PharmacoLearn

MPH203T Computer Aided Drug Delivery System, M.Pharm Semester 2

Unit 5: Artificial Intelligence, Robotics and Computational Fluid Dynamics

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5.1 Artificial intelligence: a general overview

Artificial intelligence (AI) is the branch of computer science concerned with systems that perform tasks which, done by a human, would be called intelligent: recognising patterns, learning from examples, and making predictions or decisions. Its working core in current practice is machine learning, in which the system's rules are not written by a programmer but estimated from data: given many examples of inputs with their known outputs, an algorithm adjusts its internal parameters (the estimation of Unit 1, at industrial scale) until its predictions on new inputs are accurate. The main styles are supervised learning, trained on labelled examples (this structure, that measured solubility); unsupervised learning, which finds structure such as clusters in unlabelled data; and reinforcement learning, which improves by trial and reward. Deep learning, the family behind most recent advances, uses neural networks of many layers that learn their own internal features from raw inputs such as molecular graphs, images and text, at the cost of large data requirements and decisions that are hard to inspect, the black box problem. Two disciplines from Unit 1 govern whether an AI result is worth anything: the model must be validated on data it never saw in training, and a model with too much freedom will memorise its training set and fail on new cases, the overfitting of section 1.4. AI is best understood as this subject's statistical modelling grown powerful and data hungry, not as an exemption from it.

5.2 Artificial intelligence in pharmaceutical research and development

AI applications now appear at every stage this subject has visited. In **discovery**, models predict activity, solubility, permeability and toxicity from structure (the QSAR of section 1.1 grown into deep learning), screen virtual libraries of millions of compounds, and generate entirely new candidate structures optimised against several properties at once; protein structure prediction by systems such as AlphaFold has given modelers targets that were previously unmodelled. In **preclinical and clinical development**, AI reads images and signals (pathology slides, ECGs, retinal scans), predicts which patients match a trial's biology, forecasts recruitment and flags data anomalies in the clinical databases of section 4.10. In **formulation and manufacturing**, learning models predict formulation behaviour from composition and process data, detect defects and drift from sensor and image streams beyond human vigilance, and support the control strategies of section 1.10. The working cautions are equally standard: an AI model is only as good as its training data, which in pharmacy are often small, biased toward successes and expensive to generate; performance on familiar chemistry does not guarantee performance on new chemistry; and for regulated uses the model must be validated, versioned and explainable enough for a reviewer to judge, requirements the field is still formalising.

5.3 Robotics and pharmaceutical automation

A robot is a programmable machine that senses, decides and physically acts: it moves materials, manipulates laboratory ware and executes procedures. **Pharmaceutical automation** is the wider term the syllabus pairs with it, covering robots proper, automated instruments, conveyor and storage systems, and the software that schedules and records them, wherever physical or routine work is mechanised under computer control. In the laboratory, liquid handling robots prepare plates and dilutions, automated systems

run high throughput screening and stability storage, and robotic arms tend instruments around the clock. In manufacturing, automation fills, inspects, packs and labels at speeds and consistency beyond manual work, moves materials in warehouses and cleanrooms, and operates the process equipment whose sensors feed the PAT and control systems of Unit 1. In the pharmacy itself, automated dispensing and compounding systems prepare individualised doses, including hazardous cytotoxic preparations, with barcode checked accuracy.

5.4 Pharmaceutical applications of AI, robotics and CFD

Read across the three technologies of this unit, the application map is complementary: AI decides and predicts, robotics and automation act and execute, and computational fluid dynamics (sections 5.6 and 5.7) simulates the physical processes the other two must control. A modern development programme uses all three together: AI proposes the formulation and predicts its behaviour, CFD checks that the granulator or coater will treat every particle alike at scale, automation runs the process identically every time, and the data from every run train the next round of models. Concrete applications include automated high throughput formulation screening in which robots prepare hundreds of prototype variants for AI ranked evaluation, and continuous manufacturing lines whose flow fields are CFD designed and whose quality is held by automated, model based control.

Technology	Core strength	Representative pharmaceutical applications
Artificial intelligence	Learning patterns and predictions from data	Property and toxicity prediction, virtual screening, image based QC, formulation prediction
Robotics and automation	Physical execution with speed and reproducibility	High throughput screening, liquid handling, automated filling and inspection, dispensing
Computational fluid dynamics	Simulating flow, mixing and transfer in equipment	Mixer and granulator design, fluid bed coating, cleanroom airflow, inhaler aerosol flow

5.5 Advantages and disadvantages of AI, robotics and automation

The **advantages** recur across applications. Speed and throughput rise by orders of magnitude in screening, data handling and physical processing. Reproducibility improves because machines execute the written procedure identically and record it completely, strengthening both quality and the data integrity of section 4.11. Hazardous and tedious work, cytotoxic compounding, repetitive weighing, round the clock monitoring, moves from people to machines. Prediction shortens development: programmes fail earlier and cheaper, in silico rather than in patients. The **disadvantages** are the mirror images. Capital and validation costs are high, and a validated automated system is expensive to change, which can freeze a process the science wants to improve. AI inherits the limits of its data and can fail silently outside them, while its opacity complicates the explainability regulators require. Automation deskills some roles and demands new ones, programmers, data scientists, validation specialists, that are scarce. And dependence is itself a risk: when the system is down or wrong, an organisation that has lost the manual skill has lost its fallback. The balanced syllabus position, and the industrial one, is selective adoption: automate the routine, predict the predictable, and keep human judgement on the exceptions and the accountability.

5.6 Computational fluid dynamics: a general overview

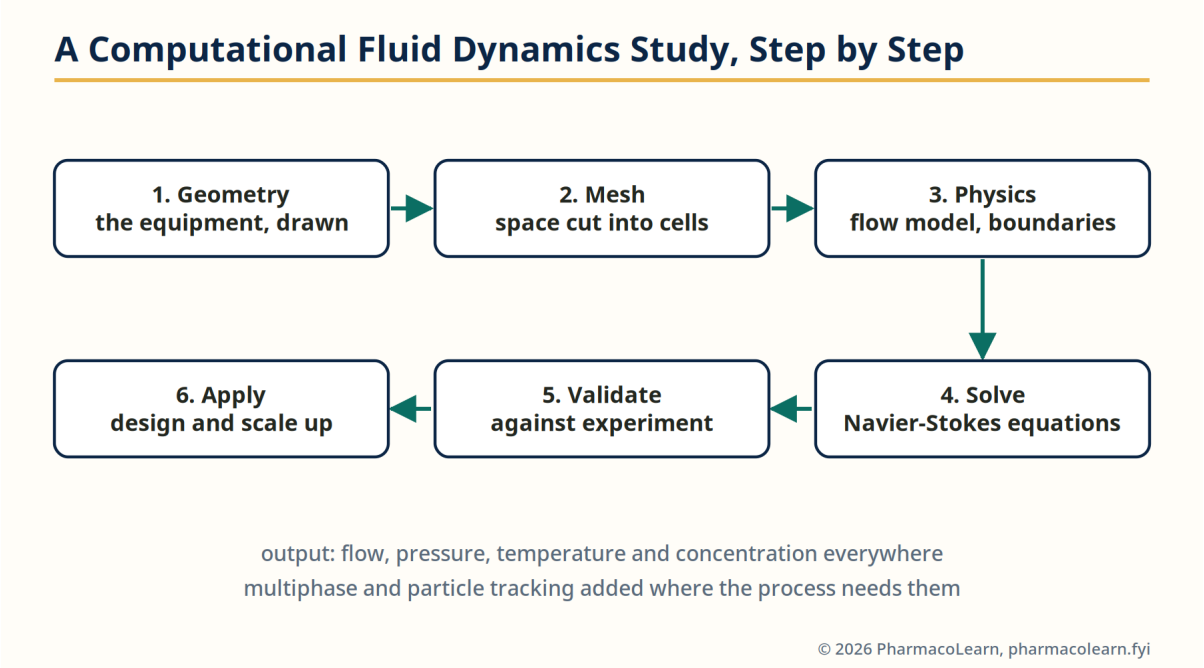

Figure: The anatomy of a CFD study. The validation step is not optional: an unvalidated simulation is a coloured picture, not evidence.

Computational fluid dynamics (CFD) simulates the movement of fluids, and with them heat, dissolved drug and suspended particles, by solving the equations of fluid motion numerically. The governing equations are the Navier-Stokes equations, the conservation laws for mass, momentum and energy applied to a moving fluid, which have no general pencil and paper solution for real geometries. CFD replaces the continuous space with a mesh of many small cells, writes the conservation equations for each cell, and solves the enormous resulting system iteratively on the computer until flows, pressures, temperatures and concentrations are known everywhere in the equipment. A CFD study has a standard anatomy: define the geometry (a stirred tank, a fluid bed coater, a dry powder inhaler), generate and check the mesh, set the physics (single or multiphase flow, a turbulence model where the flow demands one, particle tracking for suspended solids), set boundary and operating conditions, solve, and validate against experiment, because an unvalidated CFD model is a coloured picture, not evidence.

5.7 CFD in pharmaceutical applications

The established applications follow the unit operations of pharmaceutics. In **mixing**, CFD predicts blend uniformity and mixing time in stirred tanks and blenders, locates dead zones, and supports scale up by holding the right quantity constant, tip speed, power per volume or shear, a choice the simulation can test rather than assume. In **granulation and coating**, fluidised bed processes are simulated with gas flow coupled to particle motion, predicting coating uniformity, drying rates and the conditions that cause agglomeration or attrition, directly serving the products of MPH201T and MPH203T's own formulation work. In **drying and lyophilisation support operations**, airflow and heat transfer models size and arrange equipment evenly. In **cleanrooms and sterile manufacture**, CFD verifies that air change patterns sweep contaminants away from critical zones as designed. In **inhalation products**, aerosol flow through inhaler devices and the human airways is simulated to predict where particles deposit, linking device design to the pulmonary delivery of MPH201T. Across all of these the workflow is the same as Unit 4's, geometry and physics in, verified prediction out, and the answer used to run fewer, better experiments.

5.8 Current challenges

The challenges facing the technologies of this subject are shared and specific. Data are the first: models of every kind in this subject are limited by the quantity, quality and representativeness of pharmaceutical data, much of which is proprietary, negative, unrecorded or locked in incompatible systems. Validation and regulatory acceptance form the second: a prediction used in a submission must carry its evidence of correctness, and frameworks for crediting models, especially learning models that change as they are retrained, are still maturing on both sides of the submission table. The third is integration: discovery, development, manufacturing and clinical systems were bought at different times from different vendors, and the informatics vision of the subject, one coherent flow of data from molecule to patient, is still more aspiration than fact in most organisations. The fourth is people: the field needs scientists fluent in both pharmaceutics and computation, and they remain rarer than either skill alone.

5.9 Future directions

The direction of travel is toward integration and autonomy. **Digital twins**, living simulation models of a process or a product, updated continuously with its real data, are the stated goal of both manufacturers and regulators: a twin of a continuous line that predicts quality minutes ahead and adjusts the process, and in time a twin of a patient population in which doses are tested before they are prescribed. **Model informed drug development** is becoming the default regulatory language, with simulation evidence expected, not merely accepted, in areas from paediatric extrapolation to interaction labelling. **Continuous manufacturing** binds this unit's three technologies into one line: CFD designed equipment, automation executing, AI supervising. And AI itself is becoming generative, proposing molecules and experiments rather than only scoring them, which raises the premium on this subject's oldest lessons: every model, however modern, stands or falls on the estimation, validation and honest uncertainty of Unit 1.

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The subject in one chain
Statistics and QbD frame every model (Unit 1)
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   v
Disposition is predicted, transporters included (Unit 2)
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   v
Formulations are optimized by designed experiments (Unit 3)
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   v
The gut, the trial and the clinic are simulated (Unit 4)
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   v
AI, robots and CFD extend the same logic (Unit 5)
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Frequently Asked Questions

Q: What is the difference between a descriptive and a mechanistic model? A descriptive model reproduces the pattern in the data with an equation whose parameters need have no physical meaning, such as a polynomial fitted to a dissolution profile; it interpolates well but cannot be trusted outside the studied range. A mechanistic model is built from the processes believed to generate the data, dissolution, permeation, transit, clearance, so its parameters are physical quantities and it can extrapolate to new doses, formulations and populations, at the price of needing more knowledge and more data.

Q: What is population modeling, and why is it used in drug development? Population modeling fits data from all subjects at once, separating fixed effects (typical parameter values and the influence of covariates such as weight, age and renal function) from random effects (variability between and within subjects). It works on the sparse, unbalanced samples real trials produce, describes the whole distribution of behaviour rather than an average patient, and supports dose decisions for special populations who differ

from the average.

Q: What does ICH Q8 require, and what is a design space? ICH Q8 is the guideline on pharmaceutical development that defines Quality by Design: development beginning from a quality target product profile, identifying critical quality attributes, assessing risk, and building process understanding through designed experiments and models. The design space is the multidimensional region of material attributes and process parameters demonstrated to assure quality; working inside it is not treated as a regulatory change, while moving outside it is.

Q: Why must transporters such as P-gp be modeled explicitly in drug disposition? Because they break the passive diffusion picture. Efflux transporters such as P-gp and BCRP pump substrates back into the gut lumen, into bile or out of the brain, and uptake transporters such as OATP and hPEPT1 decide whether other drugs enter the body or the liver at all. A substrate's absorption, distribution and interactions cannot be predicted from solubility and lipophilicity alone; the transporter step has to be in the model, saturable and inhibitable, as Unit 2 sets out.

Q: How is a factorial design better than changing one factor at a time? A factorial design runs every combination of factor levels, so each factor's effect is measured at all settings of the others and the interactions between factors become estimable, which one factor at a time experiments can never detect. It also extracts more information from the same number of runs, and its fitted polynomial model predicts the response across the whole studied region, not only along the path the experimenter happened to walk.

Q: What is a screening design, and when is it used? A screening design identifies the few influential factors among many candidates using very few runs, by estimating main effects while accepting that interactions are confounded, as in Plackett-Burman designs that screen up to eleven factors in twelve runs. It is used at the start of development, and inside QbD risk assessment, to decide which variables deserve the full factorial or response surface study that follows.

Q: What is a virtual trial? A virtual trial is a simulation run over a population of virtual subjects, each sampled from distributions of physiology and drug parameters, instead of a single standard subject. Its output is a distribution of outcomes: mean profiles with spread, the fraction of subjects inside a target window, the variability a real trial should expect. Virtual trials size real studies, test robustness across populations and can replace trials that would be uninformative, provided their uncertainty is honestly reported.

Q: How can gastrointestinal absorption simulation support a biowaiver? A biowaiver waives an in vivo bioequivalence study on in vitro evidence. A verified absorption simulation strengthens the argument by exercising the model across the plausible range of formulation and patient variation, virtual trial style, and showing that the compared products cannot differ in exposure beyond a stated amount. Acceptance requires the model to be verified against observed data, its sensitive parameters to be measured rather than guessed, and the claim to stay within the conditions the evidence covers.

Q: What does 21 CFR Part 11 require of a computer system used in clinical development? Part 11 sets the conditions for electronic records and signatures to be trusted as equivalents of paper records: the system must be validated, keep secure audit trails recording who created, changed or deleted each record and when, restrict users by authority checks, and retain records in accurate, inspectable form. The European counterpart is GMP Annex 11, and both rest on data integrity: records that are attributable, legible, contemporaneous, original and accurate.

Q: What is the difference between artificial intelligence, robotics and automation in pharmacy? Artificial intelligence is software that learns from data and makes predictions or decisions, such as forecasting a molecule's solubility or reading a quality control image. Robotics is machinery that physically

acts in the world, handling plates, filling vials or compounding doses. Pharmaceutical automation is the wider system joining robots, instruments and control software so that a whole routine process runs, records itself and stays in control with minimal manual intervention.

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