EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

Brussels, 25 May 2021

COST 069/21

DECISION

Subject: Memorandum of Understanding for the implementation of the COST Action “Multiscale Irradiation and Chemistry Driven Processes and Related Technologies” (MultIChem) CA20129

The COST Member Countries will find attached the Memorandum of Understanding for the COST Action Multiscale Irradiation and Chemistry Driven Processes and Related Technologies approved by the Committee of Senior Officials through written procedure on 25 May 2021.

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Funded by the Horizon 2020 Framework Programme of the European Union

MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

COST Action CA20129
MULTISCALE IRRADIATION AND CHEMISTRY DRIVEN PROCESSES AND RELATED TECHNOLOGIES (MultIChem)

The COST Members through the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action, referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any document amending or replacing them.

The main aim and objective of the Action is to radically advance, through state-of-the-art theoretical, multiscale computational modelling and experimental studies, the fundamental understanding of irradiation-driven chemistry processes involving complex molecular systems (biomolecular systems, deposited metal nanostructures, metal-based nanoparticles, and composite materials) exposed to radiation, and to enable implementation of this knowledge in biomedicine, nanofabrication, and energy conversion technologies. This will be achieved through the specific objectives detailed in the Technical Annex.

The present MoU enters into force on the date of the approval of the COST Action by the CSO.

OVERVIEW

Summary
Radiation is an inevitable element of the world. It may affect life and likely was involved in its origin. The fundamental understanding of radiation was often at the heart of the most important scientific and technological breakthroughs (Maxwell theory, Einstein photo-effect, relic radiation, synchrotron, FEL, etc.) and it remains so. One of the big current challenges concerns the quantitative understanding of the complex processes in various systems, including the living ones, induced by their irradiation by photons, charged particles, or neutrons. These processes may lead, for instance, to the therapeutic effects of radiation, new pathways for the controlled fabrication of nanosystems with desired properties, energy conversion and storage, catalytic activity, or be in the heart of technologies for the construction of novel light sources. Despite a large variety of possible applications, the fundamental principles of irradiation-driven processes in different systems are similar. One of such features is the multiscale spatiotemporal nature of the processes extending the direct outcomes of irradiation over large time-&-space dimensions and linking them to a variety of relevant phenomena. The advances in this interdisciplinary area became possible only recently due to the development of powerful computers and modern experimental techniques.

The **Action MultIChem** aims to establish a broad international interdisciplinary intersectoral cooperation aiming to advance our fundamental understanding of the **multiscale irradiation-driven processes and related technologies** paving the path towards major scientific and technological breakthroughs, and socio-economic impacts. These goals require a pan-European approach and COST is the most appropriate instrument for their realization.

Areas of Expertise Relevant for the Action	**Keywords**
● Physical Sciences: Atomic, molecular and chemical physics ● Chemical sciences: Physical chemistry ● Medical biotechnology: Databases, data mining, data curation, computational modelling	● Irradiation-driven nanoprocesses ● Multiscale modelling ● Nanofabrication technologies ● Functionalised nanosystems ● Radiotherapies

Specific Objectives
To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

Research Coordination
● To combine and advance experimental, theoretical and computational modelling methods for studying, on a molecular level, irradiation-driven chemistry processes underlying radiation-induced biodamage; radiation-induced formation of nanostructures on surfaces; catalytic and radiosensitising properties of metal-based nanoparticles exposed to radiation. To exploit this knowledge for the development of industrially viable computational tools.
● To establish a comprehensive databank of irradiation-driven chemistry (IDC)-related quantities, e.g. photon, electron and ion interaction cross sections with bio- and organometallic molecules, nanoparticles and nanostructures, chemical reaction rates, diffusion coefficients for different atomic and molecular species, compositions of metal-containing nanostructures grown by focused electron beam induced deposition, etc.
● To develop computational tools based on molecular-level understanding of IDC and multiscale modelling

of biodamage phenomena (relative biological effectiveness, DNA damage response, etc.) with the aim of developing the nanodosimetry based dose delivery protocols and their utilization in new-generation treatment planning systems for ion-beam cancer therapy.
● To develop specific computational workflows for multiscale modelling in nanofabrication of nanostructures, nanoparticles and composite materials, as well as molecular-level characterisation of the IDC processes therein. This will enable optimal experimental conditions and better technological control of fabricated nanostructures and materials with enhanced catalytic and radiosensitising properties.
● To disseminate the scientific and technological outcomes of MultIChem to a broader scientific community, policy makers, and the general public.

Capacity Building
● To establish a pan-European IDC community that will combine advanced theoretical and computational methods with advanced experimental techniques for studying collision- and irradiation-induced processes involving biomolecular systems, nanoparticles and nanostructures, while fostering the development of the existing experimental and theoretical tools beyond the state-of-the-art.
● To accumulate and systematise the knowledge collected by different complementary communities working in the areas related to IDC. To formulate the key research domains of the IDC research field and determine directions for its further development.
● To consolidate efforts of different research communities studying IDC towards technological breakthroughs in the development of novel radiotherapy treatment protocols, nanofabrication methods, as well as novel radiosensitising agents and nanocatalysers.
● To establish a critical mass of scientific knowledge, infrastructure, managerial experience and open communication opportunities to ensure that the MultIChem Consortium remains active and sustainable after the completion of the Action.

TECHNICAL ANNEX

1. S&T EXCELLENCE

1.1 Soundness of the Challenge

1.1.1 DESCRIPTION OF THE STATE-OF-THE-ART

Many modern and emerging technologies exploit irradiation of molecular systems which results in alteration in both the systems' structure and morphology and hence changes in their electronic, mechanical and catalytic properties on both the nano- and the microscale. The interaction of different radiation modalities (e.g., visible and UV light, X-rays, electrons, ion beams) with molecular systems initiates quantum processes, such as electronic excitation, ionisation, radiation-induced fragmentation, e.g. via the dissociative electron attachment (DEA) mechanism, electronic and thermal relaxation of the deposited energy as well as transport of different reactive species produced in the irradiation process, such as secondary electrons or atomic and molecular fragments. These quantum transformations are followed by the next stage that includes **irradiation-driven chemistry (IDC)** leading to subsequent transformations or synthesis of complex molecular systems. Indeed, irradiation-driven processes such as induction of complex DNA strand breaks, radiation-induced formation of nanostructures or chemical reactions involved in catalysis are central to many modern technologies. A schematic time-space diagram of these processes and the corresponding research and technology areas is shown in Fig. 1.

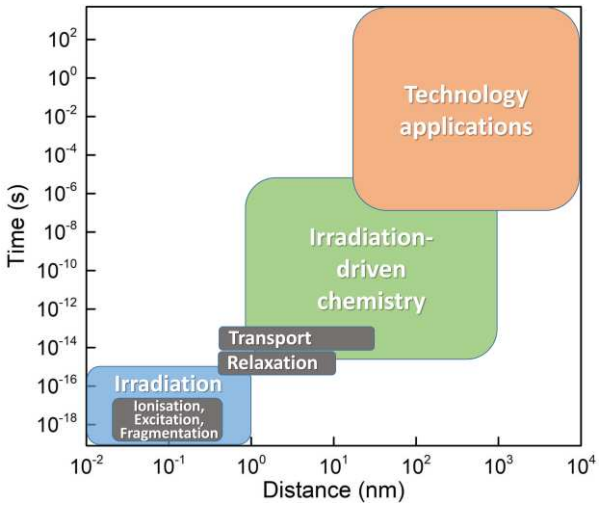

Figure 1. A space-time diagram of features, processes and disciplines associated with irradiation of complex molecular systems. Approximate scales of the key physical and physicochemical phenomena following irradiation are also indicated.

The focus of the COST Action "Multiscale Irradiation and Chemistry Driven Processes and Related Technologies" (MultIChem) is to advance our understanding of IDC by means of modern experimental techniques and pioneering computational methods, with the aim of exploiting IDC in next generation technologies. IDC is based upon a complex cascade of **irradiation-induced physical and chemical processes** taking place on different time and spatial scales, see Fig. 1. Understanding of such processes must be based on a **multiscale approach** that treats the entire multistage scenario in a consistent manner. Such an approach combines discrete experimental, theoretical and computational methods into a coherent framework that goes beyond the limitations of the particular methods.

There are many technologies that exploit irradiation of different molecular systems with different radiation modalities, and the diagram shown in Fig. 1 is therefore rather general. To be specific, three technology-related case studies suitable for exploitation of a multiscale approach have been selected for study in this Action. They represent three important technological sectors with high socioeconomic impact, namely biomedicine, nanofabrication, and energy conversion. In each specific case, as it is

described below, particular radiation modalities, irradiated systems and links to corresponding technological applications are discussed in greater detail.

(i) Biomedicine. Radiation is widely used nowadays in medical applications, particularly in modern radiotherapy treatment techniques such as ion-beam cancer therapy (IBCT) [1,2] that exploits the ability of protons and heavier ions to inactivate living cells due to induction of complex DNA strand breaks. Significant progress has been made in understanding molecular-level mechanisms of biodamage induced by different radiation modalities [3-5] allowing the next generation of radiotherapy to be developed and brought into the clinic [2]. This research has emphasized both the cross-disciplinary nature of the problem and the need to formulate a multiscale approach to the physics of radiation damage with ions [4]. Each stage of the multiscale scenario (such as ionisation of the medium by projectile ions, formation and transport of secondary species, chemical interactions, thermo-mechanical pathways of biodamage) must be treated on the basis of the appropriate fundamental theories and the interlinks between consequent stages need to be carefully elaborated. The biological stage includes relevant biological phenomena (e.g. DNA repair) and accounts for their probabilities through experiments in those cases where an explanation through physics or chemistry is impossible or lacking.

However, current clinical protocols for radiotherapy planning are still optimised by macroscale calculation of the radiation energy per unit mass of patient, a methodology termed ‘dosimetry’. This method is over-simplistic and has little correlation with tissue radiotoxicity which varies with radiation type, cell characteristics and microenvironment. It is thus desirable to develop novel treatment models that would account for the molecular-level descriptions of biodamage and incorporate this knowledge into the multiscale scenario. For this a multiscale understanding of the mechanisms underlying IBCT must be elaborated further to describe, on a fundamental level, the IDC induced by the interaction of projectile ions with the medium. This will revolutionise our understanding of radiation damage and lead to the development of ‘nanodosimetry’ as the central approach for next generation radiotherapy.

A theoretical description of the production and propagation of reactive species can be extended beyond traditional Monte Carlo (MC) approaches [6] by accounting for the coupling of the reactive products with the thermally driven movable biological medium in which they are produced. Triggered by such simulations, new damage mechanisms need to be explored experimentally, such as shock-wave induced damage and the influence of magnetic fields on the biomolecular damage. First experimental studies of the effects associated with the complex dynamics of the medium in the vicinity of ion tracks were performed recently [7] through the exploration of time-resolved picosecond dynamics of liquid water irradiated with laser-accelerated protons. The dynamics of a biological medium can also be studied through time-resolved analysis of G-values and the kinetics of different reactive species produced after irradiation of water with ion beams [8]. Finally, novel experimental approaches must be developed for studying the energy deposition in complex biomolecular systems. In particular, accurate quantification in terms of cross sections of radiation-induced damage of DNA and other critical components needs to be carried out taking also environmental effects into account. This knowledge can then be integrated into the existing models for radiotherapy planning in order to develop the next-generation of radiotherapy planning tools.

(ii) Nanofabrication. Radiation is utilised for controlling various chemical processes for specific technological needs, e.g., for the formation and controllable growth of metal nanostructures under the exposure to focussed electron or ion beams, or for the production of thin films with tailored structural properties. Many experiments have also been conducted to study electron-induced chemical transformations in organic thin films in relation to astrochemistry [9]. Such transformations take place during the formation of cosmic ices and dusts in the interstellar medium due to the interplay of molecular adsorption on a surface and surface irradiation [10].

This Action will focus on a novel nanofabrication technique - focussed electron beam induced deposition (FEBID) [11,12] that allows controlled creation of nanostructures with nanometre resolution for the electronics industry. To date, FEBID has shown its potential for controllable creation of nanostructures made of iron, cobalt, tungsten, gold, platinum and binary alloys for different technological

applications [11-13]. FEBID is based on the irradiation of organometallic precursor molecules by high-energy (typically >10 keV) electrons whilst they are being deposited upon a substrate. Electron-induced decomposition of the molecules releases its metallic component which forms a deposit on the surface with a size similar to that of the incident electron beam (typically a few nanometres).

To date, FEBID has relied on precursors developed for conventional fabrication techniques such as chemical vapour deposition (CVD); a process that is governed by thermal decomposition. The dissociation mechanisms in FEBID are, however, non-thermally driven. Consequently, the precursors used for CVD are not optimized for FEBID leading to the production of nanostructures with sub-optimal chemical composition [14]. Furthermore, although the energy of the primary electron beam in FEBID is on the order of tens of keV, the bulk of the chemical reactions are initiated by low-energy secondary electrons that are emitted from the substrate. This makes the electron-induced chemistry that governs FEBID complicated and also creates a low-energy electron flux outside the focal point of the primary electron beam, which can cause significant broadening of the structures.

Successful commercialisation of FEBID requires that the key physicochemical phenomena that govern multistep (including the irradiation and replenishment stages) process of fabrication, composition and growth of nanosystems coupled to radiation are understood. This requires a concerted approach linking fundamental knowledge on electron-driven chemistry within FEBID with rational design and chemical synthesis of novel, superior precursor molecules. By controlling the extent of these processes through rational design and synthesis of suitable FEBID precursors, the purity of the deposits, the resolution, and the deposition rate can be improved substantially. Atomistic-level modelling will allow optimal parameters (e.g., substrate type, molecular environment, additional molecular species that may facilitate precursor decomposition, etc.) to be determined. It should be stressed that these molecular-level mechanisms and phenomena are not limited to FEBID but are also relevant for other nanofabrication techniques such as ion-beam induced deposition as well as for the thin films deposition.

Until recently, most of computational simulations of the FEBID process and the growth of nanostructures have been performed using the MC approach and the diffusion theory [13,15]. These methods allow for analysis of the average characteristics of the process such as the chemical composition and the growth rate of adsorbed nanostructures but do not provide any molecular-level details of the adsorbed material, e.g. the characterization of its crystalline or amorphous structure, and the radiation chemistry involved. A deeper understanding of the underlying phenomena may be achieved using a multiscale approach that will facilitate control of the electronic, mechanical and catalytic properties of fabricated systems on the nanoscale. This multiscale analysis requires experimental information on low-energy electron induced processes in different organometallic systems such as dissociative electron attachment, neutral dissociation and dissociative ionisation, and on their relative contributions at a specific electron energy. In addition to the detection of fragment ions, neutral products need to be determined using novel mass spectrometric and spectroscopic techniques [16]. Additionally, the products of electron induced reactions in condensed environments need to be detected e.g. by mass spectrometry and optical spectroscopy [17].

(iii) Application of nanoparticles in biomedicine and energy conversion. Irradiation of free metal-based nanoparticles (NPs) and metal NPs embedded in matrices affects their functional properties which in turn determines their use in many emerging technologies based on NPs. In particular, NPs placed in a cellular environment and exposed to energetic photons or ion beams demonstrate therapeutic effects which favours their use as radiosensitisers in combination with conventional radiotherapies [18]. The radiosensitising effect of metal NPs is commonly related to strong irradiation-induced emission of secondary electrons [19] that activate hydrolysis of the surrounding aqueous medium and hence increase the yield of hydroxyl radicals and other reactive oxygen species [20] that propagate in the medium and deliver damage to biomolecules. Another broad technological area that exploits radiochemical transformations of free NPs and NP-based composites is related to photocatalysis, energy conversion and environmental applications [21-23]. These technologies exploit photocatalytic reactions and collective electron excitations that take place on the NP surface, as well as

processes occurring in the NP bulk, e.g., photoexcitation of electron-hole pairs in a metal (or metal oxide) NP and their migration to the NP surface. Photocatalytic reactions on the NP surface also offer applications in decontamination. Lastly, the potential of conducting metal-organic frameworks (MOFs) offers the possibility of a NP support acting as photosensitizer for hydrogen production and storage [24]. The combination of this technology with metal oxide [25] and noble metal [26] NPs offers multifunctional systems capable of hydrogen production and storage, pointing to energy sector applications.

Investigation of radiation-driven chemical transformations in NPs that are needed to achieve their functioning is a complex multi-parameter problem. Indeed, a vast number of parameters (e.g., the size, shape and composition of a metal core of radiosensitising NP; heterostructuring of the active NPs; thickness, composition and density of a coating surrounding the metal core; surface charge, etc.) can be varied with the aim of enhancing the production of reactive chemical species in the vicinity of NPs and improving the ease of NP recycling and reclamation, thus optimising the radiosensitising and catalytic properties of such systems. The large number of possible parameters makes it a formidable task to systematically explore each of them experimentally. A multiscale modelling framework [27] must therefore be developed for a quantitative description of structural properties of metal NPs in molecular environments or on substrates, irradiation-induced effects (such as electron emission, production of reactive species, collision-induced fragmentation of NPs and their coatings) as well as the kinetics of irradiation-induced chemical reactions in the vicinity of NPs. Such a multiscale description can provide atomistic-level insights into characterisation of the medium before and after irradiation and describe radiation-induced chemical transformations that govern the radiosensitising and catalytic properties of nano- and composite materials. These simulations therefore have the potential to significantly reduce the experimental costs for optimization, control and functionalization of NPs in biomedical and nanotechnology applications and thus facilitate significant progress in these research areas.

1.1.2. DESCRIPTION OF THE CHALLENGE (MAIN AIM)

As described in sect. 1.1.1, our limited molecular-level understanding of the IDC processes hinders the advancement of several modern technologies exploiting irradiation-driven processes.

The main aim of the COST Action MultIChem is to radically advance our fundamental understanding of IDC in complex molecular systems, therefore paving a path towards the major scientific and technological breakthroughs, and socioeconomic impacts. This will be achieved through advanced theoretical, computational modelling and experimental studies (described below in sect. 1.2.1) that will provide insights into the structural, electronic, thermo-mechanical and catalytic properties of biomolecular systems, deposited metal nanostructures, metal-based nanoparticles and NP-MOF composite materials exposed to radiation.

The Action aims at advancing the understanding of IDC and enabling its implementation in those existing technologies introduced above in sect. 1.1.1. To address this challenge, a highly interdisciplinary and intersectoral collaborative European approach is required as may be delivered through the mechanisms of a COST Action (e.g. Workshops and Short-Term Scientific Missions (STSMs)). It will bring together researchers from disparate disciplines to collaborate on delivering the scientific and methodological advances necessary to develop the IDC-based multiscale approaches for some of the most challenging problems in current science and technology.

1.2 Progress beyond the state-of-the-art

1.2.1 APPROACH TO THE CHALLENGE AND PROGRESS BEYOND THE STATE-OF-THE-ART

A fundamental understanding of the IDC processes of molecular systems embedded into large-scale molecular environments requires the inclusion of both short-time/(sub)nanoscopic scale quantum

aspects and long-time/nano-, micro- and mesoscopic scale effects due to the environment. To achieve this understanding the MultIChem Action will adopt a multiscale approach that treats the irradiation of molecular systems and subsequent chemical transformations in an inclusive and consistent manner.

From a theoretical viewpoint, a rigorous quantum-mechanical description of the IDC processes (e.g., by means of time-dependent density functional theory (TDDFT) or different realisations of quantum molecular dynamics) is feasible for relatively small systems containing, at most, a few hundred atoms and for (sub-)femtosecond time scales. These methods are utilised mainly to describe the dynamics of the electronic subsystem after exposure of a molecular system to radiation. The macroscopic analysis of steady-state processes involving much bigger systems that constitute of millions of atoms is typically conducted by various Monte Carlo (MC) schemes. However, the MC approach (represented by well-known codes e.g. GEANT4-DNA, FLUKA, PARTRAC or TOPAS) is commonly utilised to simulate particle transport in continuous/static media and does not allow explicit simulations of the post-irradiation dynamics of molecular media and related physical and chemical phenomena.

A crucial part of the multistage scenario of IDC is the analysis of intermediate time and spatial domains where the irradiated system placed in a molecular environment is far from equilibrium. In this regime different dynamical processes take place so that the steady-state picture is not applicable. Exploration of these time and spatial domains is highly relevant to the key questions addressed in this Action, e.g. for establishing the probabilities of DNA damage by reactive chemical species or for defining optimal conditions for the formation of nanostructures with desired composition and properties.

To model radiation-driven processes the Action will adopt an **innovative computational multiscale modelling approach** that requires coupling of molecular dynamics (MD) and MC schemes and use of novel computational methods such as **Irradiation Driven Molecular Dynamics (IDMD)** [28]. The IDMD methodology is designed for the molecular-level description of IDC and applicable to any kind of molecular system exposed to radiation. It accounts for the major dissociative transformations of irradiated molecular systems (topological changes, redistribution of atomic partial charges, atomic valences, bond multiplicities, interatomic interactions) and possible paths of their further reactive transformations [29] which can be simulated by means of MD with well-established reactive force fields such as ReaxFF [30] or reactive CHARMM [31].

Within the IDMD framework various quantum collision processes (e.g., electronic excitation, ionisation, DEA) are treated as random, fast and local transformations incorporated into the classical MD framework in a random manner with the probabilities elaborated on the basis of quantum mechanics. This can be achieved because the aforementioned quantum processes happen on the sub-femto- to femtosecond time scales (i.e. during the periods comparable or smaller than a typical time step of MD simulations) and involve typically a relatively small number of atoms.

The probability of each quantum process is equal to the product of the process cross section and the flux density of incident particles. Both characteristics should be elaborated for each particular case study. The cross sections of collision processes can be obtained from (i) *ab initio* calculations by means of various dedicated codes, (ii) analytical estimates and models, (iii) experiments, or (iv) atomic and molecular databases such as e.g. VAMDC [32] and RADAM [33]. They can also be treated as model parameters which may be validated via IDMD-related experiments (see below in this section). The flux densities of incident particles are usually specific for the concrete problem and the system considered. The properties of atoms or molecules (energy, momentum, charge, valence, interaction potentials with other atoms in the system, etc.) involved in such quantum transformations are changed according to their final quantum states in the corresponding quantum process.

In the course of a quantum process the energy and momentum transferred to the irradiated system are adsorbed by the electronic and ionic degrees of freedom, and chemically reactive sites of the irradiated system are created. These events lead to the changes of molecular topology of the system, the number of molecules in the system and other characteristics that may affect the dynamical behaviour of the system on long time scales. The follow-up dynamics of the reactive sites is determined by classical MD and the thermodynamic state of the system until they undergo further irradiation-driven quantum transformations.

In IDMD special attention is devoted to the accounting for the dynamics of secondary electrons and the mechanisms of energy and momentum transfer from the excited electronic subsystem to the system's vibrational degrees of freedom, i.e. to its heat. For small molecular systems the ejected electrons can often be uncoupled from the system and excluded from the analysis of the system's post-irradiation dynamics. For the extended molecular systems the interaction of secondary electrons with the system can be treated within various electron transport theories, such as diffusion or MC approach, and be considered as additional irradiation field imposed on the molecular system. This analysis provides the spatial distribution of the energy and momentum transferred to the medium through its irradiation. Finally, electronic excitations transfer the deposited energy to the system's heat via the electron-phonon coupling, which lasts typically up to the picosecond time scale. The IDMD approach accounts for the key outcomes of this relaxation process determining its duration, the temporal and spatial dependence of the amount of energy transferred into the system's heat.

The above described multiscale modelling framework combining both MD and MC schemes for the first time and based on the novel IDMD methodology will be utilised to explore IDC processes relevant for each technological challenge outlined in sect. 1.1.1. This will include modelling of: (i) radiochemistry in the vicinity of ion tracks passing through a water medium. Different irradiation and environmental conditions (ion type & energy, oxygen content, etc.) will be considered to acquire a systematic understanding of the IDC processes (formation of various reactive oxygen species and solvated electrons, their dynamics and transport) that are relevant for the advancement of IBCT; (ii) the formation and growth of metal nanostructures under electron beam irradiation. As described above, this approach will account for the probabilities of electron-induced quantum processes such as dissociative electron attachment or dissociative ionisation that play an important role in the FEBID process; (iii) the production of reactive species in the vicinity of coated metal NPs placed in molecular environments or metal NPs deposited and immobilised on surfaces, irradiated with photons or ion beams. Such simulations require taking into account the probabilities of quantum processes like ionisation, excitation or fragmentation. The unique expertise on multiscale modelling of IDC processes using advanced computational methodologies will be built up within the MultIChem Action and this know-how will be offered to industry.

The Action will include also **a synergistic experimental programme** aiming at benchmarking and validating the outcomes of the simulations. For that, MultIChem will exploit, develop and combine novel experimental techniques to study the IDC mechanisms in both gaseous and condensed phases. Experimental studies of irradiation-driven processes will be conducted with molecular systems of different complexity, ranging from small molecules that can be easily prepared in both gas and condensed phase towards thermally unstable larger macromolecules (such as oligonucleotides, G-quadruplexes, peptides and proteins [34]) that are technologically more relevant. Environmental effects will be treated by conducting experiments with clusters and in controlled condensed phase environments. Advanced techniques for producing complex biomolecular targets in the gas phase will be exploited, e.g. the laser-induced acoustic and thermal desorption techniques [35,36] and electrospray ionisation coupled to ion traps [37]. The obtained data will allow us to proceed to more complex radiation sources such as plasma sources, which are finding more and more applications in medicine.

The Action will also explore alternative experimental strategies for quantifying radiation-induced damage to large macromolecular systems, e.g. evaluating cross sections for DNA single and double strand breaks [38]. This will exploit recent works using the DNA origami technique, in which damage is directly visualized by atomic force microscopy [39,40]. Neutral fragmentation products and molecules newly formed in the course of IDC also need to be detected and quantified using mass spectrometry and novel experimental approaches involving optical spectroscopy such as Raman spectroscopy.

In addition, novel experimental techniques need to be developed that are capable of monitoring relevant transient and intermediate states with short lifetimes in order to identify the dynamics underlying IDC. To go beyond the state-of-the-art, more experimental studies are needed to explore the irradiation-driven dynamics of molecular media and condensed environments. Fast dynamics of molecular media and condensed environments can be resolved on a picosecond timescale by means of advanced

experiments with laser-driven proton and ion beams [7]. These techniques may be used to study the dynamics of the medium (including, ion-induced collective flow) in the vicinity of ion tracks.

Finally, multiscale modelling predictions will be verified at the more complex, technology-relevant level by means of in vitro and in vivo biological experiments. These experiments will aim at a complete validation of the multiscale models of radiation-induced biodamage based on the nanoscale understanding of IDC and subsequent molecular damage and related phenomena (relative biological effectiveness, DNA damage response, etc.) against cell survival and clinical (animal studies) data.

The chemistry exploited in FEBID will be studied by combining gas-phase measurements of the electron-induced fragmentation of individual precursor molecules with studies of the electron-induced decomposition of the same molecules adsorbed on a surface. Particular attention will be devoted to the implementation of different purification protocols that have been identified recently to increase the purity of metal deposits [41]. Finally, transmission electron microscopy (TEM) [42] will be used to monitor the irradiation driven structural modifications of NPs and nanostructures deposited on surfaces.

MultIChem will therefore create an interdisciplinary network of researchers with an active involvement of both non-academic and industrial partners in each technological area considered in the Action. Thus, the academic part of the Consortium will be complemented by leading European radiotherapy centres and hospitals, companies focussed on the development of experimental tools and devices for nanofabrication, companies working on fabrication and characterisation of NPs and nanostructures (either free or placed into an environment), companies working in the field of nanomedicine (production of radiosensitising agents) as well as nanofabrication and energy companies. Finally, an important role in the MultIChem Action will be played by the enterprises working on professional software development for advanced multiscale modelling.

1.2.2 OBJECTIVES

1.2.2.1 Research Coordination Objectives

The goal of MultIChem is to consolidate, at the European level, the research efforts of different communities focussed on existing technologies that exploit IDC processes. To achieve this goal a pan-European network will be established which will bring together leading researchers in diverse research fields (see section 1.2.2.2 below) with key non-academic and industrial stakeholders (hospitals & radiotherapy centres, SMEs in the field of nanofabrication, and computational modelling software developers and users).

The **main research coordination objectives** of the Action are:

1. To combine and develop existing experimental, theoretical and computational methods for studying, on a molecular level, IDC processes underlying radiation-induced biodamage; radiation-induced formation of nanostructures on surfaces; catalytic and radiosensitising properties of metal-based NPs exposed to radiation. Once developed this molecular-level knowledge will be exploited for the development of new technological protocols. Novel experimental approaches and computational tools for modelling of IDC will be offered to the clinical community and industrial companies in the field of nanostructure nanofabrication and characterisation.

2. To establish a comprehensive databank of IDC-related quantities (e.g., photon, electron and ion interaction cross sections with bio- and organometallic molecules, NPs and nanostructures, chemical reaction rates, diffusion coefficients for different atomic and molecular species, compositions of metal-containing nanostructures grown by FEBID, etc.). This will be linked to existing, well-established atomic and molecular databases such as “Virtual Atomic and Molecular Data Centre (VAMDC)” and “Radiation DAMage (RADAM)”. Such a databank is seen as one of the major resources required by the community to store and exchange scientific data, and is fully in accord with recent EU guidelines for open accessibility of data. Its cross-platform availability and universality in different communities will be achieved through developing specific formats for metadata storage that will permit easy search and retrieval of any IDC-related information in a transparent and user-friendly manner.

3. To develop prototypes of novel treatment planning systems for ion-beam cancer therapy that will combine molecular-level understanding of IDC and subsequent molecular damage and related phenomena (relative biological effectiveness, DNA damage response, etc.) with existing macroscale dose delivery protocols. Since treatment planning protocols must be designed in close collaboration with the clinical community, the Action will include research units in hospitals where irradiation is used for patient treatments. These protocols will ultimately form the basis of a new-generation approach of implementing tailored treatment plans for individual patients.

4. To develop new technological protocols enabling better control and characterisation of fabricated nanostructures, NPs and composite materials with enhanced catalytic and radiosensitising properties. The new protocols will be based upon an enhanced molecular-level understanding of IDC and thus incorporate our knowledge of the optimal experimental conditions needed to fabricate systems with tailored properties. Specific computational workflows for solving specific tasks in nanofabrication modelling and characterisation will be designed which will interlink different scales of the multiscale modelling of the IDC processes in nanostructures, NPs and composited materials.

5. To disseminate the scientific and technological outcomes of MultIChem to a broader scientific community, policy makers and general public. Specifically, a dedicated MultIChem YouTube channel will be established to permit an easy way to overview the major synergetic outcomes of the groups involved in the Action. Annual public lectures on the topics related to IDC research will be recorded and posted on this channel to allow broader impact and visibility.

1.2.2.2 Capacity-building Objectives

The Action will bring together researchers from diverse research fields such as atomic and molecular physics, physical chemistry, radiation chemistry, surface science, radiation damage of materials, nanotechnology, biophysics and radiobiology. Collaboration of researchers working in these fields will enable the formation of the first IDC network that will have a unique set of skills to advance our understanding of the multiscale scenario of irradiation-induced chemical transformations. Further consolidation with non-academic and industrial partners will aim at translating these advances into the technological applications based on IDC.

Specific **capacity-building objectives** of MultIChem are:

1. Establishing a pan-European IDC community that will combine advanced theoretical and computational methods (quantum-mechanical methods, classical MD and MC schemes, combined approaches such as IDMD, etc.) with advanced experimental techniques for studying collision- and irradiation-induced processes involving biomolecular systems, NPs, nanostructures and NP-MOF composite materials, while fostering the development of the existing experimental and theoretical tools beyond the state-of-the-art.

2. Accumulation and systematisation of the knowledge collected by different complementary communities working in the areas related to IDC. Formulation of the key research domains of the IDC research field and determining directions for its further development.

3. Consolidation of efforts of different research communities studying IDC towards technological breakthroughs in the development of novel radiotherapy treatment protocols, nanofabrication methods, as well as novel radiosensitising agents and nanocatalysers.

4. Establishment of a critical mass of scientific knowledge, infrastructure, managerial experience and open communication opportunities to ensure that the MultIChem Consortium remains active and sustainable after the completion of the COST Action.

2. NETWORKING EXCELLENCE

2.1. Added value of networking in S&T Excellence

2.1.1. ADDED VALUE IN RELATION TO EXISTING EFFORTS AT EUROPEAN AND/OR INTERNATIONAL LEVEL

The primary aim of the MultIChem Action will be to build a highly cooperative research programme to study molecular mechanisms of IDC and explore the exploitation of these mechanisms in novel technologies. Such an ambition is far beyond the capacity of a single group or research institution and therefore must be based upon research collaborations resulting from the international, interdisciplinary and intersectoral interactions between (i) academic partners (universities and research centres), non-academic institutions (hospitals and radiotherapy centres), and industrial partners including SMEs; (ii) partners in R&D-intensive countries with those from Inclusiveness Target Countries (ITCs). International cooperation with Near Neighbour Countries (NNCs) will be fostered by including a renowned research institution from Russia. The MultIChem Consortium will continue looking for new collaborations in other NNCs and International Partner Countries during implementation of the Action. Such interactions will be fostered through the MultIChem networking activities (staff exchange through STSMs, Training Schools for PhD students and Early Career Investigators, dedicated workshops and conferences) to keep Europe at the forefront of these areas of research and technology.

The European added value of this Action is evident from the leading position of European scientific community in the fields of novel radiotherapy treatments (including those with radiosensitisers), irradiation-driven nanofabrication, nanocatalysis and multiscale computational modelling. This Action is built upon aspects of previous COST Actions and European projects, such as COST Action P9 “Radiation Damage in Biomolecular Systems (RADAM)”, COST Action MP1002 “Nanoscale insights into Ion-Beam Cancer Therapy (Nano-IBCT)”, COST Action CM1301 “Chemistry for ELectron-Induced NAnofabrication (CELINA)”, COST Action CM1204 “XUV/X-ray Light and fast Ions for ultrafast Chemistry (XLIC)”, FP7 MSCA Initial Training Network “Advanced Radiotherapy, Generated by Exploiting Nanoprocesses and Technologies (ARGENT)”, H2020 MSCA European Training Network “Low energy ELEctron driven chemistry for the advantage of emerging NAno-fabrication methods (ELENA)”, and others. However, MultIChem is distinct from these earlier Actions and projects with its focus on the development of fundamental understanding of a complex cascade of irradiation-induced physical and chemical processes by means of a consistent multiscale approach up to the level enabling its implementation into the concrete technologies, and it will bring together a new set of partners from a wide range of disciplines. The added value of MultIChem is the radical advances in the understanding of IDC processes, development and validation of novel computational methodologies such as IDMD and of the corresponding experimental methods.

2.2. Added value of networking in impact

2.2.1. SECURING THE CRITICAL MASS AND EXPERTISE

An intersectoral and multidisciplinary network of collaborators will be established within the Action. The MultIChem Consortium will contain all the expertise required for achieving the Action objectives and will include leaders in: (i) computational modelling of irradiation-driven physics and chemistry, (ii) multiscale modelling of structure and dynamics of complex molecular systems, (iii) advanced experimental studies of irradiation-driven fabrication and modification (e.g. phase and morphological transitions) of nanosystems, (iv) advanced experimental studies (on the molecular level, in vitro and in vivo) of irradiation-driven processes in biological systems as well as (v) Early Career Investigators who will provide next generation leadership in multiscale modelling of IDC and in related experiments. By bringing together such a coalition Europe will have the opportunity to become the international leader in such research and therefore assume leadership in the emerging technologies discussed in this Action. It is therefore essential that technological links between the academic and non-academic partners are established. Representatives of several hospitals, radiotherapy centres and companies are among this

Action, and it is expected that more medical and industrial bodies will join the Action during its operation. Furthermore, one member represents a large research and innovation hub that will facilitate search for new collaboration partners, establishing new contacts with industry, and promotion of the commercially viable technological applications.

The Action will also realise the potential of scientific communities within ITCs and NNCs where such research can develop rapidly once training and integration with more research-intensive COST Countries is realised. Accordingly, the Action will deliver a series of training and knowledge transfer workshops and conferences which, when combined with STSMs, will allow researchers and their groups in ITCs to integrate within the wider European research and technology IDC community.

2.2.2. INVOLVEMENT OF STAKEHOLDERS

The MultIChem Consortium has been established in a way that reflects the requirements of the key stakeholders participating in the Action.

The Consortium includes leading academic groups (experimental, theoretical, and computational modelling) in the fields of atomic and molecular physics, physical chemistry, radiation physics and chemistry, surface science, nanotechnology, biophysics and radiobiology. Establishing interactions between these groups will enable the development of molecular-level models for IDC and related phenomena and validation of these models against experimental data. The Consortium will also include companies (four SMEs and two large companies are amongst the proposers) as well as medical physicists, biomedical engineers and radiotherapy practitioners.

MultIChem will establish mechanisms that will intensify interdisciplinary and intersectoral cooperations in both research and innovation with other stakeholders. As such, the Action will engage with companies involved in radiation research, fabrication of functionalised NPs for biomedical applications as well as companies providing materials and hardware for FEBID and related focussed beam-based technologies. Connections to a number of key companies working in the above-mentioned areas, e.g. Siemens, Ion Beam Application S.A., NanoH, Zeiss, TESCAN and FEI (Thermo FisherScientific) will be establihed in the lifespan of the Action, MultIChem will engage with these and other companies aiming to include their representatives in the Consortium. By demonstrating the full potential of novel multiscale modelling methods for studying IDC in complex molecular systems coupled to radiation, the MultIChem Action will open the path towards broad exploitation of IDMD by both academic and industrial research communities. Representatives of the industrial community will be invited to MultIChem meetings and conferences, and further joint activities with industrial partners will be fostered within the STSM scheme. These measures will facilitate the growth and further development of the IDC and multiscale modelling at the European level.

2.2.3. MUTUAL BENEFITS OF THE INVOLVEMENT OF SECONDARY PROPOSERS FROM NEAR NEIGHBOUR OR INTERNATIONAL PARTNER COUNTRIES OR INTERNATIONAL ORGANISATIONS

The scientific and technological challenges addressed by this Action are highly relevant to research activities conducted in many other countries across the world. Expected members of the MultIChem Consortium have strong connections with research and medical institutions from NNCs, including Russia, Ukraine and Belarus as well as with international partners from the United States, Australia, Japan and India. The Action will therefore benefit from Non-COST Country institutions joining the MultIChem network during the lifespan of the Action. Well-established experts in radiation-matter interactions from a research institution in Russia have joined the MultIChem network. It is expected to create close ties with other leading research teams from NNCs and International Partner Countries through existing collaborative links and through establishing new contacts. It is expected that research groups from NNCs will provide valuable contributions to the development of understanding of IDC

phenomena and hence to the development of the applications discussed previously. Members of the research teams from ITCs and NNCs will have or will provide access to modern large-scale experimental and computational facilities (synchrotrons; proton and ion beam facilities for molecular-level, in vitro and in vivo studies; powerful supercomputer clusters). The European Research Area will therefore benefit from multiple visits of researchers from ITCs and NNCs to other COST Countries and from the opportunity of sending some of its most active researchers to the world-class teams in these countries.

Furthermore, the topics covered by the Action are of great importance for the work of international organisations, e.g., International Atomic Energy Agency (IAEA) and CERN. IAEA acts as a 'standards agency' for international radiotherapy and develops recommendations concerning radiation damage to organic materials in nuclear reactors. One of big technological issues for CERN related to this Action is (i) the stability of solid-state detectors exposed to focussed beams of highly energetic particles and (ii) technologies for ion beam cancer therapy. Contacts with the CERN teams in these areas have already been established and it is expected to include them into the MultIChem Consortium over the Action's lifespan. The Action will also seek to organise and host some of its meetings jointly with these organisations.

3. IMPACT

3.1. Impact to science, society and competitiveness, and potential innovation/breakthroughs

3.1.1. SCIENTIFIC, TECHNOLOGICAL, AND/OR SOCIOECONOMIC IMPACTS (INCLUDING POTENTIAL INNOVATIONS AND/OR BREAKTHROUGHS)

MultIChem is a highly innovative Action that aims at providing the culture and leadership for significant advances in European research and technology related to and exploiting irradiation-induced chemistry involving complex molecular systems.

Research activities envisaged within the Action aim at developing an innovative multiscale computational approach towards the description of IDC by means of coupling molecular dynamics and Monte Carlo methods and using novel methodologies such as IDMD. Advanced experimental techniques will also be elaborated and new experiments will be conducted (on a single-molecule level as well as in vitro and in vivo) to validate or support data obtained from computational modelling and create relevant publicly available databases, etc. All these activities will contribute significantly towards achieving **major scientific impact** of the MultIChem Action. Scientific outcomes of the Action will be of immediate importance and interest to a wide range of scientific communities.

On the basis of the advancement of the fundamental knowledge in IDC the Action aims to provide a catalyst for advancing several major technologies. In particular, (i) a better understanding of radiochemistry involving biological systems and its role in the mechanisms of biodamage with ionising radiation will provide a fundamental basis for developing novel treatment planning systems that will combine the nanoscale effects and IDC phenomena with existing macroscale dose delivery protocols; (ii) a better understanding of the mechanisms of radiation-induced formation, growth and modification of nanostructures and microporous structures will enable effective optimisation of existing nanofabrication technologies, allowing more precise / better controlled fabrication, and also the targeting of specific compositions and morphologies in NPs and composite materials for optimal photophysical activity, (iii) a better understanding of the impact of structure and composition of metal and metal oxide NPs on the production of reactive species and hence on their radiosensitising and catalytic properties, and, finally, (iv) the novel computational methodologies for modelling of IDC will allow the community to go beyond the limits of standard quantum-chemistry or Monte Carlo simulation codes and thus expand

the capabilities of a molecular dynamics approach for modelling irradiation-induced chemical transformations in large molecular systems over substantially large time scales. All these activities will facilitate **major technological breakthroughs** and will enable the aforementioned technologies to advance up on the Technology Readiness Level scale from the formulation of basic principles and technology concepts to experimental proof of concept and technology validation during the Action.

As a natural consequence of these technological developments, the research and technological programme realised within the Action will have **a strong socioeconomic impact** in the medium to long term. Directions towards optimisation of radiotherapy protocols via understanding and exploiting molecular-level IDC processes will provide more successful, better targeted cancer treatments with subsequent economic and “quality of life” benefits. Novel, more efficient methods of nanofabrication will allow for miniaturisation of the created electronic nanodevices and their cost-effective production. Meanwhile, improved photophysical properties of NPs and the combination of these with MOFs points to improved technologies in the fields of water treatment and energy storage.

3.2 Measures to Maximise impact

3.2.1. KNOWLEDGE CREATION, TRANSFER OF KNOWLEDGE AND CAREER DEVELOPMENT

The MultIChem Action is structured in a way to promote, establish and strengthen links between disparate research and technological communities. MultIChem represents a highly interdisciplinary and intersectoral Consortium which includes academic and non-academic partners, representatives of technology-oriented enterprises and computational software companies. The Action will include world-class leaders in different research fields such as physics, chemistry, nanotechnology, biology and medicine.

The MultIChem Working Groups (more details are given below in section 4.1.1) are aimed at both creating new knowledge and maximising the transfer of that knowledge between the research and technology oriented communities. For example, the fabrication of radiosensitising NPs is an important research topic that links nanotechnology with clinical medicine since understanding of the mechanisms of DNA damage by chemical species requires knowledge transfer from physics and chemistry to biology and then engagement with those delivering clinical practice. Similarly, understanding of the mechanisms for the formation and growth of nanostructures and interactions between components in composite materials links atomic and molecular physics, physical and surface chemistry with nanotechnology, and then with industrial fabrication companies. Finally, all these research topics and disciplines are strongly interlinked with experiments and novel computational methods that allow us to understand and predict properties of irradiated complex molecular systems through advanced atomistic-level simulations.

MultIChem will ensure its presence at university showcase events, presenting work at events staged by member universities that aim to improve networking and cooperation with industry/SMEs. An essential part of MultIChem will be the organisation of a series of networking events to impart scientific knowledge exchange, training of Early Career Investigators (ECIs), and dissemination of the Action’s results to broader scientific and industrial communities. ECIs will be involved in the management of the MultIChem Consortium and of its Working Groups (see section 4.1.1), and will play key role in the organisation of MultIChem annual meeting and dissemination of the Action’s outcomes. These activities, in addition to STSMs to academic, non-academic and industrial partners, as well as the information exchange within the Consortium, will facilitate the career development of ECIs and will help them to achieve leading positions in either academia or industry.

In order to enhance the complementarity and synergy between the Consortium partners, particular attention will be put on cooperation and knowledge transfer between the ITCs and more research-intense COST Countries. STSMs will also provide opportunities for travelling staff to gain new knowledge, give seminars and tutorials and report results at major international conferences relevant

for the topics of this Action (e.g., Miller Conference on Radiation Chemistry, European Conference on NanoFilms, International Symposium 'Swift Heavy Ions in Matter', International Conference on Electron, Ion and Photon Beam Technology and Nanofabrication, International Conference 'Dynamics of Systems on the Nanoscale', and meetings held under the auspices of IAEA), which for the ECIs and Young Researchers will be highly beneficial additions to their CVs.

3.2.2 PLAN FOR DISSEMINATION AND/OR EXPLOITATION AND DIALOGUE WITH THE GENERAL PUBLIC OR POLICY

MultIChem will place high importance on its dissemination and outreach activities, and exploitation of the research results obtained in the course of the Action.

A dedicated website will be created to disseminate the aims and objectives of the Action and advertise its forthcoming meetings, MultIChem Conferences and Training Schools. The research results will be disseminated through publications in peer-reviewed journals (with a special emphasis on open-access publications) and presentations at scientific meetings (e.g., those listed in section 3.2.1). Co-authorship of scientific papers by the Action members will be a vital measure of the success of the Action and will be fostered through scientific exchanges at MultIChem meetings and STSMs. In addition to the usual academic practice on dissemination of research results, other measures will be taken to protect Intellectual Property (IP) that has a market value through patenting, and this will be exploited whenever possible. The principles of IP and joint ownership of collaborative work will be recognized by members of the MultIChem Consortium in line with the European Union's policies such as COST Code of Conduct.

Data generated and collected in the course of the Action will be included in a comprehensive MultIChem database containing the IDC-related quantities (e.g., photon, electron and ion interaction cross sections with bio- and organometallic molecules, coordination structures, nanoparticles and nanostructures, chemical reaction rates, diffusion coefficients for different atomic and molecular species, etc.). The constructed database will be linked to the existing, well-established atomic and molecular databases such as VAMDC [32] and RADAM [33]. The new database is seen as one of the major resources for the community to store and exchange scientific data, as dictated by recent EU open access guidelines. Its cross-platform availability and universality in different communities will be achieved through developing specific formats for metadata storage that will permit easy search and retrieval of any IDC-related information in a transparent and user-friendly manner. The data generated by the MultIChem Consortium will be stored in this database and made publicly available thus ensuring its widespread dissemination and re-use as well as securing the legacy of the Action.

Four annual MultIChem Conferences will be organized at which research conducted by the Action members will be presented. The Action will aim at organizing two of these events in Inclusiveness Target Countries to ensure wider engagement with research and industrial communities in these countries. These conferences will also host Management Committee meetings and review key tasks for the next Action period and short-term goals for the respective Working Groups (WGs). The WGs will host smaller, targeted workshops focussed on specific scientific and technical challenges. MultIChem will organise two Training Schools (TS) aimed at transferring knowledge between different disciplines and different sectors (academia - industry, universities - hospitals and medical centres, software developers - software users) and providing wider training to ECIs. TS materials will be archived such that they may be used by Action members in their own local/regional meetings to train further cohorts of ECIs. MultIChem is thus expected to generate a range of training materials with recorded lectures and seminars, webinars and videos being collected for dissemination across the community. These materials will be uploaded to the MultIChem website to create a permanent teaching resource.

To disseminate the Action results to a wider range of audiences, a strong web and social media presence will be created and sustained through appropriate social media channels (e.g., Facebook, Twitter, LinkedIn, ResearchGate). Apart from that, a dedicated MultIChem YouTube channel will be established to permit an easy way to overview the major synergetic outcomes of the groups involved in

the Action. Annual public lectures on the topics related to IDC research will be recorded and posted on this channel to allow broader impact and visibility. A series of webinars presented by members and recorded for more general dissemination will be organised presenting research tools and discussing research of the Action. A regular (biannual) newsletter will be prepared and disseminated through the generated mailing lists to inform researchers and stakeholders (including those from outside the Action) about the latest progress of the Action and will be a major mechanism for attracting new collaborators. The dissemination strategy will also be extended towards the use of "traditional" mass media (e.g. radio or newspapers) exploiting links of the MultIChem members to local and regional media.

Special efforts will be made towards broader public engagement. The MultIChem Consortium will publish more generic and public orientated articles and put illustrative materials on the Consortium website which will ensure that the MultIChem research activities are made known to society at large in such a way that they can be understood by non-specialists thereby improving the public's understanding of MultIChem's underpinning science. Public lectures organised on the occasion of international conferences, science festivals and university open days will help the MultIChem researchers to communicate their ideas and scientific results to the wider public and in return gain a better understanding of the public interest in priorities for science and technology and also the public's concerns. An exhibition will be prepared by the Consortium for display at public events organised by the partners and at more general European public forum, e.g. the ESOF meetings in 2022 and 2024.

4. IMPLEMENTATION

4.1. Coherence and effectiveness of the work plan

4.1.1. DESCRIPTION OF WORKING GROUPS, TASKS AND ACTIVITIES

MultIChem will operate through a well-defined management structure that has been proven successful in several previous COST Actions.

Management Committee (MC) will comprise of up to two representatives from each of the participating member countries, the Chair and the Vice-Chair. The MC will also have two representatives from industry and radiotherapy centres who will play an important role in the implementation of new technological achievements. The MC will be complemented by a science communication manager whose main responsibility will be to monitor and intensify web and social media presence of the Action and to communicate its results to different audiences including general public. One member of MC will be responsible for EDI (Ethnicity, Diversity and Inclusiveness) issues. The MC will meet every 12 months (preferably at Annual MultIChem meetings) and will be responsible for the overall direction of the Action. It will ensure the effective communication and exchange of best practices among the participants to maximise the scientific, technological and socioeconomic benefits of the Action.

The main tasks of the MC regarding implementation of the Action will be:

T1: Supervision and coordination of the activities of the Working Groups (WGs).

T2: Administration of the budget and preparation of reports to the COST Association administration.

T3: Implementation of gender policies aiming at a balanced representation of women in the MC itself, WG leaders, and STSMs amongst others.

T4: Monitoring the development of the critical mass of networking activities crucial for the long-term sustainability of the network.

T5: To follow the involvement of Early Career Investigators and Young Researchers in the Action and use available tools to boost their careers.

T6: To continually seek new partners (academic, non-academic, industrial), especially from Inclusiveness Target Countries but also in Non-COST Countries, to maximise the impact of the Action.

T7: To act as final arbitrator in the event of disagreements amongst partners as to resource allocation, project tasks and dissemination of results.

The research and technological activities envisaged in MultIChem are split into three dedicated WGs (WG1, WG2 and WG3). WG4 will be responsible for dissemination of the Action results and coordination of public relations activities that are crucial for the project. The description of WGs is given below.

WG1: Irradiation- and chemistry-driven multiscale phenomena

The main objective of WG1 is to acquire a fundamental-level understanding of IDC transformations of complex molecular systems exposed to different types of radiation. This will be achieved through exploiting atomistic-level theoretical and multiscale computational modelling approaches supported by highly relevant experimental studies. In order to provide a focus to the Action, research studies will be based around several specific case studies relevant for technological applications, specifically:

- ion irradiation of biomolecular systems (isolated biomolecules such as amino acids, DNA segments, oligonucleotides, etc., and biomolecular clusters, both in the gas phase and in molecular environments);
- electron beam irradiation of deposited metal clusters and nanoparticles;
- electron beam irradiation of organic and inorganic films;
- photon and ion irradiation of metal or metal oxide nanoparticles;
- electron transfer in NP-MOF composites.

The following tasks for WG1 are envisaged:

T1.1: Development of the general multiscale methodology for modelling of the irradiation-induced chemical transformations in molecular systems combining molecular dynamics and Monte Carlo schemes, thus allowing for effective multiscale modelling of the whole spectrum of the processes involved. Development of experimental techniques to benchmark models of IDC in molecular systems. Validation of the model predictions against the results of complementary experiments.

T1.2: Exploration of ion irradiation induced chemistry of complex biomolecular systems such as amino acids, oligonucleotides, DNA origami, etc. Exploration of time-resolved fast dynamics of a liquid water environment under exposure to laser-accelerated ion beams. Time-resolved analysis of G-values and the dynamics of different reactive species produced after irradiation of water with ion beams.

T1.3: Atomistic-level investigation of electron-driven chemistry in the FEBID process. Study of low-energy electron induced processes in a broad range of organometallic systems taking into account different dissociation mechanisms and their relative contributions at specific electron energies. Incorporation of this knowledge into a multiscale computational model of nanostructure formation and growth under the action of electron beams.

T1.4: Investigation of radiation-induced morphology changes as well as impact of the structure and composition of metal-based NPs on their catalytic and radiosensitising properties.

T1.5: Data handling and construction of the MultIChem database where a comprehensive databank of IDC-related quantities (e.g., photon, electron and ion interaction cross sections with bio- and organometallic molecules, nanoparticles, nanostructures and composite structures, chemical reaction rates, diffusion coefficients for different atomic and molecular species, compositions of metal-containing nanostructures grown by FEBID, etc.) will be accumulated and archived.

WG2: Intersectoral cooperation on research and innovation

The activities conducted by WG2 will aim at the efficient transfer of fundamental knowledge on IDC phenomena from the academic partners to the non-academic and industrial partners by means of the cooperation mechanisms provided within the COST Action (staff exchange, joint workshops and conferences, etc.). WG2 will work on validation of the scientific outcomes produced by WG1 at the more complex, technology-relevant level.

The following tasks for WG2 are envisaged:

T2.1: Validation of the multiscale models of radiation-induced biodamage based on the nanoscale understanding of IDC and subsequent molecular damage and related phenomena (relative biological effectiveness, DNA damage response, etc.) against cell survival and clinical (animal studies) data.

T2.2: Standardisation of the FEBID-based nanofabrication methods. Suggestions on optimisation of the existing technological solutions from the multiscale modelling of IDC in the FEBID process.

T2.3: Recommendations on optimisation of technological protocols for fabrication of nanoparticles (free structures and composites with MOF) with enhanced catalytic and radiosensitising properties.

T2.4: Optimisation of computational tools for multiscale modelling of IDC for the use in technological applications related to nanofabrication, characterisation of NPs and nanostructures. Development of computational methods for understanding the photophysical properties of porous supports as well as diffusion and sorption in these composite systems, including both MOFs and NP-MOF composites. It is expected that tools developed during the Action could substitute (or become an alternative to) expensive laboratory experiments, and thus reduce the experimental and technological costs.

WG3: Multiscale approach based technological advances

WG3 will complement the objectives of WG1 and WG2 through inter-technology cooperation. The main goal of WG3 will be to advance the existing technological solutions through the multiscale understanding of irradiation-driven chemical transformations in different molecular systems.

The following tasks for WG3 are planned:

T3.1: Inclusion of the IDC and radiation-driven nanoscale effects into the existing radiotherapy treatment plans based on macroscale dose delivery in order to facilitate technological advances in IBCT.

T3.2: Inter-technology exchange involving nanofabrication companies aiming towards advances in the electron induced nanofabrication techniques with FEBID.

T3.3: Inter-technology exchange aiming towards advances in the production of NPs with enhanced radiosensitising and catalytic properties.

T3.4: Advances in the development of novel computational tools for multiscale modelling of IDC phenomena according to the needs of industrial community in the field of nanofabrication, characterisation of NPs, nanostructures and porous supports in NP-MOF composites.

WG4: Training, dissemination and outreach

WG4 will focus of disseminating the results of MultIChem, training of the Action's participants (with a particular focus on Early Career Investigators), and coordination of public relations activities.

The main tasks for WG4 will be:

T4.1: Dissemination of the outcomes of MultIChem through the dedicated website as well as various kinds of printed (e.g. leaflets and biannual newsletters) and social media. Regular collection of news from WGs1-3 and their dissemination.

T4.2: Communication of the results to perceived stakeholders and general public.

T4.3: Organisation of MultIChem annual conferences, which should also be open to non-network members. One or several special issues in high profile journals summarising the Action's research activities may be published.

T4.4: Organisation of Training Schools (TS) for ECIs. The Action will organise two TS, at the end of the first year (Q4 of Year 1) and during the third year (Q4 of Year 3). The first TS will focus on reviewing state-of-the-art of experimental and theoretical description of IDC in various systems, and state-of-the-art of IDC-based technologies (modern radiotherapies, methods of irradiation-assisted nanofabrication, (nano)catalysis). The second TS will focus on reviewing the scientific advances made during the Action and training ECIs in new methodologies and experimental tools developed within the Action.

4.1.2. DESCRIPTION OF DELIVERABLES AND TIMEFRAME

The following major deliverables (Dx.x) and milestones (Mx) are envisaged to ensure the objectives of MultIChem will be successfully achieved:

no.	Title	WG no.	Due month
D5.1	Minutes of the MultIChem Kick-off meeting	MC	1
D5.2	Minutes of the 1st MC meeting	MC	10
D1.1	WG1 Annual report: Novel experimental, theoretical and computational methodologies for studying IDC phenomena in complex molecular systems	1	12
D5.3	Minutes of the 2nd MC meeting	MC	22
D1.2	WG1 Annual report on studying IDC multiscale phenomena	1	24
D2.1	WG2 Annual report on intersectoral cooperation on research and innovation	2	24
D3.1	WG3 Annual report on multiscale approach based technological advances	3	24
D5.4	Mid-term report	MC	25
D5.5	Minutes of the 3rd MC meeting	MC	34
D1.3	WG1 Annual report on studying IDC multiscale phenomena	1	36
D2.2	WG2 Annual report on intersectoral cooperation on research and innovation	2	36
D3.2	WG3 Annual report on multiscale approach based technological advances	3	36
D5.6	Minutes of the 4th MC meeting	MC	45
D4.5	4th MultIChem Annual Conference	4	45
D1.4	WG1 Annual report on studying IDC multiscale phenomena	1	46
D2.3	WG2 Annual report on intersectoral cooperation on research and innovation	2	46
D3.3	WG3 Annual report on multiscale approach based technological advances	3	46
D4.6	Summary report on the MultIChem dissemination programme; a series of leaflets and biannual newsletters, a collection of high-quality refereed publications	4	46
D4.7	Summary report on the outreach programme; publication of articles in research magazines and in Internet aimed at general public	4	46
D5.7	Final report	MC	48
M1	Organisation of the MultIChem Kick-off meeting	MC	1
M2	Operational MultIChem website and social media channels	4	6
M3	Organisation of the 1st MultIChem Annual Conference and 1st Training School	4	10
M4	Organisation of the 2nd MultIChem Annual conference	4	22
M5	Launching of the MultIChem database	1-3	30
M6	Validation of the multistage methodology for IDC in complex molecular systems	1	32
M7	Organisation of the 3rd MultIChem Annual Conference and 2nd Training School	4	34
M8	Release of a set of recommendations for optimisation of the existing technological solutions from the multiscale modelling of IDC phenomena	2-3	36
M9	Organisation of the final MultIChem Conference	4	45

4.1.3. RISK ANALYSIS AND CONTINGENCY PLANS

As MultIChem deals with advances in emerging technological solutions and brings together previous disparate communities, it involves certain risks which will be minimized by preventive planning intended to elaborate in advance potential alternative solutions.

The MultIChem Consortium includes representatives of large-scale synchrotron facilities, ion beam facilities and large computer centres as well as members who have already a well-established

collaboration with such facilities in France, Germany, Italy, the Nertherlands, and United Kingdom. The facilities and computer resources available at scientific partner organisations will also be engaged in case of necessity.

The identified risks, their likelihood and the corresponding contingency measures are listed below:

1) Failure to coordinate the work of multidisciplinary and inter-sectoral communities and thus to manage the project (risk level - low). The Action has considered mitigation measures for this risk to ensure constructive dialogue across the communities involved both at the start of the project and throughout. The members have considerable experience in intersectoral communication and joint work as well as in organisation of COST Actions which will also partially mitigate this risk. The MC will be used to review and provide solutions to such problems should they arise.

2) Insufficient involvement of industrial partners (risk level - low). As described in sections 2.2.1 and 2.2.2, several industrial partners have already indicated their willingness to participate in the Action. Several Consortium members have strong connections with a European association that involves industrial and non-industrial partners in the field of thin films deposition and characterisation, and nanostructure formation. One member represents a large research and innovation hub in the field bio- and nanotechnology which will facilitate search for new collaboration partners, establishing new contacts with industry, and promotion of the commercially viable technological applications. The MC will thus constantly seek for new partners to be included into the MultIChem network and operate well proven methods for engaging such partners in the Action.

3) Insufficient interaction between the working groups (risk level - low). Many of the Consortium members participated in previous COST Actions and European projects and are therefore aware of good practice in operating collaborative projects and in particular the advantages of doing so through COST Action. Within MultIChem the existing cooperations will be extended to a larger pan-European level to create a large collaboration between academic, non-academic and industrial partners.

4) Involvement of industrial partners may provoke Intellectual Property (IP) issues (risk level - medium). To address this issue, the MC will pay special attention towards IP protection measures. It will ensure that the benefits of the exploitation of R&D results are secured through legal protection and, in particular, through appropriate protection of Intellectual Property Rights, including copyrights. IP issues will be tackled in accordance with the European Union's policies such as the European Charter for Researchers and the COST Code of Conduct.

5) Restriction in movement of people for meetings and STSMs (e.g. due to COVID) (risk level - medium to high). This risk will be mitigated via holding virtual conferences and WG meetings and by delaying STSMs to later in programme.

4.1.4. GANTT DIAGRAM

The table below shows the time schedule for the different WGs and tasks described in sect. 4.1.1 as well as the deliverables and milestones described in sect. 4.1.2.

WG meetings (not shown in the Gantt chart) will take place throughout the Action and at least one per year. They will foster collaborations between the partners and provide the mechanism for scientific information exchange. Each year, an annual progress report about the overall status of the Action and each of the research/technological WGs will be prepared (deliverables D1.1 - 1.4, D2.1 - 2.3, D3.1 - 3.3) and circulated among the Action members.

		Year 1				Year 2				Year 3				Year 4			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
WG1	T1.1																
	T1.2																
	T1.3																
	T1.4																
	T1.5																
	Deliv.				1.1				1.2				1.3				1.4
WG2	T2.1																
	T2.2																
	T2.3																
	T2.4																
	Deliv.								2.1				2.2				2.3
WG3	T3.1																
	T3.2																
	T3.3																
	T3.4																
	Deliv.								3.1				3.2				3.3
WG4	T4.1																
	T4.2																
	T4.3																
	T4.4																
	Deliv.		4.1		4.2				4.3				4.4			4.5	4.6, 4.7
Mgmt.	T1-7																
	Events	K			A,T				A				A,T			A	
	Deliv.	5.1			5.2				5.3	5.4			5.5			5.6	5.7
Milestones		M1	M2		M3				M4		M5	M6	M7 M8			M9	

K = Kick-off meeting; **A** = Annual meeting (including the annual MC meeting); **T** = training school

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