

Joint Transnational Call 2017

for transnational research projects in synergy with the two FET Flagships Graphene Flagship & Human Brain Project

Call pre-announcement

FLAG-ERA (the Flagship ERA-NET) will present its second Joint Transnational Call (JTC) for collaborative research projects in synergy with the two FET Flagships on **January 12th**, **2017** at a networking event organised **in Madrid**, Spain. The call announcement will be published beforehand at www.flagera.eu and other sources of information. The purpose of this pre-announcement is to enable interested parties to start building their consortia and preparing their proposals. It provides a tentative timeline, the foreseen list of participating funding organisations, contact points, main eligibility rules and call procedures, and descriptions of the call topics¹.

FLAG-ERA gathers National and Regional Funding Organisations (NRFOs) in Europe and beyond with the goal of supporting, together with the European Commission, the FET Flagship initiatives, i.e., the Graphene Flagship and the Human Brain Project (HBP) Flagship. One of its main aims is to allow researchers to complement the current Flagship projects and to collaborate towards the achievement of their vision through the use of existing or dedicated transnational, national and regional calls. In particular, FLAG-ERA aims at launching dedicated JTCs allowing researchers from several countries to jointly contribute to the Flagship goals. Note that researchers interested to work in the framework of the Flagships can also do so using other sources of funding in combination with the Flagship association mechanisms².

Tentative Timeline

A two-step submission procedure will be used: Applicants are invited to submit short pre-proposals; Applicants who are selected in this first step are invited to submit full proposals. A tentative timeline is provided below.

Early January 2017	Call announcement publication
14 March 2017	Pre-proposal submission deadline
End May 2017	Notification of accepted short proposals
July 2017	Full proposal submission deadline
Oct 2017	Notification of accepted full proposals
Dec 2017 - March 2018	Project start

Note that this pre-announcement is for information purposes only. It does not create any obligation for the FLAG-ERA consortium nor for any of the participating funding organisations, and the official call announcement shall prevail.

² http://graphene-flagship.eu/project/partnering/Pages/Partnering-Mechanisms-under-Horizon-2020.aspx, https://www.humanbrainproject.eu/partnering-projects.



Participating NRFOs and indicative budgets

The table below provides the list of NRFOs participating to the call. Note that the list of participating NRFOs depends on the Flagship and, for the Graphene Flagship, on the sub-call (basic research or applied research and innovation). Budgets figures are indicative.

			Graphene (k€)		HBP (k€)
Country		Funding organisation	Basic research	Applied research and innovation	Basic and applied research
BE	Belgium ⁱ	FNRS	200	-	200
BG	Bulgaria	BNSF	175	-	175
DE	Germany	DFG	2000 -		-
ES	Spain	MINECO	560		560
FR	France	ANR	1250		1250
GR	Greece	GSRT	500	200	-
HU	Hungary	NKFIH	250		250
IT	Italy	MIUR	-	100	100
LT	Lithuania	LMT	100		100
LV	Latvia	VIAA	200		-
NL	Netherlands	FOM	1000	-	-
PL	Poland	NCBR	-	500	-
RO	Romania	UEFISCDI	250		250
SE	Sweden	VR & VINNOVA	500	500	500
SI	Slovenia	MIZS	210		420
SK	Slovakia	SAS	240		240
TR	Turkey	TUBITAK	1000		1000
	•	Total:	9735		5045

ⁱ French-speaking community only



National Contact Points

	Country	Funding organisation	Name	Email	Phone
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¹ French-speaking community only

For further information, please visit us on the FLAG-ERA website: http://www.flag-era.eu.

For general questions about the JTC and national eligibility criteria, please contact your national or regional contact point (see above).

For technical questions regarding the JTC (electronic submission, etc.), please contact the Joint Call Secretariat: fabien.guillot@agencerecherche.fr.



Eligibility of Consortia

Each consortium submitting a proposal must involve at least **3 partners from 3 different countries** and fulfil at least one of the following two options:

- At least 3 partners requesting funding from 3 different countries participating in the JTC, or
- At least 2 partners requesting funding from 2 different countries participating in the JTC plus
 a Flagship Core Project partner from a different country, not requesting funding in the
 framework of the JTC and securing its own funding.

While applications will be submitted jointly by groups from several countries, each group will be funded by its respective national or regional funding organisation. The applications are therefore subject to eligibility criteria of individual funding organisations.

Duration

Projects may be funded for a period of **up to 3 years** and according to individual funding organisation regulations.

Procedure

A two-step submission procedure applies. At each step, a joint transnational proposal (or preproposal for the first step) shall be prepared by the applicants, and must be submitted electronically by the coordinator. The proposal shall include a draft application to become a Flagship Partnering Project.

Evaluation and Selection of Proposals

Proposals are assessed by an independent international Scientific Evaluation Panel with the help of external reviewers. They are evaluated and ranked according to the following criteria:

- Relevance to the JTC (first step only);
- 2. Scientific and/or technological quality;
- 3. Implementation;
- 4. Potential impact.

On the basis of the ranking and of available funding, the Call Steering Committee, composed of the NRFOs participating in the JTC, will prepare a list of projects invited to submit a full proposal (after the 1st step) or recommended for funding (after the 2nd step).

Association to the Flagship

Projects recommended for funding will be invited to proceed with the formal association to the Flagship, using the Flagship standard association procedure. Any issue at this stage will be treated through classical project risk management.



Research areas

The FLAG-ERA JTC 2017 comprises two topics, one for each Flagship. The Graphene part of the call is sub-divided into two sub-calls, one for basic research and one for applied research and innovation. There are thus three sub-calls in total. Each sub-call covers a specific list of research areas listed below and described in the following pages. Relevant parts of the Flagship and contact points for each area are provided on the call web page.

Graphene JTC areas (Basic research)

- 1. Synthesis and characterization of Layered Materials (LMs) beyond graphene
- 2. Large scale production of heterostructures based on LMs
- 3. Vertical and lateral epitaxy of Graphene and Related Materials (GRMs) for optoelectronics
- 4. Functional ceramics incorporating GRMs
- 5. Inks for printing stable, GRM-based, semiconducting thin films
- 6. Modelling charge and heat transport in GRM-based composites
- 7. Ecotoxicology of GRMs
- 8. Nanofluidics using GRMs
- 9. Novel device concepts based on GRMs for quantum communication
- 10. Beyond CMOS switches and new computing paradigms based on GRMs

Graphene JTC areas (Applied research and innovation)

L. In-situ and ex-situ quality control of GRMs

- 2. Controlling doping in high quality large-area graphene
- 3. GRMs for smart textiles
- 4. Functional coatings using GRMs
- 5. GRMs for corrosion prevention and as lubricants
- 6. GRMs for thermal management and thermoelectrics
- 7. Biorecognition of specific disease markers using GRMs
- 8. Highly selective gas sensors based on GRMs
- 9. GRM-based bioelectronic technologies

HBP JTC areas

(Basic and applied research)

- 1. Human brain intracranial data and their relationship to other aspects of brain organisation
- 2. Comparing morphology and physiology of cortical cell types in human and non-human primates
- 3. Comparative aspects of brain function and connectivity
- 4. <u>Cross-species multi-scale data constraints for visuo-motor integration</u>
- 5. The neural bases of spatial navigation and episodic memory
- 6. Models of auditory processing
- 7. Representation of perceived or memorised information in multi-level systems
- 8. Modelling dendrites within active networks
- 9. Testing predictive coding and attractor network models
- 10. Biological deep learning
- 11. Disease modelling and simulation
- 12. Innovative modelling for allosteric drug discovery
- 13. <u>Integration of simulation tools, neuromorphic computing and robotics with brain and behavioural studies</u> for developing next-generation brain-computer interfaces
- 14. Text mining of cellular, synaptic, connectomic or functional properties of the brain



Graphene - Basic research

1. Synthesis and characterization of LMs beyond graphene

Layered materials (LMs) are crystals where robust chemical bonding within the planes coexists with weak van der Waals coupling of those layers to the environment or in heterostructures, with properties suitable for electronics and optoelectronics applications. Further capability building is needed in:

- growth of atomically thin stable LMs (such as hBN, MoS₂, MoSe₂, MoTe₂, WSe₂, GaS, GaSe, GaTe, and InSe) using molecular beam epitaxy (MBE), chemical vapour deposition (CVD) and/or atomic layer deposition (ALD);
- finding chemical routes for repairing defects and damage in LMs produced by growth or exfoliation from bulk layered crystals;
- synthesis of novel semiconducting and metallic layered compounds that can be exfoliated into monolayers.

Proposals should foresee a balanced approach to materials fabrication and characterisation and plan for both growth/synthesis activities and suitable structural, optical, scanning microscopy, and/or electronic transport characterisation of the produced LMs. Projects are expected to gather teams with complementary expertise in growth and characterisation, with ready access to the necessary facilities. Developments should be benchmarked against the same materials already produced worldwide, showing that the material quality can advance electronic or optoelectronic devices beyond state of the art.

2. Large scale production of heterostructures based on LMs

The objective is to produce van der Waals heterostructures in a reliable, scalable and reproducible manner. The existence of a wide range of LMs gives the opportunity to create atomically thin pnjunctions, Schottky barriers, or tunnel junctions as these materials have strong intralayer bonding but only exhibit weak van der Waals interactions between adjacent layers. Applications are foreseen in functional electronics or high-end instrumentation development (e.g. detectors or sensors) in industrial sectors such as electronics and energy.

Materials may include mono-atomic layers (graphene, silicene, and phosphorene), compound mono-layers (BN, GaX) as well as other unit-cell thick materials such as transition metal dichalcogenides (TMDs). The scalable synthesis of heterostructures resulting from the formation of atomically sharp interfaces between strongly bonded oxides can also be considered. The approach may be wet-chemical assembly, including layer transfer or direct growth with chemical vapour, as well as physical vapour deposition, molecular beam epitaxy (MBE) or sputtering technologies. It should be explicitly shown that atomically thin interfaces are produced in the fabrication process. In order to assess the properties and functionalities of the heterostructures, characterization of the heterostructures is mandatory.



3. Vertical and lateral epitaxy of GRMs for optoelectronics

Graphene and related material (GRM) heterostructures offer a variety of novel functionalities determined by material choice and structure design, and give high performance due to atomically clean and sharp interfaces. Devices based on these heterostructures enable a wide range of applications such as light-emitting diodes, photovoltaic devices, and photodetectors. To further develop and use combinations of these structures, heteroepitaxial growth is needed for both vertically stacked heterostructures as well as in-plane connected GRM heterostructures.

The quality of the materials, as well as of the heterostructures, needs to be evaluated including the crystal orientation, relative orientation of the different materials and the sharpness of the interfaces. Also important is the evaluation of the interlayer coupling, in the context of the desired applications. The GRM range includes graphene, transition metal dichalcogenides (TMDs) and also GaX. The role of graphene is to be an efficient electrical contact for semi-conducting LMs. Devices fabricated based on the grown structures and demonstration of their functionality for opto-electronic applications, such as photodetectors, modulators, transceivers, light emitting diodes, single photon emitters—are required. This includes an evaluation of the performance of the devices, such as efficiency and speed.

4. Functional ceramics incorporating GRMs

The use of GRMs as nano-additives in composites is one of the most mature research areas for these promising materials, with GRM-polymer composites already on the market. GRM-ceramic composites have received comparatively little attention, even if the use of ceramics as coating tiles, refractory material or bio-implants is a major industrial field. Effective development of GRM-ceramic composites is challenging due to the poor processability of both materials and the high temperatures involved in ceramic production.

The goal is to develop new GRM-ceramic composites, using the unique properties of GRMs to have structural, chemical, optical or electronic functionalities that cannot be obtained with other types of additives. Fundamental research is required, as example to better understand and control the (opto)electronic properties of GRM-ceramic interfaces. A clear vision of how the new functionalities developed shall solve existing problems, or allow new technological applications of ceramics, is needed.

5. Inks for printing stable GRM-based semiconducting thin films

Printing and solution processing are established approaches for low cost and high volume manufacturing, but the availability of printable materials exhibiting stable semiconducting properties and high enough charge carrier mobility (>40cm²/Vs) for practical electronic applications is limited. Solution-based GRMs with semiconducting properties are very promising for the realization of large scale printed electronic applications.

The main challenges that need to be addressed include: manufacturing of semiconducting GRM powders and dispersions in bulk volumes; formulation of semiconducting GRMs into inks with a stable rheology without compromising the electrical properties of the materials; GRM inks



formulation in friendly solvents; printability of the produced inks into stable semiconducting thin films on standard substrates. In addition, the following key processes should be developed: substrate conditioning for optimal printing; post-processing of the printed structures to optimize the electrical performance and/or stability; contacting of the semiconducting thin film. The functionalization of the semiconductor material or thin film for specific properties would also enable further applications such as sensing. Devices utilizing printed semiconducting GRMs should be demonstrated with a mobility $> 40 \text{cm}^2/\text{Vs}$ and an ON/OFF ratio $> 10^5$, and the performance of the inks should be benchmarked against state-of-the-art materials, using the charge carrier mobility and the devices stability as key performance indicators.

6. Modelling charge and heat transport in GRM-based composites

Charge transport in graphene has been intensively studied. However, most studies focus on charge transport in defect-free graphene, or graphene nanoribbons. GRMs are often produced as highly non-ideal structures. Point defects, amorphous pockets, wrinkles, mismatching crystalline grains are found at the microscale, while stacking and inter-sheet interactions play critical role for the overall physical properties at the macroscale. Besides electrical transport, also heat transport requires a deep understanding of the physics and structure of complex GRM-based composite materials, and the details of inter-sheet interactions. For GRMs to have a real impact, one thus needs a deeper understanding of charge and heat transport in large scale models of thin conductive layers of GRMs composed of large number of overlapping sheets, or three-dimensional percolating layers present in bulk composites.

Multiscale experimental, theoretical and computational tools should be developed to study the charge and heath transport of systems composed by large numbers of interacting GRM nanosheets, and of the interfaces present in such systems. Projects should investigate the charge transport properties and/or the thermal conductivity of GRM-based composites, through the development of a full hierarchy of computational and theoretical models, for example ranging from two-dimensional continuum elasticity to atomistic modelling of charge and heat currents in very large size systems. The structural morphologies of studied materials and transport results should be cross-validated with experimental data of relevance for applications.

7. Ecotoxicology of GRMs

The study of the interactions of GRMs and living organisms must be extended to a wider array of materials and to the toxic substances frequently present in polluted environments, whose action might be promoted or inhibited by GRMs. The aim is to promote safety-by-design, meaning that potentially toxic properties could be engineered out in order to have new, improved, non-toxic materials, still retaining their desirable properties. Because ecotoxicology has to provide the regulatory assessment tools related to the future GRMs in the environment, it is necessary to design new protocols relevant to natural exposure conditions. Understanding the global mechanisms of interaction and effects of GRMs under natural conditions could be achieved by designing experimental trophic chains and bio environments using representative organisms and cell models in aquatic and terrestrial setting.



Areas of special interest are:

- 1) Characterization of materials properties and interplay with pollutants in connection to potential GRMs ecotoxicity. A combination of well-characterized, "custom-designed" materials (i.e. materials with systematic variation in properties, such as lateral dimensions or number of layers) needs to be investigated in comparison to others that are relevant from an industrial and commercial point of view, and released in use conditions or simulated use conditions, together with different arrays of heavy metals and organic contaminants. The effects need to be assessed on ecologically relevant organisms (e.g. soil organisms, nitrogen fixing bacteria and cyanobacteria, mycorrhizal fungi, or autophototrophs), aquatic model organisms and different relevant unicellular models.
- 2) Physico-chemical and biological biodegradation processes and sedimentation of GRMs in soil and water ecosystems. The numerous physico-chemical interactions between these materials and humic colloids, e.g. humic and fulvic acids, need to be studied spectroscopically in order to describe the potential impact of the environmental matrices ("eco"-corona) on the biodegradation and sedimentation processes.

8. Nanofluidics using GRMs

GRMs show great potential for many applications (including separation of gases, heat exchanges, water filtration, energy storage, biomedical applications, and various sensors) where understanding of the nanofluidic properties of GRM laminates plays a crucial role. Further research is needed to use GRMs to develop structures or laminates with a significant performance improvement over current technologies, and to exploit the new opportunities offered by GRMs.

Projects should outline a credible route towards higher technology readiness levels and, ultimately, new industrial products. They should combine experimental and theoretical efforts, based on the expertise in GRM fabrication, characterisation and modelling of their relevant structural and nanofluidic properties.

9. Novel device concepts based on GRMs for quantum communication

The rapid technological advances in quantum communication have triggered increased interest for commercial applications. An important roadblock is the limited performance of single photon detectors and controllable sources of single photons or entangled photon pairs. GRMs offer new ways to control single photon emission, for example from localized emitters such as quantum dots embedded in the material.

There is a strong need to gain better control and understanding of the exciton localization and the ability to tailor the localization in terms of position, emission properties, ability of electrical control, etc. Ideally the emission wavelength should be expanded from visible to shortwave-infrared, up to 1.5 μ m, covering the telecommunication window. It is important to integrate the emitters with cavities in order to enhance the emission efficiency, and to enable efficient coupling with integrated photonic systems. In addition, controllable emission of entangled photon pairs is required. For a single-photon detection platform, there is a need to employ GRMs for single photon detection with high quantum efficiency. One promising approach is the implementation of GRM-based



superconducting bolometers. The sensitive wavelength range should extend up to and preferably beyond 5 μ m. Benchmarking of the devices with existing technologies is essential.

10. Beyond CMOS switches and new computing paradigms based on GRMs

The geometric scaling of silicon transistors is approaching fundamental limits and solutions in the beyond CMOS area are required. GRMs offer several different possibilities to realize beyond CMOS switches and devices enabling novel computing paradigms.

Proposals should focus on the experimental demonstration of proof-of-concept devices based on GRMs for beyond CMOS switches or devices enabling novel computing paradigms. If applicable, the implementation of these devices into new computing architectures may additionally be addressed. Specific devices within the scope of this call topic include, but are not limited to: (Vertical) tunnelling transistors, ballistic switches, devices based on GRM heterostructures, devices utilizing the spin degree of freedom, quantum devices or similar. Projects may include also theoretical work in order to provide an outline on the ultimate performance of the devices, to develop models for the devices or to reduce the parameter space for further improvement.



Graphene - Applied research and innovation

1. In-situ and ex-situ quality control of GRMs

Fast and reliable characterization of GRMs is an important step for production quality control and industrialization of material synthesis. Therefore it is essential to develop techniques, in-situ and exsitu, to monitor the quality of these materials and provide feedback for process control or material grading.

Areas of special interest are: (i) in-situ techniques that are able to detect in real-time (a) different oxidation states of the catalyst; (b) identify monolayer growth and area coverage; (c) number of layers and (d) estimation of the grain size; (ii) Ex-situ techniques that can quickly provide information on the film morphology, thickness, composition, surface and electrical properties are also required.

Demonstrators should target the characterization of at least one property of mono- or multilayer GRM over a large set of experimental samples.

2. Controlling doping in high quality, large-area graphene

Doping is an essential process to engineer the conductivity and work function of graphene. Besides electrostatic doping, other techniques such as chemical doping need further exploration. The two major approaches involving chemical doping of graphene include substitutional and adsorbate-induced doping. Substitutional doping involves replacement of carbon atoms in a graphene layer by other atoms, such as nitrogen and boron. It is difficult to control, and it significantly disrupts the graphene lattice, thus deteriorating the charge carrier mobility. Adsorbate-induced doping, on the other hand, exploits the 'surface-only' nature of graphene to modulate the charge carrier concentration via physisorption of molecules. This type of doping takes place via charge transfer between dopant and graphene. While the controllability is more favourable compared to substitutional doping, the weak nature of the physisorbed interaction limits the robustness, hence feasibility, of this routine.

Alternatively, chemical modification could provide a means that is controllable, as well as being chemically and thermally robust. Chemical functionalization can form ${\rm sp}^3$ defects at the points of covalent attachment. Covalent attachment of molecules to graphene is also a known method of inducing doping. Thus, covalent functionalization provides a platform in which to tackle simultaneously the issue of band gap tuning and charge carrier doping. The high degree of surface coverage control over the extent of modification and homogeneity make covalent functionalization an attractive protocol. However, a major drawback to chemically modifying graphene is that the unique electronic structure (${\rm sp}^2$ based) can be destroyed. In general, due to the use of highly reactive species, required because graphene has a relatively low chemical reactivity due to the delocalization of the π electrons over the entire two-dimensional network, the chemical modification of graphene cannot be spatially ordered and the covalent attachment occurs randomly. This results in a significant reduction of the charge carrier mobility, for which a solution must be found. Other problems such as scalability, combination with the graphene transfer, robustness and reproducibility arise at when fabricating and patterning graphene components into integrated circuits, especially in ambient



conditions. Current state-of-the-art methods do not offer viable graphene components to compete with the present materials in use, hence alternative strategies are demanded.

The target is to devise an efficient strategy for large area doping of graphene, while preserving key properties such as mobility and scattering time. This needs to be combined with large area transfer processes. All approaches must result in a material that is CMOS compatible, in terms of metal and other impurities, as for CMOS fab rules.

3. GRMs for smart textiles

Current advanced (or smart) textile technology relies on a heterogeneous platform of multilayers printed or coated in sequence onto fibres or directly deposited on the final fabric. Current conducting fibres for smart textiles mainly use thin Cu or Al wires bundled with cotton or coated with polymers, and the main components are textile-integrated (into/onto the textile surface). The future in this field will lead to having the components being textile-based (the textile itself being the functional component). The full realisation of advanced textiles could benefit from a new platform exploiting fully flexible, tuneable and processable materials to give new functionalities (e.g. light emission, photovoltaic activities, sensing, energy storage, heating or mechanical actuators). GRMs can provide the high conductivity, high flexibility and chemical tuneability needed for this task.

The goal is to develop new GRM-based smart textiles, using the unique properties of GRMs, to have structural, chemical, optical or electronic functionalities that cannot be obtained with other types of materials. Addressing the issues of durability of the target systems upon standard textile washing and enhanced biocompatibility in contact with human skin will represent an added value. Encapsulation techniques (although not preferable) might also be suitable as a solution.

4. Functional coatings using GRMs

Due to their layered structure, GRMs are ideal candidates for coating and thin film applications, and with new production technologies emerging, graphene is now available in useful quantities to address its implementation in various areas. Additionally, the field of functional LMs is not limited to pristine graphene but also includes doped derivatives, transition metal dichalcogenides (TMDs), polymers and others or nano-composites based on such materials.

Areas of interest are coating formulation, application and testing, addressing functionalities such as (but not limited to): electrical conductivity, gas barrier properties or gas separation, improved chemical resistance, heat dissipation, temperature stability, catalytic activity, electromagnetic interference shielding or self-monitoring.

Such functionalities can have many applications ranging from gas barrier coatings, separation membranes, anti-statics, radiation shielding or flame-retardance to more sophisticated devices like in-situ strain measurement sensors, catalytically active surfaces and electrodes or flexible electronics. Within this field a diversity of formulations and recipes can be addressed, for instance powder based dry coatings, paints, specialized inks for different printing technologies or direct deposition on the substrate.



5. GRMs for corrosion prevention and as lubricants

The planar nature of GRMs makes them promising for the protection of surfaces, including those of construction materials, aerospace metals, composites and machine components.

Areas of special interest are (i) coatings for improved chemical and water barrier properties, corrosion resistance or thermal performance; (ii) lubricant systems where GRMs lead to lower friction, reduced wear, reduced corrosion and higher efficiency of heat transfer. In the context of coatings, a scalable deposition methodology must be developed (e.g. direct growth, spray coating, dip coating).

For both coating and lubricants applications it is expected that new formulation techniques may have to be developed. The addition of GRMs to the coatings and lubricants should show improved performance in both short-term and accelerated tests conducted in service relevant-conditions, such as hot salt spray chambers.

6. GRMs for thermal management and thermoelectrics

The ability to tailor the electron density of states and thereby influence the Seebeck coefficient in GRMs makes them attractive candidates for thermal management. This is particularly applicable to GRM-based heterostructures, and to grainy materials with controlled grains size, shape and distribution. While the former could lead to sufficient electronic level difference to tune electron transfer and electron contribution to the thermal conductivity, an important research questions is to what degree this affects the nature of the interfaces and the concomitant interface thermal resistance. The latter, if studied with a statistical approach to take into account the variations in the real GRM grain structure and estimate their contribution to the interface thermal resistance within certain bounds, will provide a means to have a degree of predictive insight as to what to expect in terms of thermoelectric parameters and performance of such materials.

Proposals should address novel experimental methods on near-field and far-field radiation and thermal measurements, and advanced configurations arising from phonon engineering for optimization of thermal management in GRM-based hybrids. The reliability and reproducibility of the experimental methods and material structures should be emphasized, as well as its integration and large scale production perspectives.

7. Biorecognition of specific disease markers using GRMs

The identification and accurate measurement of disease biomarkers at the level of individual patient in response to specific therapies is instrumental to the development of personalized medical treatments. Toward this goal, new devices capable of high sensitivity, parallel measurements of multiple disease biomarkers (either circulating in the bloodstream or found in phenotypically characterized (live) cell subpopulations), are strongly required. In this context, graphene-based opto-electrical platforms (e.g. fluorescence quenching, impedance related electrochemical measurements and paper/plastic-based platforms) are ideal candidates as cost-effective, highly sensitive devices for



the analysis of protein and/or DNA biomarkers in small sample volumes. Disease biomarkers detection platforms might result from synergies between various GRMs, nanoparticles, specific biofunctionalization protocols and sensing technologies.

To allow further industrialization, production of high quality functionalized graphene, (reduced) graphene oxides and/or graphene quantum dots, with thickness control and high quantum yield, should be demonstrated through easily scalable processes and overall with appropriate functional groups, compatible with physiological media and able to maximize the interaction with the disease biomarkers.

8. Highly selective gas sensors based on GRMs

The major challenges in the emerging gas sensing concepts are concentrated on selectivity. Highly sensitive GRM-based gas sensors analysing e.g. the charge carrier response to the adsorbed gases have inherent limitations in the selectivity, similar to the more conventional material systems such as functionalised oxides and their matrices. The only viable alternative for the next phase selective gas sensors is in the direct measurement of the spectral fingerprints of the gases.

Areas or special interest are: GRM based spectroscopic systems for the measurement of the characteristic vibrational spectra of gaseous substances at far-IR / THz region and/or dissociation spectra in the UV region; potentially (non-dispersive) IR/THz gas sensors or waveguide-based sensors; potentially employing bolometric or thermoelectric effects in GRMs.

Systems should be operating at ambient or room temperature and the stability with respect to humidity and thermal fluctuations should be controllable. The spectral features under analysis should be narrow and distinguishable enough to allow selective detection irrespective to the presence of other gases and this, as well as the benefit of GRM in relation to more conventional material solutions, should be rigorously justified in the proposal.

9. GRM-based bioelectronic technologies

The call aims at projects exploring GRM-based bioelectronic technologies and devices for in-vitro and in-vivo applications.

Projects addressing the topic of in-vitro cell interfaces should aim at developing novel technologies based on GRMs for studying in-vitro cell or tissue related processes (growth, electrical and chemical signalling, etc.) or at exploiting these technologies for sensing (cell-based drug screening, etc.). Beyond demonstration of novel technology concepts (electrical, optical, mechanical, etc.) taking advantage of GRM characteristics as well as their combination with other materials, the projects should aim at integrating the technologies into prototype platforms, including engineering of functionalities such as microfluidics and electronics.

Projects addressing the topic of bioelectronic devices for in-vivo applications should aim at developing GRM-based flexible devices that, via nerve/tissue stimulation or recordings (central or peripheral nervous systems), can be used to restore or maintain healthy conditions or to study cognitive functions or neural disorders. In particular, the call targets technologies for control of



artificial limbs or devices, neuromodulation, and rehabilitation (spinal cord injury, stroke, pain, speech disorders, etc.), as well as applications involving organs different than the brain (cardiovascular, such as pacemakers, etc.). The developed technologies must be designed and evaluated together with clinical organizations (leading the therapeutic assessment) as well as industrial partners (leading the commercial exploitation) and tested on relevant preclinical models for studying functionality, efficiency, safety and mechanisms of action.



HBP - Basic and applied research

Projects should contribute to the aims of the HBP and address ambitious research questions in the field of brain research including medical research, brain inspired technologies, robotics & computing and/or contribute to technological development. The proposed activities should be based on the latest scientific knowledge, and include innovative concepts that bring the field closer to the solution of a concrete and important problem in an interdisciplinary research approach. Objectives should be realistic and measurable, and reproducibility should be ensured. Proposed activities should demonstrate their potential to shape the evolving HBP ICT platforms (Subprojects 5-10), e.g. showcasing the value that these platforms can add to the neuroscience community, and/or foster their development. Ideally they cut across existing HBP Subprojects, including neuroscientific and platform Subprojects and/or the 'Ethics and Society' Subproject.

1. Human brain intracranial data and their relationship to other aspects of brain organisation

Human intracranial data are optimal to bridge levels of observations and understanding between animal electrophysiology and human non-invasive recordings (fMRI, EEG, MEG). It would be extremely valuable to provide intracranial data collected during cognitive tasks, e.g. multi-unit recordings, to integrate them into the Human Brain Atlas, and to analyse them, for example with respect to other aspects of brain organisation (structural, functional), ideally in collaboration with experts in other recordings scales (monkey or non-invasive human recordings). There is an added value for the Human Brain Atlas and for modelling and simulation.

2. Comparing morphology and physiology of cortical cell types in human and non-human primates

Simulating human brain neuronal circuitry based on data-driven models is one of the major goals of HBP. The simulation of the somatosensory cortical column of rodents provides a roadmap for data-driven modelling and simulation of human circuitries. However, early results on neuronal morphologies and physiologies revealed that several properties of human neuronal circuits in the cortex are strikingly different from rodent cortical circuits. To understand whether these differences are specific to human neocortex or whether they extend also to non-human primates, research is needed on the morphology and physiology of neuronal circuits in the non-human primate neocortex subserving similar functions in both species.

3. Comparative aspects of brain function and connectivity

Studies on homologies of the human brain and the brains of other species are central for understanding how far data from animal models can be transferred to human brain research. It is proposed to study neuronal activity/connectivity across species for the same task and experimental set-up. This would concern preferably comparisons between mouse, monkey, and human brains.



For example, fMRI can be used to compare brain activations obtained during cognitive tasks in different species, and to establish quantitative, functional connectivity matrices across homologous areas and networks in multiple species under varying states and task conditions. Such in-vivo connectomes are needed to build and simulate multimodal computational architectures of the cortex incorporating ex-vivo histological and receptor-density data in the same models.

In addition, comparative fMRI experiments in monkeys and human patients that have to undergo surgical resection of epileptic foci may be performed with the goal to identify potentially functionally homologous regions in the temporal pole. Based on the fMRI maps, equivalent portions of monkey cortex can be dissected as in the patients. Both brain samples could then be prepared for slice recordings to perform a detailed physiological and morphological characterization of cells in both samples. This would allow a direct comparison of neurons in human and monkey association cortex which are likely contributing to similar perceptual or cognitive processes.

4. Cross-species multi-scale data constraints for visuo-motor integration

Multi-scale object recognition and sensorimotor integration neural simulation models are being developed in the HBP based on both experimental data and conceptual models. The present research area targets contributions from additional multi-scale data from multiple simultaneous electrophysiological recording data from relevant brain areas in non-human primates (e.g. visual, parietal, subcortical, premotor, motor) performing the same or similar sensory-motor tasks. Additional high-resolution fMRI and EEG human data for other sensory-motor tasks could provide useful constraints for validating and generalising the simulation models.

5. The neural bases of spatial navigation and episodic memory

Spatial navigation represents a complex function of the vertebrate brain. It requires the brain to remember a sequence of locations and events stored in episodic memory to be able to navigate. Central to this information processing are circuits in the entorhinal cortex and hippocampus. Much is known regarding specific cell types, connectivity and transmitters. It is proposed to translate this extensive knowledge into an understanding of the circuits generating navigation, to identify the input sources and the output that forwards information to the motor centres.

6. Models of auditory processing

The auditory system is important for navigation and to sense the environment, but has not been considered in HBP so far. The present research area aims to develop data-driven models of auditory processing, from the level of the cochlea up to the auditory cortex (including brain stem and thalamic nuclei) with a focus on the "awake" auditory processing. The models should be implementable in neuromorphic hardware and ideally run in real-time, for being used in neuro-robotics applications, or sensori-motor navigation paradigms.



7. Representation of perceived or memorised information in multi-level systems

In various HBP projects both bottom-up and top-down approaches are pursued for understanding the linkage between low-level, e.g. single neurons and local microcircuits, and high-level systems, e.g. networks distributed across multiple areas, in relation to behaviour, perception and cognition. Novel, emerging techniques such as 2-photon calcium imaging or high-density silicon probe recordings now allow researchers to study the relations between these multiple levels in combination with behavioural paradigms. The present research area aims to investigate how these different levels are connected and organised to understand the neural representation of perceived or memorised information.

8. Modelling dendrites within active networks

Dendrites are important to understand how neurons integrate information but little is known about dendritic function in activated states of the brain. The goal of this research area is to design models of dendrites with unprecedented dynamical realism, directly constrained by experiments. The experiments should directly visualize (using voltage-sensitive probes) the activity of cortical dendrites, during "active" network states, either in vivo or in vitro. Models are then designed (or existing models improved) directly based on these data. The goal is to understand dendritic processing in vivo, ultimately in awake animals.

9. Testing predictive coding and attractor network models

The construction of world models by the brain has been conceived in terms of multiple theoretical models, such as Predictive Coding networks (where incoming sensory information is predicted based on prior experience), Attractor networks (recurrently connected dynamic networks) and Hierarchical models of feature detectors. This research theme should examine (i) whether model predictions can be verified or rejected by physiological and behavioural data; (ii) whether sensory and memory systems may realistically combine models within one overall architecture; (iii) what computational properties such joint models have.

10. Biological deep learning

Deep learning networks have turned out to be very efficacious in addressing complex problems such as playing games (e.g. Go), image classification and object recognition. The next challenge is to implement such networks in biological brains. The present research area aims to research whether less realistic properties of deep learning algorithms could be replaced by more biological properties, i.e. realistic bioelectric behaviour of neurons, and how the functionality of networks could be further augmented using knowledge about the brain.



11. Disease modelling and simulation

The Medical Informatics Platform aims to achieve biologically based classifications of brain diseases, and thus to take advantage of rich data available in hospitals. The objective of this area is to promote clinical proof-of-concept studies of the Medical informatics and the simulation platforms. Projects will have access to data and bioinformatics methods (machine learning, data intensive network analysis, pathways analysis in large volume of data) to gain new clinical insights, derive mechanisms of disease causation and mechanisms of action of known therapeutic agents. Possible research themes include mechanisms of disease causation, mechanisms of action of known therapeutic agents, screening of drug candidates, and developing theory-driven models of disease directly constrained by experimental data in human and animals from the biological signatures of disease and the disease classifications identified by researchers using the Medical Informatics Platform.

12. Innovative modelling for allosteric drug discovery

Innovative neuromedicine approaches require a detailed understanding of the molecular and systems-level organization of the human brain, the causes and mechanisms of diseases, their progression, and the response to treatments. Because of the high level of complexity of the nervous system and of intersubject variability in molecular brain organization, behaviour and disease, addressing these issues for any neuropathology appears a daunting task. Indeed, for most neurodegenerative diseases, such as Alzheimer's and Parkinson's, there is currently no cure in spite of the very large investments from academia and industries. The discovery of new drugs against brain diseases thus has high ethical priority for the on-going neuroscience research. HBP offers novel insights and computational methods to design and in silico select original classes of drugs.

Allosteric pharmacology, or the design of drugs targeting sites topographically different from the endogenous ligand binding site, is one of the most recent innovative approaches to drug discovery. Classical neuroactive drugs were designed on the basis of their similarity-isosteric competitivity with compounds of natural origin. The allosteric interaction paradigm, instead, offer alternative drug-discovery opportunities.

There is a need for novel molecular-simulation based research efforts to accelerate the discovery of new and more effective treatments, based on allosteric mechanisms, reducing the problem of side effects, whilst speeding up and drastically lowering the cost of drug discovery.

13.Integration of simulation tools, neuromorphic computing and robotics with brain and behavioural studies for developing next-generation brain-computer interfaces

Using expertise on brain organization, cognitive and theoretical neuroscience, as well as brain simulation and neurorobotics, the present research area proposes to develop next-generation interfaces for controlling brain states and neural population activity subserving neuroprosthetics, brain stimulation techniques, optogenetics (highly specific control of neural circuits by genetic manipulation and light, in animal models) and other forms of real-time feedback to brain systems.



14. Text mining of cellular, synaptic, connectomic or functional properties of the brain

Basic semantic data mining capabilities are available in the Neuroinformatics Platform of the HBP. This research area aims to develop HBP text mining tools (Sherlock, a UIMA based text mining engine) or adapt open source community toolkits and workflows in the text mining community to extract information relevant for HBP modelling and predictive work. Of particular interest in this effort are cellular, synaptic, connectomic, and functional properties of all scales of the health and diseased brain.