat.					
Materiale Inventariabile		2 HD da 18 Giga Bytes	3	**3**	
Costruzione Apparati					
		Totale		**16**	

Note:

Mod. EN. 2 (a cura del responsabile locale)

ISTITUTO NAZIONALE DI FISICA NUCLEARE

Preventivo per l'anno **2001**

Nuovo Esperimento	Gruppo
MODA2	5

Struttura
ROMA II

PREVISIONE DI SPESA: PIANO FINANZIARIO LOCALE

PER GLI ANNI DELLA DURATA DEL PROGETTO

In ML

ANNI FINANZIARI	Miss. interno	Miss. estero	Mater. di cons.	Trasp.e Facch.	Spese Calcolo	Affitti e manut. appar.	Mat. inventar.	Costruz. apparati	TOTALE Competenza
2001	5	8					3		**16**
2002	5	8							**13**
TOTALI	**10**	**16**					**3**		**29**

Note:

Osservazioni del Direttore della Struttura in merito alla disponibilità di personale e di attrezzature:

Mod. EN. 3

(a cura del responsabile locale)

ISTITUTO NAZIONALE DI FISICA NUCLEARE

Preventivo per l'anno **2001**

Nuovo Esperimento	Gruppo
MODA2	5

Struttura
ROMA II

PREVISIONE DI SPESA

Piano finanziario globale di spesa

In ML

ANNI FINANZIARI	Miss. interno	Miss. estero	Materiale di cons.	Trasp.e Facch.	Spese Calcolo	Affitti e manut. appar.	Mat. inventar.	Costruz. apparati	TOTALE Competenza
2001	5	8					3		**16**
2002	5	8							**13**
TOTALI	**10**	**16**					**3**		**29**

Note:

Mod. EN. 4

(a cura del rappresentante nazionale)

ISTITUTO NAZIONALE DI FISICA NUCLEARE

Preventivo per l'anno **2001**

Nuovo Esperimento	Gruppo
MODA2	5

Struttura
ROMA II

PROPOSTA DI NUOVO ESPERIMENTO

Vedi Proposal Allegato

ISTITUTO NAZIONALE DI FISICA NUCLEARE

Preventivo per l'anno **2001**

Nuovo Esperimento	Gruppo
MODA2	5

Struttura
ROMA II

PROPOSTA DI NUOVO ESPERIMENTO

Vedi Proposal Allegato

Modelling Biological Systems by Computer Simulations

G. La Penna[1)], S. Letardi[2)], V. Minicozzi[3,4)], S. Morante[3,4)], G.C. Rossi[3,5)] e G. Salina[5)]

1) IMAG - CNR, Genova
2) Casaccia - ENEA, Roma
3) Dipartimento di Fisica, Universitá di Roma "*Tor Vergata*", Roma
4) INFM, Unitá di Roma "*Tor Vergata*", Roma
5) INFN, Sezione di Roma 2, Roma

Abstract and General Proposal Description

The aim of this project is to model mesoscopic systems of biological interest, such as cell membranes and micelles or other smaller macromolecular aggregates resulting from specific recognition mechanisms, and to explore their dynamic and thermodynamic behaviour either by numerical simulations, like Molecular Dynamics (MD) and Monte Carlo (MC) methods, or by means of a more speculative approach based on stochastic equations of the Langevin type. The first strategy is more suited in the case of systems endowed with translational or rotational symmetries, like cell membranes and micelles, while the second is more appropriate in the study of the slow dynamics that controls protein-protein or protein-DNA aggregate formation.

Directly in the first case and indirectly in the second one, because of the need of computing diffusion coefficients and other physical quantities entering in the diffusion equations, deterministic MD simulations or MC methods will play in any case a central role. The problem with these algorithms is that their computational complexity grows quadratically with the number of elementary components (atoms) of the system, thus limiting in a substantial way the size of the system that can be studied and the length of the simulated trajectory or the number of independent configurations that can be generated. We plan to significantly improve over this situation by implementing the most advanced and sophisticated MD and MC simulation strategies, like Multiple-Time-Step (MTS) integration, Hybrid MC (HMC) or Jump-Walking Hybrid MC (JWHMC) algorithms, etc., on the most powerful parallel platforms that are today available in Europe. These are the computers of the CRAY and APE series to which we have access, as users belonging to the scientific Institutions participating to this project.

- We will model cell membranes as bilayers of phospho-lipid molecules, each layer being composed by an adequately large number of molecules, typically O(1000) molecules. A similar kind of amphiphilic molecules is used to construct (inverse or direct) micelles. These are spherical aggregates formed by about 20 such molecules, in the interior of which an appropriate number of positive counter-ions (to balance the negative charge carried by the heads) and water molecules are segregated. Inverse

micelles are formed when the amphiphilic molecules are immersed in an apolar solvent. The interest of studying inverse micelles is twofold. On one hand they represent useful simplified models of lyposomes, on the other they offer the unique possibility of investigating the peculiar properties of confined water. The development of efficient codes on parallel machines will allow to analyse the thermodynamic properties of both bilayers and inverse micelles and, in particular, the study of the structure of their phase diagram [1] as function of temperature, density or of other relevant physical parameters.

- The mechanisms that mediate the recognition processes between biological macromolecules are at the basis of the events that, among others, modulate the immunological response and regulate the DNA expression. Their investigation in terms of deterministic processes guided by classical dynamics is both physically inadequate (many essential features of the interaction that are usually modelled by various kinds of stochastic forces are completely ignored) and numerically impossible to carry out in practice (the energy landscape of the system is as complicated as that of a spin glass [2], a problem which computationally is known to belong to the class of NP-complete problems). Exploiting the fact that there is a strong experimental evidence showing that only short portions of the involved macromolecules play a role in the interaction, we propose, instead, to attack the problem in terms of stochastic diffusive equations in which one fragment of the first macromolecule diffuses in the average local potential due to the presence of the other interacting system.

State of the Art

Theoretical models describing the dynamic and/or the thermodynamic properties of mesoscopic systems, such as cellular membranes or other molecular aggregates of biological relevance, are based either on a detailed atomistic description of the system, whose dynamics is then investigated by means of the deterministic approach of Molecular Dynamics (MD) [3], or on stochastic evolution equations describing appropriate diffusive processes in an average force field [4].

The first strategy is more useful in the study of cellular membranes and micelles, although also Monte Carlo (MC) [5] methods in their various formulations have proved to be of much help in modelling the solvent or in investigating the equilibrium properties of the system. MD and MC are, in fact, complementary algorithms in this respect, as they allow to sample the *micro-canonical* and the *canonical ensemble* of a system, respectively. As it is well known, MD simulations give also access to dynamic and off-equilibrium properties.

The second approach is more suited for attacking the problem of understanding the nature and the molecular basis of the processes underlying the various known instances of recognition mechanisms both among proteins and between DNA fragments and proteins. Parameters entering in the diffusion equations are anyway computed by means of deterministic MD simulations or MC methods. Let us discuss in turn what is the scientific background behind the two approaches.

1) As is well known, MD provides a microscopic classical description of the system, which consists in following its time evolution by solving numerically the Newton equations of motion of its elementary constituents (atoms). The MC algorithm is, instead, based on the construction of a Markov process by means of which a sequence of configurations of the system is generated, that are distributed with probability given by the Boltzmann energy factor. In both cases the existence of pair-wise interactions between the atoms of the system

make the complexity of the computation grow like the square of the number of atoms, N^2. This circumstance puts a severe limit on the size of the system that can be studied and on the length of the dynamical trajectory or on the number of (independent) configurations that can be generated in MD or in MC simulations, respectively. It is then clear that in any research project in this domain a lot of effort must be devoted to the problem of trying to beat the intrinsic N^2-law of this type of numerical methods.

A good deal of work has already been done by the Roma2 INFM group in this direction. In connection with the present research project we list below some of the most significant scientific results achieved in this domain.

- Simple models of lipid bilayers, formed by up to 2x256 phospho-lipid molecules have been constructed and a first survey of their thermodynamics properties has been carried out by means of extensive MD simulations performed by using the APE100 parallel platforms [6].
- A Hybrid Monte Carlo (HMC) algorithm [7] has been implemented both on parallel and on more standard serial computers. The novelty of this work lies in the fact that the MTS integration method is employed to most efficiently carry out the MD simulation part of the algorithm by which trials configurations are constructed.
- A model of realistic dimensions of an inverse micelle with counter-ions and water molecules in its interior has been constructed. The study of the interaction of the full system with an apolar solvent (CCl_4), equilibrated by using the HMC algorithm described above, has already been started [8].

2) Different levels of approximation of the Mode-Coupling Diffusive Dynamics have been developed in the literature, starting from the lowest order one, given by the Optimised Rouse-Zimm Local Dynamics [9][10]. Higher order corrections have been constructed in the maximum correlation approximation [11]. This general computational set up has been successfully used to deal with the dynamics of various types of macromolecules, ranging from elastomers and proteins to polysaccharides and DNA fragments in double helix configurations. Results of this approach have been compared to the exact solution in simple cases [12] and, in more complicated ones, shown to match with available NMR relaxation data [13].

From a methodological point of view especially interesting are the applications of this computational strategy to study the slow dynamics of DNA fragments (such as double helix bending, groove deformation, etc.), as the latter is directly related to the DNA biological activity [14][15]. Different levels of approximations have been tried, leading to results in rather good agreement with NMR experimental numbers. The interplay between deterministic MD simulations and the stochastic evolution equations that drive the dynamics of the system is crucial in this case, as the different approximated forms of the employed diffusive operator are determined from MD data averages.

Objective

In correspondence with the two complementary theoretical approaches described above, we now briefly illustrate the main objectives of the present project.

1) Schematically, a cell membrane consists of an almost spherical bilayer of phospho lipid molecules, separating the interior of the cell from the external world. Phospho-lipids are molecules composed by a hydrophilic head and one or two hydrophobic tails. These peculiar hydropathicity properties lead to the well known bilayer-like structure of the membrane, in

which the hydrophilic heads are in contact with water, present both outside and inside the cell, while the hydrophobic tails are more or less tail-to-tail, pair-wise aligned.

It appears experimentally that an important parameter governing the reaction rate of many biological processes taking place inside or in the near vicinity of a membrane is its “permeability" [16] . From this point of view a membrane can be thought of as a system made out of two layers of a smectic fluid, with a permeability which depends “critically" on temperature, density, the detailed chemical composition of the constituent phospho-lipids, the concentration of chemicals possibly dispersed in the membrane itself or in the solvent, etc..

It is clear that a detailed simulation of the dynamics of the membrane of a living cell is just impossible and one has to resort to a number of simplifications. A fortunate circumstance in this respect is that it appears experimentally that the nature and the location of the phase transitions, which control a number of important physico-chemical properties of the membrane, are essentially related to the bulk ordering properties of the hydrophobic tails [15]. Thus a first step in the direction of simulating a realistic system, which is the one that has been also largely followed in the literature (see refs. [17] to [21]), is to take a bilayer consisting of the largest possible number of lipid molecules (compatible with the available computing power) and proceed to study

- the role of water as a solvent,
- how the relevant order parameters behave as functions of temperature and density,
- how the presence of foreign molecules (drugs, small peptides, etc.) interacting with the hydrophobic tails may affect the structure of the phase diagram.

In particular we would like to test the validity of the idea that the role of water, with the electrostatic interactions that go with it, is simply that of making lipid heads soluble, thus allowing the formation of the typical “two-sheet" structure in a water-rich biological environment. Once the bilayer is formed in the polar fluid, its structural and thermodynamic behaviour will be mainly governed by the packing and flexibility properties of the hydrocarbon tails [16]. Most of the effects of water on the physico-chemical behaviour of the membrane are of secondary importance for the kind of questions we are addressing here. In the picture we have, in fact, water is important in that it behaves as a sticky medium for the lipid heads, which modulates the superficial density by more or less penetrating into the bilayer [22]. Thus water penetration should be held responsible for the difference one sees in the increase of disorder in the head region, as compared to what happens to the tails, only to the extent it affects the superficial density of the bilayer. The different behaviour between heads and tails may in turn be at the origin of the great sensitivity of the structure of the phase diagram to molecular composition and tail length. To study the role played by water we will have to set up for comparison different bilayer models, with and without water. Of course in the first case Coulomb interactions cannot be neglected and will have to be very carefully treated. We will not dwell here on the complicated technical problems posed by the presence of long range forces in numerical simulations, but we refer to the vast literature on the subject (see for instance [3] and the many references quoted there).

In the case of micellar systems we would like to clarify with the help of sufficiently long simulations the dynamics of the formation of inverse micelles in an apolar solvent and the peculiar physico-chemical properties of the hydration zone. To this end a detailed (all atom) description of the amphiphilic constituent molecules will have to be used. This is a significant

improvement over the existing simulations [23], where the hydrocarbon tail of the constituent molecules was modelled by a Lennard-Jones sphere and the dipolar head by two point-like charges connected by a harmonic potential. As for the simulation of the solvent, we will use the HMC algorithm or a variant of it, the so-called Jump-Walking Hybrid MC (JWHMC) algorithm. HMC is a straightforward modification of the MC method in which the trial configurations to be subjected to the Metropolis test are constructed using an MD algorithm. This allows to perform collective moves of the system with a consequent much better sampling of the system phase space, without spoiling the “canonicity" of the algorithm [5][7]. The JWHMC algorithm is in turn an evolution of the HMC method in which from time to time along the Markov chain Metropolis tests are performed at values of certain physical parameters of the system (like temperature, force field parameters, etc.) significantly different from the actual ones. This trick, which conceptually is very similar to the “simulated tempering" of [24], helps a lot in preventing the system to remain trapped in some much-too-long-lived metastable configuration. Given the complexity of the system in study, stochastic algorithms, like the JWHMC we have just described, seem to be much more appropriate than deterministic approaches of the MD type.

We conclude by observing that the whole computational scheme discussed above is completely classical. However, it should be observed that quantum effects of particular relevance could be included with not too much effort. The Car-Parrinello [25] method, in fact, reduces the quantum computation of the interatomic potential to a sort of MD in an enlarged space where not only atomic degrees of freedom, but also electronic ones are let to evolve. The skills that the INFM-Rome2 group has developed in the field of MD simulations could be, if necessary, exploited to deal with this interesting possibility.

2) The physico-chemical processes that regulate the formation of protein-protein and protein-nucleic acid complexes play a fundamental role in biology, as they control two of the most essential events that permit and maintain life, namely immunological response and DNA expression. Thus it is a task of the utmost importance to try to uncover the nature of the mechanisms which are responsible for the formation of biological macromolecule complexes. A direct approach to this problem, based on a brute-force extension of standard MD methods to these situations, is doomed to failure, because of the enormous complexity of the phase space available to the combined system. In fact, despite the fact that only short bits of the involved macromolecules actually play a significant role in the interaction, the complexity of the phase space is so high that impossibly long simulation times would be necessary for the system to overcome the energy barriers in between nearby minima. The use of stochastic or diffusive equations, in which the evolution takes place in some kind of external average force field, is then mandatory.

The approach developed in the references [9] to [15] is very promising in this respect. Our goal will be to extend its application to a systematic study of protein-nucleic acid complex formation. Accurate tests of this strategy will be possible, thanks to the many NMR experimental data existing in the literature. Comparison with experiments will help in shaping the form of the force fields and determining the level of approximation to which the relevant diffusive equations should be solved. We are confident that this approach will be very successful and will help in understanding the general features underlying the recognition mechanisms between biological macromolecules.

References

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Description of the groups involved in the proposal and their contribution to the research activity

- The Biophysics group of the University of Rome "Tor Vergata", which is associated to INFM (Istituto Nazionale per la Fisica della Materia) Sect. B is, since many years, involved in the study of biological macromolecules and their aggregates. Within the group there exist complementary competences in different areas of Biophysics, covering both theoretical (pattern recognition in genomic and amino acidic sequences, numerical simulations) and experimental (X-ray spectroscopy) aspects of the field. As for the present proposal, the expertise of the proponent group on the use of MD simulations and MC methods for the study of the dynamic and thermodynamic properties of biological systems, like phospho-lipid bilayers, micelles and lyposomes, is internationally widely recognized.
- The CNR (Consiglio Nazionale delle Ricerche) group has a leading position in the field of stochastic equations, as its components have been among the people involved in the development of the application of diffusive evolution equations to the modellization and the study of the dynamics of complexes formed by locally interacting macromolecules.
- The INFN (Istituto Nazionale di Fisica Nucleare) group possesses specific mathematical and programming competences that are essential in the task of implementing on the available parallel platforms (machines of CRAY and APE series) the different simulation strategies which we plan to employ in the various stages of the project.

Interdisciplinary added value

The study of complex systems as those that are of interest in this proposal require a large amount of interdisciplinary knowledge, ranging from biology to programming and from modern mathematics to NMR and X-ray spectroscopy. All these competences are fortunately present in the collaboration that has been set up for this project. In this way many useful methodologies developed even in distant scientific contexts will be immediately ready for the use here, with the added benefit that the most advanced and sophisticated programming techniques will be available for the needs of the present project.

Requested Co-Funding of the proposal

- CNR - 20 Mlit for the two years, to be used for travelling expenses of the proponents, for co-funding of a dedicated research fellowship and for the acquisition of computers and software allocated to this project.
- INFM - 20 Mlit for the two years, to be used for travelling expenses of the proponents, for co-funding of a dedicated research fellowship and for the acquisition of computers and software allocated to this project.

Project Milestones

2001 Milestone value

Extensions of the standard HMC method will be developed with the aim of incorporating different “walking" strategies, according to the possible different choices of system parameters (temperature, torsional potential coefficients, external fields, etc.) that one is willing to vary. These new MC-like algorithms will be cross-checked in simple cases, by comparing their performances with MD simulations and with more standard MC methods. Whenever possible, NMR and X-ray spectroscopic data will be used to test the validity of the scheme.

The loss of information on the local molecular motion that one ends up with in this approach may be partially recovered by resorting to diffusive equations of the kind described before (see sect. 2 and references therein), appropriately generalized to encompass the cases which are of interest for this project. Extending these stochastic methods to, say, the case of a bilayer is not a trivial problem because of the strong spatial anisotropy of the average forces felt by the constituent molecules, which are in contact partly with water and partly with a hydrophobic medium. Besides these developments the application of these methods to the study of biological complexes will be still actively pursued.

2001 Achievements & Deliverables (Synthetic Description)

In the first year of the project we plan to

- implement the JWHMC algorithm on standard serial platforms 04/2001
- perform the first tests of the JWHMC algorithm on simple systems 06/2001
- extend the existing stochastic methods to anisotropic cases. 09/2001
- accomplish the porting of the JWHMC algorithm on parallel platforms of the SIMD type (APE1000) 12/2001

2002 Milestone value

Successful tests of the JWHMC algorithm will allow interesting applications to the case of phospho-lipid bilayers and inverse micelles, as a next step. JWHMC simulations have proved, in fact, to be a viable alternative for situations in which MD or standard MC techniques have problems in adequately sampling the phase space of the system, because the conformational landscape is extremely rough with configurations separated by large energy barriers. The huge number of degrees of freedom that enter in the atomistic description of systems, like bilayers or micelles, require a substantial speed up of the simulations. From this point of view we consider a milestone of this project the implementation of JWHMC on multi-processor platforms of the SIMD type, where the very nature of the algorithm in principle allows to reduce the CPU-time required for the simulation by a factor of the order of the number of processors. The CPU-time required to collect a given number of configurations is, in fact, expected to scale linearly with the inverse of the number of nodes, as

different nodes can be arranged to run different “walkers" and nodes will be made to communicate only occasionally to allow energy comparison and, when necessary, exchange of configurations. From these simulations we will be able to extract a large number of useful information concerning the physico-chemical properties of the investigated systems that will be compared with the available experimental data.

In parallel with a systematic exploitation of the JWHMC approach, we will continue the development of the complementary strategy based on stochastic diffusive equations. The latter will be used in a variety of cases ranging from the study of the dynamics of complex formation to the computation of order parameters in bilayers and micellar systems.

2002 Achievements & Deliverables (Synthetic Description)

In the second year of the project we plan to

- perform simulations on phospho-lipid bilayers and inverse micelles
- apply stochastic methods to complex formation studies and order parameter computation.

Criteria suggested by the proposer for the Evaluation of the Project and Beneficiaries

Proposed Criteria for the Evaluation of the Proposal

It is suggested that the project should be evaluated on the basis of the high level of interdisciplinarity that goes into problems that, like the ones we consider here, are related to biology. Problems of this sort require, in fact, the development of the whole path-way of scientific knowledge, that, starting from the experimental observation, aims at understanding the physics of the phenomenon in terms of a suitable mathematical model, based on previous experience and/or theoretical prejudisms. In dealing with biological questions, a key aspect of this gnoseological process is that one easily risks to end up with a model which is of a complexity comparable with that of the system one is investigating. In evaluating this proposal it should be then particularly appreciated the fact that the modellizations we propose for the biological systems we wish to study lead to well defined, though innovative, computational schemes that can be adequately implemented on the existing most advanced computers.

Beneficiaries

Many of the theoretical ideas and numerical algorithms that we plan to develop in the framework of this project are rather new and, as such, will be of interest for the Biophysics community at large. In particular we think that a joint effort should be made by the scientific community as a whole to set up computing packages for the investigation of dynamic and thermodynamic properties of biomolecule aggregates. We hope that this project may be a first, perhaps non negligible, contribution in this direction.

List of participants (2001)

	Title & Full-Name	**RU,Institution**	**FTE** (%)
INFM	Prof. Silvia Morante Professore Associato	Unità INFM di “Tor Vergata”	100

	Dr. Velia Minicozzi Dottorando	Unità INFM di “Tor Vergata”	100
INFN	Dr. Gaetano Salina Primo Ricercatore Prof. Giancarlo Rossi Professore Ordinario	Sezione INFN di Roma2 Sezione INFNdi Roma2	15 15
CNR	Dr. Giovanni La Penna Ricercatore Dr. Sara Letardi Borsista	IMAG, CNR Genova ENEA Casaccia	20 20

ISTITUTO NAZIONALE DI FISICA NUCLEARE

Preventivo per l'anno **2001**

Codice	Esperimento	Gruppo
	MODA2	5

Struttura
ROMA II

COMPOSIZIONE DEL GRUPPO DI RICERCA

N	RICERCATORI Cognome e Nome	Qualifica: Dipendenti Ruolo	Dipendenti Art. 23	Incarichi Ricerca	Incarichi Assoc.	Affer. al Gruppo	Percentuale
1	Minicozzi V.				Dott.	5	100
2	Morante S.				P.A.	5	100
3	Rossi G.C.			P.O.		4	15
4	Salina G.	I Ric				5	15

N	TECNOLOGI Cognome e Nome	Qualifica: Dipendenti Ruolo	Dipendenti Art. 23	Incarichi Ass. Tecnol.	Percentuale

Numero totale dei Tecnologi

Tecnologi Full Time Equivalent

N	TECNICI Cognome e Nome	Qualifica: Dipendenti Ruolo	Dipendenti Art. 15	Incarichi Collab. tecnica	Incarichi Assoc. tecnica	Percentuale

Numero totale dei Ricercatori	**4,0**	Numero totale dei Tecnici
Ricercatori Full Time Equivalent	**2,3**	Tecnici Full Time Equivalent

Mod. EC/EN 7

(a cura del responsabile locale)

ISTITUTO NAZIONALE DI FISICA NUCLEARE

Preventivo per l'anno **2001**

Codice	Esperimento	Gruppo
	MODA2	5

Struttura
ROMA II

COMPOSIZIONE DEL GRUPPO DI RICERCA (cont.)

LAUREANDI Cognome e Nome	Associazione SI	Associazione NO	Titolo della Tesi
Relatore	O SI	O NO	
Relatore	O SI	O NO	
Relatore	O SI	O NO	
Relatore	O SI	O NO	
Relatore	O SI	O NO	
Relatore	O SI	O NO	
Relatore	O SI	O NO	
Relatore	O SI	O NO	

	Denominazione	mesi-uomo

SERVIZI TECNICI

Annotazioni

INTERAZIONI CON LE INDUSTRIE (COMMESSE HIGH TECH)

DENOMINAZIONE	DESCRIZIONE PRODOTTO O COMMESSA

(a cura del responsabile locale)

ISTITUTO NAZIONALE DI FISICA NUCLEARE

Preventivo per l'anno **2001**

Codice	Esperimento	Gruppo
	MODA2	5

Struttura
ROMA II

REFEREES DEL PROGETTO

Cognome e Nome	Argomento

MILESTONES PROPOSTE PER IL 2001

Data completamento	Descrizione
4/1/2001	Implement the JWHMC algorithm on standard serial platforms.
6/1/2001	Perform the first tests of the JWHMC algorithm on simple systems.
9/1/2001	Extend the existing stochastic methods to anisotropic cases.
12/1/2001	Accomplish the porting of the JWHMC algorithm on parallel platforms of the SIMD type (APE1000)

COMPETITIVITA' INTERNAZIONALE

The problem of modelling mesoscopic systems, as the biological ones, is of the utmost importance not only from a methodological point of view but also for its practical applications. A lot of work has gone in this direction ranging from spin-glass inspired models, to deterministic (MD) or stochastic (MC) simulations. This project is at the forefront of the today's research activity in this field both for the level of sophistication of the mathemathical tools we are setting up to work and for the unprecedented amount of computing power that the envisaged massive use of parallel platform will provide us. It is only in this framework that one can hope to attack problems like the effects of drugs on membrane permeability, the formation of ionic channels, the formation of protein-protein or protein-DNA complexes.

LEADERSHIPS NEL PROGETTO

Cognome e Nome	Funzioni svolte
Morante Silvia	Responsabile Nazionale

(a cura del responsabile nazionale)

Esperimento	gruppo	Rappresentante nazionale	Struttura res_naz	nuovo_continua
MODA2	5	S. MORANTE	ROMA II	nuovo

STR.	ESPERIM.	Missioni interno	Inviti ospiti stran.	Missioni estero	Mater. di Cons.	Spes Sem	Tras. e Fac.	Pub. Scien.	Spese Calc	Aff. e Manut. App.	Mater. invent.	Costruz. apparati	TOTALE
ROMA2	Personale												
	Ricercatori	4,0	Tecnologi		Tecnici						Servizi mesi uomo		
	FTE	2,3	FTE		FTE								
	Rapporti (FTE/numero) Ricercatori	**0,58**	**Ricercatori+Tecnologi**										**0,58**
	MODA2	5		8							3		**16**
	di cui sj												
	Totali	5		8							3		**16**
	di cui sj												
	Richieste/(FTE ricercatori+tecnologi)	**6,96**											
TOTALI													
	Totali	5		8							3		**16**
	di cui sj												
Confronto con il modello EC4													
	Mod. EC4 dati	4		9							5		**18**
	Totali-Dati EC4	1,0		-1,0							-2,0		**-2,0**
Personale													
	Ricercatori	4,0	Tecnologi		Tecnici						Servizi mesi uomo		
	FTE	2,3	FTE		FTE								
	Rapporti (FTE/numero) Ricercatori	**0,58**	**Ricercatori+Tecnologi**										**0,58**
	Richieste/(FTE ricercatori+tecnologi)	**6,96**											