Graduate Research Training Program

Pharmacometrics & Computational Disease Modelling

at the Martin-Luther-Universitaet Halle-Wittenberg and the Freie Universitaet Berlin, Germany

Launch of the Graduate Research Training (GRT) Program 'Pharmacometrics & Computational Disease Modelling' in Germany

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(2) Hamilton Institute/NUIM, Ireland & MATHEON/Freie Universitaet Berlin, Germany;

(3) Elected representatives from Industry Partners in the Extended Steering Board

Background of Initiative

- Pharmacometrics & computational diseae modelling *(PM & CDM)* are *highly interdisciplinary disciplines* involving the understanding of the underlying biological/pharmacological/pharmaceutical mechanisms and the formal mathematical/statistical methods and gaining *increasing attraction* and are becoming internationally established.

- In Germany, qualifying in PM & CDM is *difficult to master for a PhD student,* due to its interdisciplinary character and the lack of a curriculum for graduate students at universities.

- At the same time, there is a *high demand for thoroughly trained young scientists* with sophisticated knowledge and expertise in these fields[1,2] that can boost the disciplines in academia as well as in research-driven pharmaceutical companies.

Aims

A novel initiative in Germany has been launched as a *University program* to

- Thoroughly train junior scientists in PM & CDM
- Advance theory and applications in PM & CDM
- Implement PM & CDM in the academic environment
- Promote PM & CDM within and outside academia and bridge the gap between academia and industry

Key Characteristics of Realisation

- **Thematic orientation in a promising, rapidly expanding area**
- **Trans-disciplinary approach (Pharmacy & Mathematics)**
- **Close partnership with Pharma Industry (``Public-Private-Partnership'')**

Academic and Industry Partners

Academic Partners:

- *Charlotte Kloft* (MLU Halle-Wittenberg), *Wilhelm Huisinga* (Hamilton Institute/NUIM, MATHEON/FU Berlin)

Industry Partners

- *Abbott, Bayer Schering Pharma, Bayer Technology Services, Boehringer Ingelheim, Merck, Sanofi-Aventis*

Steering Board: responsible for conceptual, structural & financial aspects.
Extended Steering Board: responsible for main strategic intent within the scope and aims of GRT Program & admission process

> Steering Board
>
> Extended Steering Board (2+2)

Research training curriculum

- Academic *(A) modules* of 30 h en bloc (1 week), subdivided into i) theoretical concepts & methods (2/3) and ii) practical hands-on exercises (1/3)

- Industry *(I) modules* of variable duration

A-Module characteristics

- Introduction to the field: framework, theoretical concepts and methodology
- Conveying method and software expertise in PM & CDM
- Illustrative examples of relevance to drug discovery & development and use

I-Module characteristics

- Insight into the mission and tasks of pharmaceutical companies
- Learn about the value chain of drug discovery and development
- Learn about fields of application of modelling approaches

Semester	Research training modules			Research
1st	**A-module 1:** PK/PD modelling (March 2008)	**A-module 2:** PBPK modelling (April 2008)	**I-module 1:** Drug discovery/ development (1 week)	**Continuous work in research project for PhD thesis**
2nd	**A-module 3:** Population analysis	**A-module 4:** Systems Biology	**I-module 2:** Internship (1+ week)	
3rd	**A-module 5:** Stats & data analysis			
4th		**A-module 7:** Pharmacology[a]		
5th	**A-module 6:** Biometrics & Trial design/simulation			
6th				

(a) during 1st–4th semester at host university

A1 module: Introduction to PK/PD modelling

(Non)clinical PK, (Non)clinical PD, PK/PD models, Laplace transformation, Nonlinear regression, Curve-fitting algorithms, Numerical integration of ODE, Model diagnostics, In silico simulations (Bootstrap, Monte Carlo simulation)
Hands-on exercises

A2 module: Introduction to PBPK modelling

From empirical to physiological models, Whole body PBPK models, Ionization and protein binding, A priori prediction of tissue distribution, Models of GI absorption, Hepatic metabolism and renal excretion, Drug-drug interactions, Variability
Hands-on exercises

Setting a frame for the Program

Important questions had to be agreed on between all partners:

- *How to deal with Results / IP and publications*
- *Role and involvement of Industry Partners*
- *Research topics: generic vs. specific*
- *Location of PhD Students*

Host Universities

The GRT Program is hosted at the Host Universities, and as such embedded into the respective departments.

- Department of Clinical Pharmacy, Institute of Pharmacy, MLU
- Department of Mathematics & Computer Science and Bioinformatics, FUB

Research and Training

The interdisciplinary PhD program is designed as a 3-year program including

- a research project on generic topics of high interest in PM & CDM
- a structured research training curriculum of advanced academic & industrial modules
- mentoring by an Industry Partner

Attractiveness to PhD students

The new program offers its GRT students a unique opportunity to experience research in the area of drug development and optimising drug therapy jointly within academia and industry along with a competitive research fellowship.

Application process

- Exclusively online via *www.pharmacometrics.de* → application
- Selection based on application, letters of recommendation, number of scholarships (max. 12 per year), and personal interviews

Perspectives

- The GRT program will continuously be monitored to ensure a successful realisation: Evaluation by all partners mid/end 2009
- Integration and expansion of international Faculty Network
- Exchange with other initiatives/colleagues and their experience is sought and highly welcome

Contact: Cornelia Boehnstedt (coordinator), **contact@pharmacometrics.de**

References: [1]Holford, Karlsson, Clin Pharmacol Ther, 82:103, 2007 [2]Powell, Gobburu, Clin Pharmacol Ther, 82:97, 2007

Pharmacometrics & Computational Disease Modelling;   http:// www.pharmacometrics.de