Graduate Research Training Program

Pharmacometrics PharMetrX & Computational Disease Modelling

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

INNOVATIVE GRADUATE RESEARCH TRAINING PROGRAM
'*PHARMACOMETRICS & COMPUTATIONAL DISEASE MODELLING*'

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(1) Martin–Luther–Universitaet Halle–Wittenberg, Dept Clinical Pharmacy, Halle, Germany;
(2) Hamilton Institute/NUIM, Ireland & MATHEON/Freie Universitaet Berlin, Germany;
(3) Elected representatives from Industry Partners in the Extended Steering Board

data collection > > > modelling > > > analysis > > > in silico prediction > > > trial design and opti-misation of drug therapy > > > data collection

Background of Initiative

- Pharmacometrics & computational disease 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 lack of a curriculum 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, a*dvance 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 as ``Public–Private–Partnership''

Academic and Industry Partners

Academic Partners/Chairs
- 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

Extended Steering Board (2+2)

Steering Board: responsible for conceptual, structural & financial aspects.

Extended Steering Board: responsible for main strategic intent & admission process

Setting a frame for the Program
Important questions had to be agreed on between all:
- 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 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 fields of application of modelling approaches
Learn about the value chain of drug discovery and development
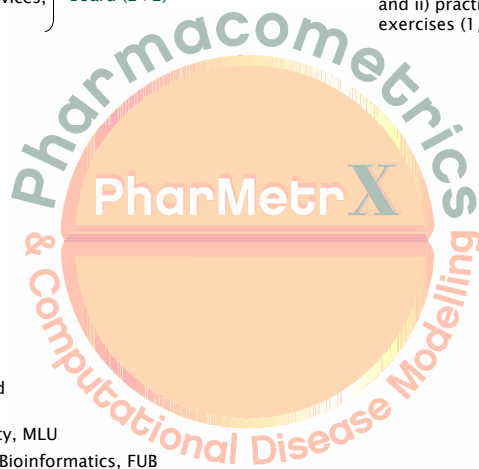
Semester	Research training modules			Research
1st	A-module 1: PK/PD modelling (March 2008)	A-module 2: PBPK modelling (April 2008)	I-module 1: Drug discovery/ development (1 week)	Conti-nuous work in research project for PhD thesis
2nd	A-module 3: Population analysis	A-module 4: Systems Biology	I-module 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			

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

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/protein binding, A priori prediction of tissue distribution, GI absorption models, Hepatic metabolism/renal excretion, Drug-drug interactions, Variability
- Hands–on exercises

Application process

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

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 of € 1400.– + allowance)

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