# **WP5: Chemical deuteration**

Lead Partner: ESS

Involved Partners: ILL, STFC, FZJ

Observers: ANSTO

# Summary for publication (online)

## Summary of the context and overall objectives of the project

Per-deuterated materials are rarely available from commercial suppliers except through costly custom synthesis, and this limits the experiments that can be performed, and forms a bottle-neck for advancing the applications of neutron scattering. The development of new synthesis, purification methods and materials forms the foundation for leveraging the full potential of the neutron scattering and new facilities such as the ESS, particularly in the areas of soft condensed matter, functional materials and the biomedical sciences.

To broaden the range of compounds available, and to provide a cost-effective service and coordinated user access, we propose to establish a European platform for chemical deuteration (DEUNET) in the form of a network between the ESS, ILL, STFC, and FZJ, with the Australian National Deuteration Facility at ANSTO as an observer. The platform will use the complementary expertise of the partners to achieve the most cost-effective syntheses and to develop synthetic routes for a broad range of compounds, as well as by sharing and recycling deuterated raw materials where possible. During the SINE2020 project, particular attention will be paid to consulting the user community about the requirements for the services and cross-fertilisation of ideas through collaborations and staff visits between the facilities. The platform will operate and provide user access on a collaborative basis during this project, with the goal beyond SINE2020 being to provide transnational access to the service as well as to extend the collaboration internationally.

## Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

*This section must be completed on-line (see above).*

In the period from October 1 2015 until March 31, 2017, partners have initiated work on reaching the objectives of WP5: *Chemical Deuteration*. The STFC Deuteration Facility has synthesized wide variety of both routine and non-routine deuterated precursors and surfactants for non-UK users and DEUNET partners, which has resulted in several successful neutron experiments at ISIS, with publications in preparation. ILL has initiated the production, analysis and purification of deuterated membrane lipids in cell cultures, which will enable the use of biologically relevant unsaturated lipids in many different types of neutron experiments related to cell membrane function in health and disease. At ESS, a new laboratory (DEULAB) has been set up for the synthesis of small deuterated molecules with precursors to the first target molecule lactic acid and polymer supports for enzyme catalysis synthesized and characterized. At FZJ, deuterated polyisoprene and polyhexylthiophene (P3HT) have been synthesized via new, improved routes allowing better control of the polymerization and therefore the properties of the commercially and technologically important polymers to be investigated by neutron scattering. The participation of our observer partner ANSTO NDF has enabled many useful discussions about both synthesis and the operation of a user deuteration facility.

## Progress beyond the state of the art, expected results until the end of the project and potential impacts (including the socio-economic impact and the wider societal implications of the project so far)

A significant fraction of the materials that will be synthezised within the DEUNET platform have industrial applications or recognized innovation potential. Detailed neutron scattering studies enabled by chemical deuteration are of crucial importance for understanding the function and improving the efficiency of new materials and technologies. Our joint effort for developing new lipid extraction methods, new polymer synthesis and enzyme-technologies for the synthesis of complex small molecules, particularly chiral compounds, will considerably enlarge the experimental possibilities by providing neutron users with deuterated compounds that have been inaccessible until now.

The DEUNET network will ensure the provision and development of expertise on a broad range of deuterated materials for the European science community beyond the frame of the present SINE2020 project and guarantees sustainability in a rapidly developing field where there is a trend towards increased soft matter experiments at all neutron scattering facilities.

# **WP5: Chemical deuteration**

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# Explanation of the work carried out by the beneficiaries and Overview of the progress – WP5 Chemical Deuteration

*Explain the work carried out during the reporting period and include an overview of the project results towards the objective of the action including summary of deliverables and milestones, and a summary of exploitable results and an explanation about how they can/will be exploited[[1]](#footnote-1).*

In the period from October 1 2015 until March 31, 2017, partners have initiated work on reaching the objectives of WP5: *Chemical Deuteration*. All partners are on track to provide their deliverables and milestones stated in the proposal. Several highlights, including technical developments are provided, demonstrating the progress made toward the objectives outlined in section 1.1.

The STFC Deuteration Facility regularly produces a large number of deuterated precursors through catalytic deuterium hydrogen exchange, including aliphatic hydrocarbons such as fatty acid, bromoalkanes, and organic ligands. A wide variety of both routine and non-routine deuterated precursors and surfactants (listed in section 1.2.1.) have been synthesized for non-UK users (D5.7) and DEUNET partners (D5.1), and have resulted in several successful neutron experiments at ISIS, with publications in preparation.

ILL has initiated the production, analysis and purification of deuterated membrane lipids in cell cultures (Task 5.2), and is currently investigating the effects of growth conditions on the lipid composition produced in deuterated and non-deuterated cultures. The developments made will enable the use of biologically relevant unsaturated lipid membranes in many different types of neutron experiments related to cell membrane and membrane protein function in health and disease.

At ESS, a new laboratory (DEULAB) has been set up for the synthesis of small deuterated molecules (Task 5.3) and precursors to the first target molecule lactic acid (D 5.4) and the polymer supports for enzyme catalysis have been synthesized and characterized. The development of enzyme-technologies for the synthesis of complex small molecules, particularly chiral compounds, will enable future neutron experiments with deuterated compounds that have been inaccessible until now. The synthesis of lactic acid enantiomers will enable the synthesis of tailored polylactic acid polymers (FZJ) for user experiments investigating the dependence of polymer microstructure, physical properties and dynamics on the chemical structure, which will provide new understanding on the properties of this important class of biodegradable plastics with biomedical and technological applications.

At FZJ, deuterated isoprene (D5.3) and polyhexylthiophene (P3HT) (D5.5) have been synthesized via new, improved routes allowing better control of the polymerization and therefore the properties of the commercially and technologically important polymers to be investigated by neutron scattering. An investigation into the synthesis of polylactic acid (D5.8) from the lactic acid synthesized at ESS via lactide has been carried out that will enable the synthesis of designer biodegradable plastic polymers for neutrons scattering studies.

The observer partner ANSTO NDF has sent a representative to the workpackage and SINE2020 meetings, which has enabled many useful discussions about both synthesis and the operation of a user deuteration facility. ANSTO regularly performs deuterated synthesis for European users within their capacity and has an active collaboration with ESS on the synthesis of asymmetric, unsaturated phospholipids for neutron scattering experiments in membrane-binding antiobiotics (Yepuri et al. 2016).

The partnership has had several networking, dissemination and outreach activities of the platform (DEUNET) coordinated by ESS (D5.5), including visits to discuss collaborations, design of our own web-pages - [deuteration.net](http://deuteration.net/) (D5.1), a [user survey](https://docs.google.com/forms/d/e/1FAIpQLSfeUwzAfQiUgO-BktixBRFhRqw3-QP6WbhOjdUqX6MbB7i67A/viewform?c=0&w=1)  and organization of a joint user workshop in Oxford 15-17th May 2017 (<https://indico.esss.lu.se/event/756/)>that will form the basis of collecting the research community’s input into the scope and strategy for DEUNET (D5.6). WP5 disseminates our member’s capabilities, on-going work and new/events through regular blogs on our website and via Twitter, with links to other user sites including neutronsources.org, the SINE2020 project home page and more to come. DEUNET has been publicized by our members in presentations at conferences and seminars both in Europe and overseas.

The dissemination activities have led to interest from external groups wishing to obtain services from DEUNET, as well as to contribute specialty deuterated products such as ionic liquids, and our plans for a database of deuterated chemicals and their producers on deuteration.net have received very positive feedback from user groups.

## 1.1 Objectives

The objectives of WP5 are to carry out R&D activities to develop the basis for:

* **A cost-effective platform** to provide access to a broad range of materials and expertise
* **New synthetic** methods and products
* **Synthesis of innovative materials** in collaboration with partners
* **Coordinated service** for European neutron users

The tasks of WP5 are:

**Task 5.1. Chemical deuteration by catalytic H-D exchange and synthesis of surfactants** (STFC M6-30) 24 PM

* ***Provision of starting materials*** to the other partners to enable the synthesis of compounds currently unavailable, for example polymers and selectively labelled lipids (D5.1, 5.5)
* ***Expanding access*** to the existing compounds for ***European (non-UK) researchers*** (D5.7)
* Improved syntheses for the production of deuterated ***unsaturated fatty acids*** *(D5.7, D5.11)*
* ***Development of routes to novel bio-surfactants*** in collaboration with ILL and ESS (D5.11).

**Task 5.2. Extraction and purification of small molecules from deuterated cell cultures** (ILL M6-42) 36 PM

The ILL for Soft Condensed Matter (PSCM), will set up procedures for the separation, purification and analysis of small, deuterated biological molecules derived from cell cultures, with main task will be to develop methods for the ***separation and purification*** of:

* Main amphiphilic lipid components of biological membranes
* Raft forming molecules such as gangliosides and cholesterol
* Polysaccharides

This will include optimization of procedures for the production, partial labeling and purification; lipid separation; polysaccharide fractionation (D5.9) and analysis using tools available on the EPN campus (D5.10).

**Task 5.3. Synthesis of complex deuterated molecules** (ESS M6-42) 48 PM

The ESS node (DEULAB) will focus on the ***chemical synthesis of complex deuterated molecules*** based on both biological and non-biological starting materials, and on developing ***novel deuteration methods***. Some of the key compounds that are urgently required include:

* chiral, cyclic or unsaturated compounds
* compounds synthesized from natural components such as sugars and lipids
* monomers for polymer synthesis, polymer-modified lipids

The aim at ESS is to develop a range of methods for chemical reactions using deuterated materials, and ii) synthesize a selection of labelled compounds in collaboration with STFC, ILL and FZJ (D5.11). In particular, the ESS will develop the ***enzyme-catalysed synthesis*** of chiral deuterated compounds, such as L- and D-lactic acid (D5.4 from which polylactic acid polymers (biodegradable plastics) will be polymerised at FZJ (D5.8).

**Task 5.4. Polymer synthesis** (FZJ M6-30) 18 PM

The Jülich lab will develop ***new synthesis procedures*** for deuterated monomers and polymers of topical interest that cannot be obtained via commercial suppliers, including isoprene (D5.3), the basis of natural and synthetic rubbers, and polythiophenes, which are of high relevance for photovoltaic or LED applications. We will devise synthesis routes for thiophene-based labelled monomers in collaboration with ISIS (D5.5). In addition, FZJ will collaborate with ESS in the synthesis of polymer modification of lipids (PEGylated lipids) (D5.11) for biomedical applications and in the synthesis of biodegradable polymers based on polylactic acids (D5.8).

**Task 5.5. Network coordination and platform activities** (ESS M6-48) 12PM

The ESS node will coordinate the WPactivities and the establishment of the platform by:

* Organising the networking events, annual meetings and dissemination of results
* Organising a User workshop to define scope and strategy for DEUNET (D5.6)
* Setting up a collaboration network (neutron facilities, university laboratories, user organisations)
* Coordinating the establishment of the platform management, operation and access (D5.12)
* In collaboration with WP2 (Dissemination), setting up a webpage and user portal (D5.1)
* In collaboration with WP3 (e-learning), providing e-learning material about deuterium labelling
* In collaboration with WP4 (Industry), developing industry-specific outreach material

## 1.2 Explanation of the work carried per WP

### 1.2.1 Work Package 5 Chemical deuteration

**Task 5.1 (STFC) Chemical deuteration by catalytic H-D exchange and synthesis of surfactants**

The STFC Deuteration Facility receives two proposal calls annually for deuteration compounds from the UK and international ISIS neutron user community and also through ILL neutron proposal calls. The STFC Deuteration Facility regularly produces a large number of deuterated precursors through catalytic deuterium hydrogen exchange, including aliphatic hydrocarbons such as fatty acid, bromoalkanes, and organic ligands. A wide variety of compounds (also the corresponding protonated versions if not commercially available) has been synthesized, for example, in 2016 we received 83 requests, of which 63 were supported. For the work in WP5 (Tasks 5.1) Dr. Kun Ma was recruited on a fixed term at the end of October 2016 (M13) and has so far fully supported four proposal requests, including one from the ESS in Sweden. He has produced 11 deuterated surfactants in for user beam time and produced four deuterated fatty acid precusors.

The following projects have been support by the STFC Deuteration Facility through SINE2020 WP5 funding in period 1 (M1-18) are listed below.

1. A large quantity of perdeuterated ligands (>25gram in total) for Professor P Santini (Università di Parma, Italy), for a project on Spin dynamics of the Mn12 prototype nanomagnet unravelled by 4-dimensional inelastic neutron scattering (D5.2, D5.7). The experiment is part of an ILL PhD studentship pf Simon Ansbro and the national Italian FIRB project “New challenges in molecular nanomagnetism: from spin dynamics to quantum information processing”. The experiment was a success, and a publication is currently in preparation.
2. The routine deuterated CTAB, SDS, AOT and nonionic surfactants(C12E6) for non-UK users of ISIS (D5.7), including Andrew Jackson (ESS) for applying self-assembly in deep eutectic solvents to templated ionothermal synthesis; a joint PhD project of Adrian Sanchez-Fernandez with Professor Karen Edler (University of Bath).
3. 11 surfactants with different counterions for non-UK users (ESS) (D5.7) for beamtime on the SANS2D instrument, which was completed.
4. Synthesis of several non-routine compounds to non-UK users (D5.7), for example deuterated Triolein, and Tween 80 detergent for Tommy Nylander (Lund University).
5. Deuterated resorcinol, urea, benzyl alcohol and choline chloride Mr F D M del Monte, CSIC, Instituto de Ciencia de Materiales de Madrid, Spain (D5.7) for the study of deep eutectic solvent dilutions: nanometer size domains and molecular reorganization for an experiment on NIMROD that was successfully completed.
6. Deuterated trimethylglycine for Professor M Ricci (Università di Roma Tre, Italy) (D5.7) for an experiment on the SANDALS instrument scheduled in early 2017.
7. Method development and synthesis of 15g of deuterated quinolin-8-ol ligand for Prof.Caretta Stefano (Italy) (D5.7) and Richard Winpenny for ISIS experiments.
8. Deuterated chemicals for DEUNET partner laboratories (D5.2), such as deuterated pentadecanoic acid as precursor to methyl pentadecanoate to be used as internal GC standard in lipid analysis for Hanna Wacklin (ESS) and help with deuterated factty acids (Rachel Morrison, ILL).
9. The facility is currently optimising the unsaturated fatty acid synthesis (D5.7) and has produced intermediates.

The STFC Deuteration Facility is co-organizing the STFC Deuteration User meeting jointly with the DEUNET workshop at the Oxford Spires Hotel, 15-17 May 2017.

**Task 5.2 (ILL) Extraction and purification of small molecules from deuterated cell cultures (ILL)**

Work at ILL has started on preparing deuterated lipids derived from cell cultures. Initially we investigated the adaption of three acetobacter stains to perdeuterated media, however, the bacteria did not grow to high enough cell densities in either hydrogenated or deuterated media and therefore it was concluded that these strains are not useful for the large-scale production of lipids. Additionally, the fatty acid profile of the lipids produced by the bacteria was not as we had hoped for, as they did not produce any lipids with oleic acid chains – instead a different isomer (vaccinic acid – 7-cis octadecenoic acid) is produced by these bacteria.

We have therefore decided to return to the yeast strain that we have previously used for lipid extraction as we know this strain can successfully grow in deuterated media. We had previously found that while phospholipid class homeostasis was maintained, the composition of fatty acids was impacted with significantly higher C18:1 produced under deuterated conditions (De Ghellinck. *et al.* PLoS One, 9 (2014) 9). We are currently studying how the growth conditions of the yeast affects the type of lipids produced to enable more comparable hydrogenated and deuterated lipids to be produced. Preliminary results have indicated that both the growth temperature and carbon source have an effect.

We have also investigated methods for the separation of phospholipids. We were initially interested in the molecular species separation of the lipids, however, after reviewing the literature and discussing with several experts in the field we have since decided that this is not practical due to the difficulty and small amount of material which would be recovered. We are therefore going to focus on separation based on either chain length or saturation level which we believe will be easier to achieve. We also hope that by ensuring that both the hydrogenated and deuterated samples are equivalent then less separation would be required.

Rachel Morrison visited ESS to learn lipid extraction and separation techniques in February 2017. She also attended a course run by the James Hutton Institute on Fatty acids and lipids which gave a good overview of the field and an insight into different techniques which can be used for lipid analysis.

**Task 5.3 (ESS) Synthesis of complex deuterated molecules (ESS)**

***D5.4 Synthesis of L- and D-lactic acid***

ESS has made considerable progress within Task 5.3 towards completing deliverable D5.4., including:

1. Synthesis and characterisation of a deuterated precursor to the enzymatic reaction for producing lactic acid (sodium pyruvate-*d*3).1-2



Figure 1. Production of sodium pyruvate-*d*3 from pyruvic acid in D2O.2

1. Synthesis of the monomer acryloxysuccinimide for co-polymerisation with acrylamide.
2. Synthesis of the polymer to serve as support material for the enzymatic reaction (poly(acrylamide-co-*N*-acryloxysuccinimide) (PAN). The reported initiator AIBN is no longer available so an alternative catalyst (ACHN) was used, which required some changes in reaction conditions. The literature method3 and the method we employed are summarised in Figure 2.



Figure 2. (Left) Literature method for the synthesis of PAN with Mn = 6900 amu and 512 μmol active groups/gram;3 (right) the method employed in our laboratory.

The effects of changing catalyst and reaction temperature on the polymer product (molecular weight and number of active groups) are being investigated using UV-Visible spectroscopy and Dynamic Light Scattering (DLS) at Lund University, where we have arranged to access analytical equipment not available at ESS. We expect to complete the polymer characterisation and lactic acid synthesis by M24 (September 2017).

An automated flash chromatography system (Biotage Isolera) was procured for the purification of the compounds synthezised. In addition the materials (enzymes, co-factors, hydrogenous test-substrates and reaction vessels etc.) and equipment required for the immobilisation of the enzyme have been procured. The best system for monitoring the reaction progress by pH-STAT titration (Metrohm 907 Titrando) has been identified and will be procured shortly after the end of P1.

We have concluded that a deuterated reaction solvent is not required for the production of per-deuterated lactic acid from pyruvate, reducing the cost of the synthesis significantly. The only deuterated co-factor needed is the formate substrate of the NADH-regenerating enzyme formatted dehydrogenase). This is commercially available but can also be synthesized in-house to reduce the overall cost of lactic acid production.

We will also investigate the physical entrapment of enzymes in dialysis tubing as an alternative method of enzyme immobilisation.

We have begun investigation of the isolation and purification of the lactic acid produced by using a racemic, non-labelled sample of DL-lactic acid (85% solution in H2O). Continuous solvent extraction has been identified as a suitable method for the isolation of the deuterated enantiopure D- and L-lactic acid from the reaction mixture.

***D5.11 Synthesis of novel deuterated lipids and surfactants***

For this project, we have begun to set up the analytical equipment and processes to allow us to isolate molecules from cell cultures for further derivatisation by chemical or enzymatic synthesis including

1. Analysis of the composition of unlabelled cell cultures known to contain high-value lipid components;
2. Production of promising cell cultures under deuterated conditions at our collaborating laboratory at Lund University (Lund Protein Production Platform LP3) and analysis/ purification of components
3. Enzymatic conversion of biological lipid mixtures as a potential new route to complex deuterated lipids.

The possibilities of combining chemical synthesis with biological expression have attracted interest from several university collaborators at Lund, Umeå, Oslo and in Canada for deuterated cell components as mixtures, single molecular species, or synthetic derivatives such as for new collaborations that have recently submitted beamtime proposals to ISIS and ILL.

**Task 5.4 (FZJ)**

***D5.3 Synthesis of deuterated isoprene***

The Jülich Centre for Neutron Science as a part of the Forschungszentrum Jülich (FZJ) contributes to the project with its knowledge in the field soft matter. Especially, deuterium labeled polymers are of high importance for science and industry when they are applied in neutron science. The synthesis of such polymers is a complex process, usually starting from the synthesis of monomers. As deuterated monomers are in many cases not commercially available, they have to be synthesized in the laboratories. Moreover, the variety of potential starting materials is scarce and therefore limiting the number of potential chemical transformations. One goal of the project is to develop new synthetic routes to deuterated monomers, important in applications. Exemplarily, isoprene, a monomer for the synthesis of synthetic rubber is highly desired, but cannot be obtained in the required high purity. The synthesis of poly(3-hexylthiophen-2,5-diyl) (P3HT) is another example, a material which is relevant for light emitting diodes (LEDs) and organic solar cells, as well as poly(lactic acid) being relevant as a renewable plastic with high biocompatibility for medical applications.

Synthetic rubber, which is industrially used as a component in rubber tires, can be made of isoprene and is therefore of high relevance for industrial applications and science. To study the polymer (polyisoprene, PI) by neutron scattering, it is necessary to gain access to its deuterated form which is accomplished by the synthesis of deuterated isoprene monomer. There is an established route to this compound, however with certain disadvantages such as multiple steps, low selectivity including a high temperature elimination step. To avoid these circumstances, a new method leading to highly pure, deuterated isoprene was established (D5.3), and is shown in Figure 3.

The method starts from the selective α-oxidation of acetone-*d6* to the corresponding diketone typically using selenium dioxide as the oxidant. An access of acetone-*d6*, which can be recovered, is needed to avoid overoxidation to pyruvic acid. Ideally, the next step would be a two-fold Wittig reaction using a deuterated C1 Wittig reagent. Unfortunately, the diketone (methylglyoxal) strongly tends to oligomerisation. This problem was overcome by the use of protective group chemistry allowing a subsequent Wittig reaction after deprotection.

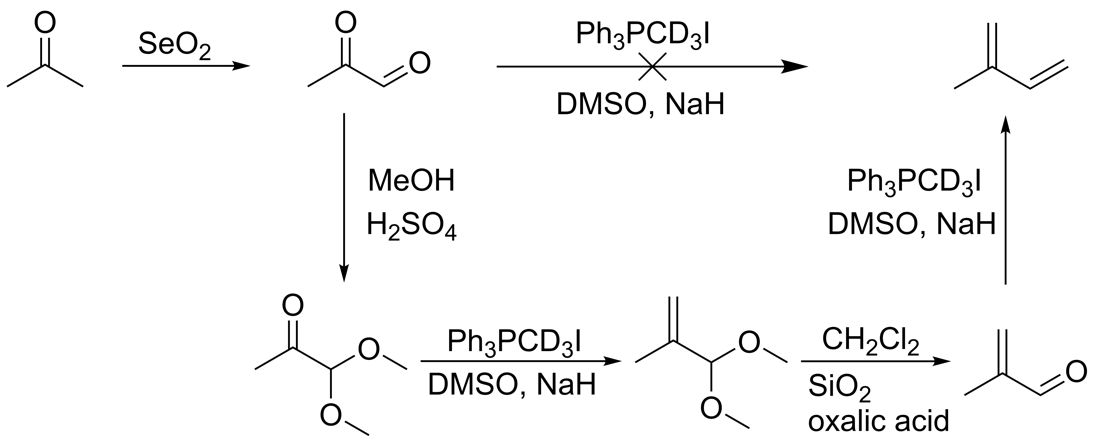


Figure 3: Overall reaction scheme of the synthesis of isoprene-*d8.*

***D5.5 Synthesis of P3HT***

Poly(3-hexylthiophen-2,5-diyl) (P3HT) is a conductive polymer which can be applied in organic light emitting devices (OLEDs) or organic solar cells and therefore relevant in the field of renewable energy (D5.5). For structural investigations, it is necessary to establish a route for high molecular weight block copolymers consisting of P3HT and polyethylene oxide (PEO). There are some synthetic routes described in literature which may lead to this material, however they were not tested for high molecular weight materials with narrow molecular weight distribution. Therefore, different approaches were screened in laboratory in order to get the best material possible. While the starting material (P3HT) could be synthesized with even better properties than claimed in literature, end-group functionalization, storage conditions and purification needed to be optimized by using special techniques. The synthesis of the block-copolymer (P3HT-b-PEO) was tested by several methods including polymerization from a macro P3HT starting material, Steglich esterification, Suzuki cross-coupling, and click chemistry. While most of the given reactions could not be applied successfully under these conditions, click chemistry showed best results. Azido functionalized PEO (PEO-N3) was used together with ethinyl-functionalized P3HT in a 1,3-dipolar copper catalyzed cycloaddition (Figure 4).

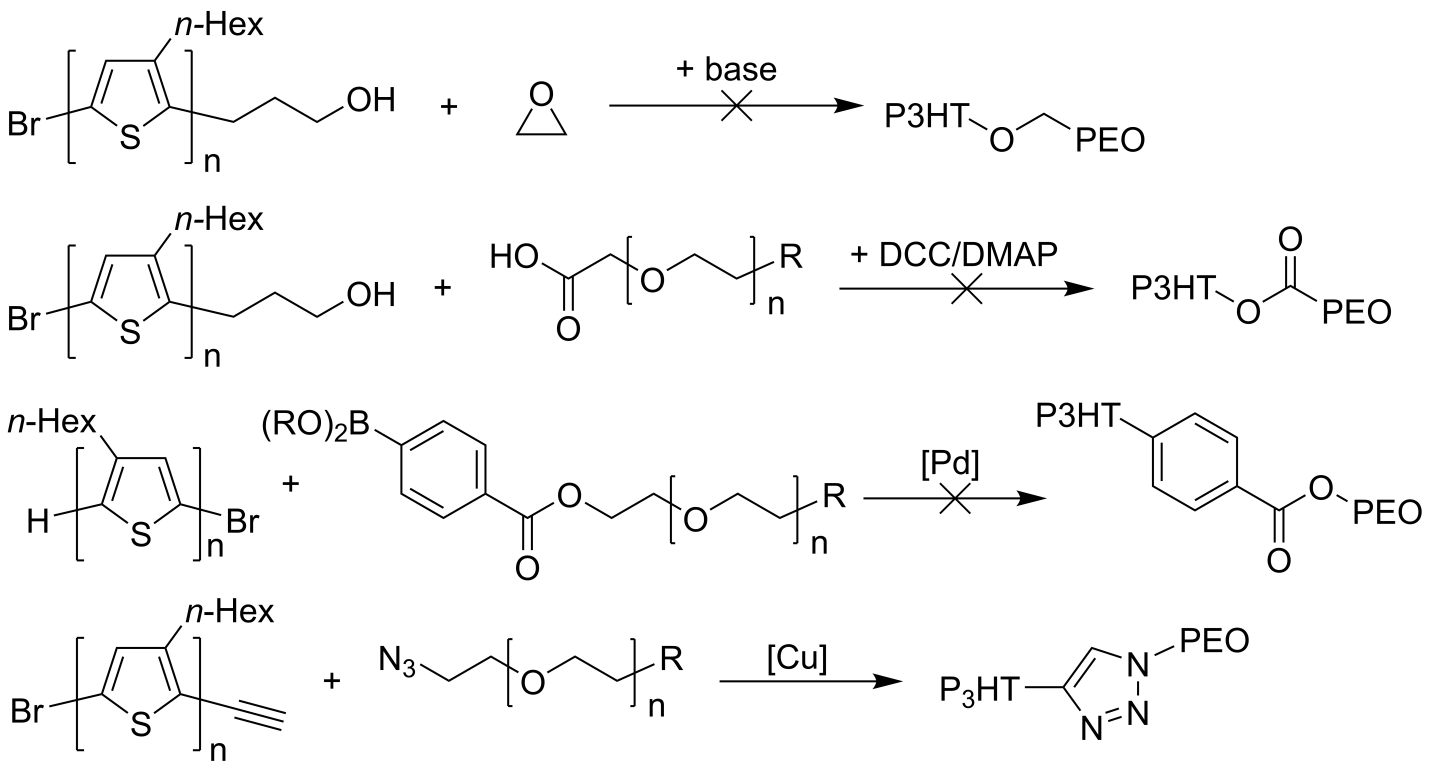


Figure 4: Synthetic approaches to P3HT-b-PEO.

***D5.8. Synthesis of deuterated polylactic acid***

Poly(lactic acid) (PLA) is relevant for renewable plastics and medical applications. The synthesis of its deuterated form for neutron scattering is planned in cooperation with ESS who will deliver the deuterated chiral lactic acid monomers which are produced by a biotechnological process (D5.11). For the production of PLA with narrow molecular weight distribution, it is necessary to use lactide – the dimeric condensation product of lactic acid. It was found that the lactide formation is usually carried out by an oligomerization-depolymerization process including loss of material and stereoinformation. Especially, the loss of material is highly undesired in the case of deuterated starting materials. Therefore, it was decided to follow a new attempt as reported by B. Sels (Science 2015, 349, pp 78-80). The authors use special zeolites in order to achieve lactide formation under relatively mild conditions. Another advantage would be the ability to recover unreacted material.

Task 5.5 (ESS)

The ESS has coordinated the networking and platform activities during period 1, which have included several dedicated Workpackage meetings (listed in Table 1), and a user workshop to be held in Oxford in May 2017. For disseminating the work done in the WP, we have set up pages for the workpackage on sine2020.org, and have started our own website for DEUNET (deuteration.net) to communicate to and connect with the user community (D5.1). To collect input for the scope and strategy of the future user platform DEUNET, we are carrying out an international user survey and have distributed it to the wider network via email, the website and twitter. The Deuteration.net website is being populated with information about the Network members, current projects and news/events (D5.1) and hosts regular blogs, updates and our event calendar. On advice from the user community we are in the process of setting up a deuterated chemicals data base that will enable users to search if the compounds they are interested in have been deuterated before and at which facility or commercial provider.

Table 1. Progress towards Deliverables:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Title (WP#)** | Sample – chemical deuteration WP5 | | | | |
| **Lead Beneficiary** | ESS | | | | |
| **Period** | M1- M18 (Oct 2015 – March 2017) | |  | |  |
| Task 5.1 (STFC) | Chemical deuteration by catalytic H-D exchange and synthesis of surfactants | | | | |
| Task 5.2 (ILL) | Extraction and purification of small molecules from deuterated cell cultures  - visit to ESS laboratory to learn lipid extraction and analysis techniques (D5.10)  -work ongoing on the optimising growth conditions of yeast to ensure H and D batches are comparable (D5.10)  -work ongoing in optimising lipid extraction, separation and analysis methods for the prepared deuterated samples (D5.11) | | | | |
| Task 5.3 (ESS) | Synthesis of complex deuterated molecules  - synthesis of deuterated precursor as substrate for enzymatic reaction; synthesis and analysis of immobilization matrix; enzyme immobilization work ongoing for production of deuterated lactic acid; student recruited from Lund University to work on this project; pH controller system procured for enzymatic reactions (D5.4)  - visit to FZJ on 1st December to discuss deuterated lactic acid requirements (D5.4/5.8)  - hosted visit by Rachel Morrison; trained Rachel to use the lipid extraction and analysis methods used at ESS (D5.10)  - work ongoing on the analysis and isolation of fatty acids from yeast cell cultures to produce novel deuterated lipids and surfactants (D5.11) | | | | |
| Task 5.4 (FZJ) | Polymer synthesis  - the synthesis of deuterated isoprene was completed (D5.3)  - synthesis of conducting polymer P3HT is being finalised (D5.5)  - hosted Hanna Wacklin and Anna Leung on 1st December to discuss deuterated poly(lactic acid) project (D5.4/5.8)  - route to lactide from lactic acid solution established (D5.4) | | | | |
| Task 5.5 (ESS) | Network coordination and platform activities  - WP5 meeting held at the ILL 18-19th January 2017.  - planned User Workshop for 15-17th May 2017 in Oxford; user survey created to accompany registration to gather data.  - user survey distributed to wider network via email, the website and twitter  - Deuteration.net website populated with information about the Network members, current projects and news/events; one person from each institution nominated as website editor (D5.1) | | | | |
| **Deviations** | D5.4 (Synthesis of L- and D-lactic acid): delay expected due to late recruitment of Anna Leung at ESS (M9). | | | | |
| **Corrective action** | A meeting between ESS and FZJ took place in December. To mitigate the expected delay in perdeuterated, enantiopure lactic acid delivery, FZJ have begun working on the polymerisation process from the unlabelled racemic analogue, in order to be ready to proceed once the precursor is synthesised. | | | | |
| **Deliverable** | **Due date (title)** | | | **Expected/ Achieved Date** | |
| D5.1 (ESS) | M9 (Webpage & user portal) | | | M9 completed | |
| D5.2 (STFC) | M12 (Synthesis precursors of surfactants) | | | M12 completed | |
| D5.3 (FZJ) | M15 (Novel route for isoprene synthesis) | | | M15 completed | |
| D5.4 (ESS) | M18 (Synthesis of L- and D-lactic acid) | | | M24 expected | |
| D5.5 (FZJ) | M20 (Synthesis of deuterium labelled poly…) | | | M20 expected | |
| D5.6 (ESS) | M24 (scientific impact & requirements…) | | | M24 expected | |
| D5.7 (STFC) | M28 (Synthesis of deut. surfactants…) | | | M28 expected | |
| D5.8 (FZJ) | M30 (Synthesis of deut labelled poly …) | | | M30 expected | |
| D5.9 (ILL) | M36 (Optimization of techniques…) | | | M36 expected | |
| D5.10 (ILL) | M42 (Physico-chemical charac…) | | | M42 expected | |
| D5.11 (ESS) | M42 (Synthesis of novel deuterated lipids…) | | | M42 expected | |
| D5.12 (ESS) | M48 (DEUNET platform) | | | M48 expected | |
| **Meetings/Conferences/Workshops attended on project resources** | | SINE2020 kick-off meeting 16 Oct 2015 Copenhagen  HW, GF attended STFC Deuteration Facility meeting 25-26 November 2016  WP5 kick-off meeting at ISIS 27 November 2015  HW visit ANSTO NDF March 2016  SINE2020 AGM Coimbra 7-8 September 2016  AR, JA attended MML Workshop, Hamburg, 2016  RM, AL, HW attended Smart Biomaterials workshop at Malmö University 25-27 October 2016.  AL, HW attended ASMSC Conference Materials of Tomorrow at Chalmers university 8-9 November 2016  AL/HW visit to FZJ 1 December 2016 to discuss/plan lactic acid project.  Internal meetings (participants,organising beneficiary etc), any external conferences attended?  Visit to FZJ by Hanna Wacklin and Anna Leung, 1st December 2016.  WP5 meeting at ILL, Grenoble, January 2017  RM visit to ESS 24 October 2016 and 30th January – 10th February 2017 | | | |
| **Publications** | | 1. N.R. Yepuri, T.A. Darwish,\* A.M. Krause-Heuer, A.E. Leung,R.Delhom, H.P. Wacklin,\* P.J. Holden, “The synthesis of perdeuterated 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC-d82) and the characterisation of its lipid bilayer membrane structure by neutron reflectometry“, ChemPlusChem 81 (2016) 315-321. DOI: 10.1002/cplu.201500452 2. Z. Fisher, A.Jackson, A.Kovalevsky, E.Oksanen, H.Wacklin\*, Biological Structures, in: Neutron Scattering – Applications in Chemistry, Materials Science and Biology, F.-A. Felix, L.P. David (Eds.) Experimental Methods in the Physical Sciences, vol. 49, Academic Press, 2017. ISBN: 9780128053249 | | | |
| **Presentations at conferences/seminars/meetings** | | HW, oral presentation, 2 November 2015 CoNEXT University of Copenhagen project annual meeting Birkerod, Denmark  HW, oral presentation, 25 November 2015 STCF Deuteration Facility workshop Oxford  HW, invited presentation 10-14 June 2016 SXNS Conference Stony Brook University/Brookhaven National Laboratory  HW, invited presentation 22 September 2016 Physical Chemistry Division Lipid Minisymposium, Lund University  HW, Invited presentation; AL, Poster, ASMSC Conference Chalmers University 8-10 November 2016.  HW presentation, iNEXT JRA (Membrane protein enabling technologies) kick-of meeting EMBL Hamburg 19 November 2016  HW Invited presentation, NSSM Oslo university 12-13 January 2017  Raba, A.; Allgaier, J.; Frielinghaus, H., Polythiophene Based Block Copolymers for Neutron Scattering. Poster, MML Workshop, Hamburg, 2016. | | | |

## 1.3 Impact

The deuteration activity of WP5 constitutes one of the key support services for present and future neutron sources and provides the basis for a broad range of science in soft condensed matter, biology and biomedicine using neutron scattering techniques.

The SINE2020 project aims to contribute to the readiness of the neutron scattering community for ESS and addresses the challenge of providing a common infrastructure across Europe that will facilitate the seamless integration of ESS and efficient use of ESS from day one. The DEUNET platform WP5 follows exactly this line by enabling the creation of a sustainable network of laboratories with the joint capabilities to produce a wide range of deuterated compounds. DEUNET prepares the experimental ground for future experiments by developing new synthetic capabilities, sharing competence and resources, necessary for scientific results with increasing high societal impact. This is particularly important in areas requiring either highly specialised materials (e.g medicine) or multidisciplinary approaches (e.g. advanced nanomaterials) for neutron scattering.

The DEUNET platform will provide a network and a web-based interface for both neutron scattering experts and new users from industry and academic partner institutions to meet experts in deuteration laboratories to familiarize them with the possibilities offered by different deuteration techniques and to develop new applications of neutron scattering enabled by deuteration.

Key Performance Indicators:

Number of industrial researchers attending user workshops and extended RTD meetings – non yet

Number of user access and samples provided – 26 samples for 8 user groups

Number of publications - 2

Number of participants in user workshops – none yet – workshop organized for 60 in M20

Presentation of the DEUNET platform at international conferences 8

# 2. Update of the plan for exploitation and dissemination of result (if applicable)

Include in this section whether the plan for exploitation and dissemination of results as described in the DoA needs to be updated and give details.

# 3. Update of the data management plan (if applicable)

Include in this section whether the data management plan as described in the DoA needs to be updated and give details.

# 4. Follow-up of recommendations and comments from previous review(s) (if applicable)

Include in this section the list of recommendations and comments from previous reviews and give information on how they have been followed up.

# 5. Deviations from Annex 1 and Annex 2 (if applicable)

## 5.1 Tasks

*Include explanations for tasks not fully implemented, critical objectives not fully achieved and/or not being on schedule. Explain also the impact on other tasks on the available resources and the planning*.

D5.4. delayed from M18 to M24 due to the relatively late recruitment of post doc at ESS (M9) and the need to set up the lab and procure equipment. Due to this, the FZJ partner has started working on the on the polymerisation process ahead of time, using the unlabelled racemic analogue, in order to be ready to proceed once the precursor is synthesised.

## 5.2 Use of resources

The resources have been used as planned taking into consideration the starting date of the new recruits at each facility.

### *5.2.1 Unforeseen subcontracting (if applicable)*

### *5.2.2 Unforeseen use of in kind contribution from third party against payment or free of charges (if applicable)*

**References**

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1. Beneficiaries that have received Union funding, and that plan to exploit the results generated with such funding primarily in third countries not associated with Horizon 2020, should indicate how the Union funding will benefit Europe's overall competitiveness (reciprocity principle), as set out in the grant agreement. [↑](#footnote-ref-1)