MINUTES 17/09/15
Lucideon, Trent, UK – Hosting partner

ATTENDEES

Name	Organisation
Phil Jackson (PJ)	Lucideon Limited
Stuart Maclachlan (SM)	Lucideon Limited (Part of meeting)
Jean-Christophe Maurin (JM)	University Claude Bernard, Lyon
Christelle Goutaudier (CG)	University Claude Bernard, Lyon
Pierre Colon (PC)	University of Paris
Vinvenzo Farano	ESR
Federico Lizzi	ESR
Delihta Fernando	ESR

EXCUSED / APOLOGIES:
Brigitte Grosgogeat (BG) – University Claude Bernard, Lyon
Kerstin Gritsch (KG) – University Claude Bernard, Lyon

In addition, PJ had decided not to ask Mark Cresswell (MCr), Ben McCarthy (BM) and Ian Campbell (IC) to attend the meeting. This is because they currently interacted with the ESRs on an almost daily basis. As such, the ESRs were constantly receiving feedback, ideas from these supervisors. Also PJ had decided to invite James Kent and KTN Ltd to annual meetings only.

OVERVIEW

Each ESR in turn presented their work to date as well as their targets ahead of their return to Lyon later this year. After each presentation the supervisors were able to ask questions which helped the ESRs firm up on their work plans.

PC in particular helped the ESRs focus on the challenges associated with their target end product.

SUMMARY OF ISSUES DISCUSSED

1) DELIHTA FERNANDO (DF)

DF reminded the meeting that her aim was to form insoluble Si-P-Ca-Na sol-gels with a surface area ~350 m2g-1. Final materials should ideally be 100% amorphous and white (cleared or organic residues)

White powders can only be obtained by avoiding the use of Na or by having no surfactant present. Na has the potential to lower the melting point of the sol-gel materials. By having no sacrificial organic surfactants, it becomes impossibly to deliver the target porosity.

There was discussion concerning what happens as the formed gel is heated / sintered. The 700 °C required to dissociate nitrate from starting materials is probably too high to avoid melting of the powder. DF now favoured use of acetates for Na, since 400C was sufficient for organic burn-out (however, the high pH generated speeds up sol-gel reactions so use of acetic acid is needed to control reactions). PJ suggested Dynamic XRD could be invaluable in defining the % amorphous material present before and during the sintering ramp-up phase. CG indicated that Raman spectroscopy could perform a similar job.

DF had looked into solvent extraction as an alternative method to sintering for organic removal.

DF data showed a strong tendency for silica crystalline phases in the final sintered product. PJ and PC encouraged Delihta to calculate the composition for the amorphous phase once the composition and wt% of crystalline phases had been subtracted out. A review of Ca-P-Na-Si phase diagrams may show how easily the amorphous phase melts upon heating to potentially block porosity.

DF will carry out a Factorial Experimental Design (FED) study before returning to Lyon in which sintered T, Ca:Na ratio and pH are varied. Inclusion of 2 centre points would be good. This means 8-10 experiments.

PC feedback on end product (i.e. primer layer containing fine sol-gel powder):

- The presence of crystalline material in powders may not be a problem from a bioactivity viewpoint
- Primers tend to be acidic (methacrylic acid) and this might lead to incompatibility with the sol-gel powders.
- What do we want the mesoporous bioglass to do? Stimulate cell-induced re-mineralisation in dentine areas near the pulp? Anti-bacterial properties? DF indicated that the sol-gel porosity should provide a greater surface area for bonding to the organic phase.
- The primer, as applied, could be based on ethanolic or acetone sol-gel powder suspensions.

2) FEDERICO LIZZI (FL)

FL outlined his plan to generate phase-separated glasses in which B3+, K+ and Ca2+ leach out of the weaker glass phase to help re-mineralisation, reduce sensitivity (K+) etc.

FL had worked with PJ to create a FED plan using Stat-Ease software in which the effect of varying the relative levels of 3 oxides on degree of phase separation would be assessed. All compositions had been melted and heat treated to induce phase separation. Visually it appears that some samples had phase separated more than others.

FL now planned to analyse the samples (XRD to check for crystals rather than two glass phases, milling and leaching to check for final porosity).

FL needs to work on defining a standard leaching protocol: mineral vs organic acid? Which organic acid chemistry? etc. Analysis after different leaching times would be based on ICP (liquid phase) and BET (remaining porous solid).

CG asked FL not to forget the role of powder particle size in dissolution behaviour. FL responded that he intended to mill all FED samples to a fixed size of <50um

PC reminded the meeting:

- Glass powders in GIC must offer both optical and mechanical properties
- The composition of the glass is absolutely critical to setting time, quality of set material in GICs
- It would be useful if FL could assess his glass powders in a GIC composition as soon as possible. FL should do literature work to understand how GIC properties can be measured and what represents good performance.

The use of DSC as an analytical tool for “as-melted” and “phase-separated” glass was encouraged. DSC should perhaps be applied to the best compositions (not all compositions).

CG suggested XRD analysis of one or 2 “as melted” glasses should be included as part of testing (as well as full XRD analysis of “phase separated” glasses to check that the milky appearance is not due to crystal formation).

A further suggestion was to melt Si-K-B formulations (i.e. no Ca2+ or Al3+ present) to act as a baseline powder in GIC work. FL to consider appropriate Si-K-B formulations and then mix /melt.

Other points raised on discussions concerning FL studies were:

- Note that species can deposit on phase separated glass powder surfaces following leaching
- Are there alternatives to Al3+ in GICs (concern over health and safety). For example what about other M3+ species like Cerium? Would 4+ ions deliver even better set properties?
- There are essentially three phase separated glass powder species that can be added in GICs based on FL work.....
- CG asked whether molten glass could be spray atomised to spheres like metal alloys? If so, would this generate a useful powder material for GIC? PJ thought that attaining small particles sizes via spray atomisation might be challenging.

FL has set 23rd October as his target date for returning to Lyon. This is based on making and milling all FED glasses (plus XRD analysis) at Lucideon. Leaching and analysis of remaining glass phases would be carried out at Lyon.

3) VINCENZO

VF outlined his P-Ca-Na sol-gel work, stating that 53% P2O5 represented a good compromise between slow solubility (>55%) and excessive solubility (<50%). In terms of altering compositions, changes to the Ca/Na ratio will be an initial focus (with increased CaO levels reducing dissolution.

In all work, alkoxides are being used as the precursor for all 3 elements.

Issues faced so far include the observation that 250 C heating does not cause complete carbon removal. Also there are instances of high crystallinity in the product and poor yield after filtration.

Since methoxyethanol cannot be boiled off (health and safety) any heating is typically performed in a closed system.

Success has been achieved by using a reflux condenser. Eventually the whole mass of starting materials gel (with ~100% yield) and a subsequent 250 C heat treatment gives a white colour (successful burn-out of organics?). XRD and XRF results are awaited.

VF also wants to introduce SrO into the sol-gels formed.

There was some discussion on XRD data for P-Ca-Na sol-gels containing Sr. Often ~80% amorphous phase was created along with 10% each of Sr and Na nitrates. The Sr nitrate can be explained as unreacted starting material. However, with no other obvious source of nitrate available, there must be some reaction with the Na alkoxide to form Na nitrate. VF was encouraged to look closely at the XRD data and take note of all vol%, wt% and mole values to check (a) whether the levels of nitrate seen in XRD data can have originated from the amount of Sr nitrate starting material and (b) the composition for the 80% amorphous phase (how close is it to the target sol-gel composition?)

It was agreed that Sr acetate would be worth investigating as an alternative starting material for sol-gels.

VF estimated that he would be involved with sol-gel synthesis until mid-November. This would include scale-up work if the XRD, XRF data alluded to above was encouraging. BET, ICP analysis should follow (until mid-December) with anti-bacterial training at Lyon then taking place until mid-January 2016.

GENERAL ISSUES:

There was some confusion as to the function of the supervisory board. Also Naima Hamacha appeared to suggest meetings in both March and April 2016. It was not clear what the objectives of each meeting were. PJ to check with Naima.

PC, CG, PJ and SM all suggested potential seminars, exhibitions, workshops. Aside from those mentioned in PJ slides, examples included:

- ConsEuro, 14th-16th May in Bologna, Italy
- A phase separation glass conference in march 2016 (CG suggestion)
- EDF Congress, 24th -28th Nov 2015 in Paris
- International Dental show in Germany, March 2016

SM felt that a sabbatical to a centre for process scale-up at Wilton in north-east England might be a useful training for the ESRs.

The following courses are available to ESRs in Lyon..... French Language School (start Jan ’16); Academic writing course; a course on industrial processing (given in French).

The meeting felt they needed guidance on the Biodensol web-site. Potentially a webinar-based training session to show the different areas and how useful information could be added to password protected areas? We need some clarification on whether DropBox and / or the web-site should be used to share documents.

A date for the next meeting (to be held in Lyon in April 2016) was not set. It was decided that Brigitte should be consulted.

ACTIONS (scientific)

1. CG to find out if Dynamic XRD is available at University of Lyon. If not, CG to work with Delihta on Raman analysis of sol-gel samples.
2. DF to calculate composition of amorphous phase in instances where crystalline phases are present ..... then look at literature phase diagrams to see if sintering in the 400-700 C range is likely to melt the amorphous compositions calculated? ... or do crystalline phases form direct from initial amorphous sol-gel materials at very low temperatures (Dynamic XRD, Raman will prove)
3. DF to arrange a Skype call between Lucideon and University of Lyon staff after completion of her FED experiments and associated XRD, BET analysis etc. This will lead to further decisions being made on DF work in Lyon.
4. ESRs to consider Focus Ion Beam Microscopy (FIM) to image porous particles
5. ESRs to work with PJ on securing XRD awareness training (especially how % amorphous vs crystalline phases are determined) with XRD expert Giles Blundred.
6. PJ to see MS about the following training at Lucideon
   - FED (re-run of two day course PJ had attended)
   - Intellectual property (re-run of recent ½ day course run by Lucideon's patent attorneys)
7. PJ to organise business cards for the ESRs.
8. PC, CG, SM to supply details for the events they mentioned in the meeting (see above) .....
9. ..... PJ to create a table of potential seminars / events for ESRs to consider. ESRs to then update the table as they make decisions on attending.
10. SM to ask Robert Quarshie (Knowledge Transfer Network Ltd) about options for spending time at the Wilton centre.

ACTIONS (management)

11. PJ to ask Naima about the supervisory board and how it differs from the meetings held to check ESR technical progress
12. PJ to work with Brigitte Grosgogeat on deciding a date for the April 2016 meeting in Lyon