

MOLECULAR DATA FOR INFECTIOUS DISEASES (MID)

(Course leader: Gert Van der Auwera)

MID is a course for molecular biologists on the implementation of molecular techniques, and more specifically the use of molecular data in tropical low-resource settings. In MID, molecular techniques and data are discussed in the context of clinical and epidemiological field studies on infectious diseases.

Pathogen and vector identity, dynamics, and transmission often form an integral part of such studies. These phenomena can be documented using DNA and RNA techniques. Despite rapid advancements in molecular methods, their implementation in low-resource environments often remains cumbersome due to logistic, financial, and human resource constraints. MID focusses on the selection and analysis of appropriate assays and their implementation in a particular research setting.

Course participants work in small groups to critically discuss peer-reviewed papers and to develop their own protocol and implementation plan.

NUMBER OF CREDITS

5 ECTS

MODE OF STUDY

This course (component) is organized :

- Distance learning (Online)
- Face-to-face (Antwerpen)

LEARNING OBJECTIVES

At the end of the course the student should be able to:

- plan accurate molecular data collection and analysis in a resource-limited context, while ensuring sufficient samples for obtaining meaningful results.
- infer research conclusions given the limitations of the proposed methods and sample.
- select the appropriate molecular methods for detection or characterization of an aetiological agent or vector, in order to answer specific questions in a clinical or epidemiological research context, and given the restrictions in terms of infrastructure, logistics, personnel, ethics, and budget.
- present the selected methodology and implementation plan orally and in writing, with clear argumentation of relevance and feasibility.
- work actively in a team to design and present the implementation strategy.
- explain clinical and epidemiological study designs and concepts.

CONTENT

The course is taught in English and offered in a blended format:

- E-learning: students receive an introduction on basic concepts and skills, in order to level all participants with relation to background knowledge and software proficiency before the face-to-face part.
- Face-to-face: students are coached to develop and present a study protocol and implementation plan for using molecular data in support of a clinical or epidemiological study in a low-resource setting. At the end of the course they need to understand study designs in clinical and epidemiological research, and be aware of ethics, biosafety, and quality.

E-learning programme

- Pathogen models: HIV, Ebola, *Mycobacterium*, *Salmonella*, *Plasmodium*, *Schistosoma*, *Leishmania*, *Trypanosoma*
- Molecular methods: fragment-based methods, DNA sequencing, nucleic acid isolation, PCR
- Software: MEGA, R, BLAST, Structure, Splitstree, spreadsheet, database

Face-to-face programme

- Group assignment: develop, present, and peer evaluate a study protocol for gathering and analysing molecular data in a multi-disciplinary team
- Critical analysis of molecular methods and data analysis based on papers published in peer-reviewed journals
- Study context: epidemiology, clinical studies
- Phylodynamics: bacteria, viruses
- Population dynamics: protozoa
- Molecular diagnostics: bacteria, viruses, protozoa
- Study preparation: ethics, Good Laboratory Practice (GLP), logistics
- Molecular data handling: protocol writing, data collection tools, database tools, quality control

TEACHING AND LEARNING METHODS

E-learning programme

In this part the student is offered a combination of online tutorials, manuals, and videos to acquire the necessary background knowledge. The student studies the provided material and answers a short assessment after studying each individual topic. For the software proficiency, the student installs each freeware package on the laptop he will bring to Antwerp, and familiarizes himself with a given list of functionalities. The student uploads software-generated output to the online learning platform Moodle for evaluation. All students passing the online tests are invited for the face-to-face programme.

Face-to-face programme

The face-to-face part is built around a central assignment that is developed in groups of 2 to 4 students. Each group submits a written study protocol for gathering and analysing molecular data in a given context, and presents the selected methods orally to fellow-students, faculty, and invited ITM scientists at the end of the course. During the course, students integrate the acquired knowledge into their protocol. The protocol contains several chapters, each related to a particular course session. Besides this assignment, students will be instructed on basic epidemiological and clinical study designs and concepts, on which a written test is taken.

The learning process is as follows:

- At the start of the course, students select one of the studies suggested by the course faculty, and form the groups after consultation with the faculty, and taking into account interest and complementarity. Students can also suggest a topic of their own interest, given it fits the course scope. An appropriate topic studies a pathogen aspect related to the clinic or epidemiology of an infectious disease in a specific low-resource setting, using molecular data. These molecular data relate to the use of DNA or RNA to characterize or detect pathogens. Serological methods are not covered by the course. Students form small groups to develop each protocol. Examples of suited (hypothetical) topics are:
 1. Between 2014 and 2016, the number of sepsis patients infected by bacteria that show extended-spectrum beta-lactamase (ESBL) production increased in Loja province, Ecuador. Different classes of genes can cause this resistance phenotype. Seven hospitals in the region participate to an epidemiological study to determine the prevalence of the different ESBL-genes per bacterial species. Design a protocol to gather and analyse ESBL gene sequence data from all collected samples.
 2. Early 2017, an outbreak of visceral leishmaniasis has been discovered in elevated slopes (altitude above 500 m) in western Nepal. For studying the transmission cycle, clinical and environmental samples are gathered from vectors, and symptomatic as well as asymptomatic humans and animals. Design a protocol to molecularly detect and characterize *Leishmania* parasites in all these samples, and to determine the collected sandfly species.
 3. In Burkina Faso, a clinical study compares the efficacy of chloroquine with artemether-lumefantrine in a two-armed trial. The study is conducted in five villages for each arm, in the Nanoro region. When a patient is diagnosed with malaria after treatment, it is important to recognize a new infection from recrudescence. In order to know whether the number of new infections versus recrudescences differs between the two arms, the *Plasmodium* parasites must be characterized and compared on a molecular basis. Design a protocol to achieve this.
- During the interactive lectures and practical sessions, students gradually use the acquired knowledge to critically interpret literature and other publicly available information, with the aim to select appropriate molecular techniques. Some sessions are followed by a written test.
- After selection of the molecular methods, each group develops an implementation plan accompanied by protocols, validations, a database, worksheets, and budget for preparing experiments and reporting results.
- The protocols and accompanying files are peer-reviewed by fellow-students, and presented orally to all students and faculty for plenary discussion.
- Based on this feedback, the implementation plan and protocols are further improved.
- Finally, each group submits the written documents for evaluation by the faculty, and presents the methods orally, with supporting slides, to faculty, fellow-students and invited ITM scientists. This presentation is followed by a discussion, moderated by a peer jury composed of fellow-students who have read the presented assignment.

ASSESSMENT

The overall score of each student is graded with a maximum of 100 points (60 individual and 40 group score). To obtain the credit certificate, a minimum of 50/100 points is required.

- **E-learning:** The online assessments represent **10/60 points in the individual score**.
- **Written tests: 30/60 points individual score.** Students complete a written test on several course sections (diagnostics, phylogenetics, population dynamics, study designs, concepts in epidemiology), which are scored on a total of 30 points.
- **Written protocol: 30/40 points in group score.** The developed protocol (method, implementation plan and accompanying documents) is evaluated by the course faculty and other ITM scientists, both on content and clarity. Different pre-defined sections will be scored: method selection,

implementation plan, quality and appropriateness of supporting documents (SOPs, database, data collection forms, ...). The score obtained on this evaluation is valid for each student in the group.

- **Peer assessment: 10/60 points individual score.** The contribution of each group member in different sections of the assignment is evaluated by the other group members. Students who contributed above average are graded higher than those who provided less input.
- **Coach assessment: 10/60 points individual score.** As the coaches work closely with their groups, they have a good overview of the progress made by individual group members. Each coach grades all the students in the group accordingly.
- **Oral presentation: 10/40 points group score.** Each group presents the protocol with slides in 15 min, followed by 15 min of discussion. Three ITM scientists will grade the presentation and answers to the discussions. The total on 10 points is added to the score of each group member.

In case a student fails, he/she will get the opportunity to hand in an improved written protocol, and to present this in a tele-conference, within one month after the end of the course. The tests cannot be retaken.

ADMISSION REQUIREMENTS

- A primary university degree (min. 4 years) equivalent to 240 ECTS (in the European Union called a master's degree) in Life Sciences.
- Proficiency in English. If your mother tongue is English or you did university studies in English, you are exempted of a language certificate. If this is not the case: an officially recognised language proficiency certificate is mandatory. Required level for English: TOEFL paper-based 580, computer-based 230, Internet-based 88 or IELTS 6.5 (ITM Toefl Code is 7727).
- At least two years of professional experience.
- To participate in the online part, access to a computer and internet connection is required. Ideally, students use the same laptop as the one used during the face-to-face part, as this allows pre-installing the required software.
- Minimum computer skills: create, edit and save documents in a word processing (e.g. MSWord), spreadsheet (e.g. MS Excel) and presentation (e.g. MS PowerPoint) program; receive, open and send e-mails with attachments; use an internet browser and conduct searches; download and upload documents; install software.
- Relevant experience in molecular biology in one or several of the following techniques: conventional PCR (gel-based) / real-time PCR / quantitative PCR / DNA extraction / RNA extraction / sanger (dideoxy) sequence analysis / next-generation sequence analysis / molecular cloning / fragment analysis / primer and probe development / phylogenomics. At least in one of these techniques, the student must be able to develop an assay or analysis pipeline given a specific research question.
- For the face-to-face part, students must have passed the e-learning assessments (min. 50%).

Note: you will need to provide the following documents during the online application procedure:

Obligatory: a motivation letter, your CV, a certified copy of all your university diplomas and all your grade sheets, a digital passport size photograph, a copy of your passport, contact details of 2 references (plus they have to send in a reference letter) and the 'molecular biology experience form'

Optional: a list of publications, an official language certificate (TOEFL or IELTS) if your university studies were not done in English, the 'DGD scholarship application form' if you meet the DGD requirements, the 'Funding of studies' form if you are not eligible for a DGD scholarship.

(Forms are presented in the second stage of the application procedure.)

SELECTION CRITERIA

- Prior education showing background in molecular biology
- Relevance of work experience
- Motivation
- Bench experience in molecular biology, ranked as follows:
 1. **SOP execution:** student has carried out a written standard operating procedure
 2. **Trouble shooting:** student has dealt with unexpected outcomes, and solved them adequately
 3. **SOP writing:** given a protocol from literature, student has transformed it into an SOP, and carried out the experiment
 4. **Method development:** given a specific research question, student has studied literature, and based on existing knowledge has developed, evaluated and validated his own procedure.

These ranks are given for each of the following techniques: Conventional PCR (gel-based), Real-time PCR, Quantitative PCR, DNA extraction, RNA extraction, Sanger (dideoxy) sequencing and analysis, Next generation sequencing and analysis, Molecular cloning, Fragment analysis, Primer and probe development, Phylogenomics

Additional Info:

- Students may be invited for a tele-conference call to allow a better understanding of their practical experience.
- Each student who successfully completes the e-learning part is invited to attend the face-to-face sessions.

REMARKS

After academic selection, candidates will be screened for DGD scholarship eligibility (requirements for the DGD scholarship: please check <http://www.itg.be/E/scholarships>).

Publications recommended for MID students:

Banoo, S., Bell, D., Bossuyt, P., Herring, A., Mabey, D., Poole, F., Smith, P. G., Sriram, N., Wongsrichanalai, C., Linke, R., O'Brien, R., Perkins, M., Cunningham, J., Matsoso, P., Nathanson, C. M., Olliaro, P., Peeling, R. W., Ramsay, A., 2010. [Evaluation of diagnostic tests for infectious diseases: general principles. Nat. Rev. Microbiol. 8, S17-S29.](#)

[Barbe, B., Verdonck, K., Mukendi, D., Lejon, V., Lilo Kalo, J. R., Alirol, E., Gillet, P., Horie, N., Ravinetto, R., Bottieau, E., Yansouni, C., Winkler, A. S., van, L. H., Boelaert, M., Lutumba, P., Jacobs, J., 2016. The Art of Writing and Implementing S](#)

Field, N., Cohen, T., Struelens, M. J., Palm, D., Cookson, B., Glynn, J. R., Gallo, V., Ramsay, M., Sonnenberg, P., Maccannell, D., Charlett, A., Egger, M., Green, J., Vineis, P., Abubakar, I., 2014. [Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases \(STROME-ID\): an extension of the STROBE statement. Lancet Infect. Dis. 14, 341-352.](#)

Key teachers:

- Conor Meehan

- Frederick Van den Broeck
- Katja Polman
- Eline Kattenberg

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