Modeling human homeostatic capability: multivariate analysis of cardiorespiratory and metabolic exercise tests for health assessment

1 Context and positioning

Homeostasis is the process by which living organisms maintain a stable internal balance necessary for their survival and optimal functioning. This process typically involves feedback mechanisms that detect deviations from a target state and activate responses to correct these deviations and return the system to a stable level. Homeostasis is recognized as one of the eight core concepts in biology and is considered fundamental in systems physiology. Therefore, it is imperative to provide training for physicians to proficiently grasp this concept [Modell et al., 2015]. Indeed, the homeostasis capabilities of an individual are used to support medical decision making. In particular, they are already used for patients' peri-operative risk stratification in lung cancer surgery [Brutsche et al., 2000, Fang et al., 2014].

The homeostatic abilities of an individual can be assessed through exercise testing, which is the traditional clinical method for evaluating patients' health status and overall systemic dynamics. A series of tests is designed to measure features representative of the individual's homeostatic capabilities, with one significant metric being the maximal oxygen uptake (VO2max). These measurements are obtained through routine functional tests and maximal exercise sessions, aimed at challenging the entire organism to evaluate physiological adaptive responses. This encompasses, but is not limited to, respiratory, circulatory, and metabolic functions [Fletcher et al., 2013]. When exercise performance or maximal aerobic capacity is limited for a given patient, the medical doctor has to identify the failing physiological function and to provide a coherent system failure mechanics analyzing the monitored data. However, medical doctors still analyze the collected physiological data in a univariate approach as historically developed [Guazzi et al., 2016].

On the other hand, the homeostasis concept and approaches have evolved from Claude Bernard pionneering works to Arthur Guyton introduction of control theory tools to describe human functionning. Currently, in the research community, the human body is considered as a dynamic physiological complex system and specific tools from statistical physics and information theory are used [Goldberger et al., 2002]. Recently, the framework of network physiology was proposed, giving a central role to homeostasis [Bashan et al., 2012, Bartsch et al., 2015]. It provided interesting results in the study of how various components of specific processes interact with each other, such as muscle fibers activation [Garcia-Retortillo et al., 2023]. Nevertheless, all the works in the network physiology domain are conceptual and mostly realized on laboratory small healthy samples.

To broaden theoretical knowledge and to fill the gap between current research and medical practice, the Exercise Test Laboratory of Hôpitaux Universitaires de Marseille built its own activity database composed of 2500 exercise tests.

2 Objectives

This thesis aims at exploiting the aforementionned clinical dataset in order to provide a global understanding and interpretation framework of the multivariate data generated during maximal exercise testing to improve patients' homeostasis phenotyping through their homeostatic capabilities. Phenotyping of an individual involves the comprehensive characterization and analysis of observable traits, behaviors, and physiological markers specific to that person.

We aim to develop a medically and statistically consistent approach to identifying and quantifying determinants of overall performance as well as aerobic performance from monitored variables. This would provide physicians with improved analytical tools to achieve a more relevant and precise patient exercise phenotyping. To this end, we will begin by adapting recent work in unsupervised classification, developed at LIS for diagnosis [Marino et al., 2017], to recorded multivariate physiological time series. The developed multivariate method will be compared to the usual medical univariate sequential approach in terms of predictive power for the occurrence and severity of medical events occurring after the exercise test.

The thesis project aims to go further and provide physicians with a quantitative decision support indicator. It will be developed by focusing on the dynamic interactions between the recorded variables. Such indicators have been developed within LIS for industrial applications [Melhem, 2017, El Jamal et al., 2022]. Here, we consider in particular adapting the framework of physiological networks to the mesoscopic and macroscopic case of exercise tests, linking cardiac, vascular, respiratory, pulmonary, and muscular data. This would provide crucial information to the physician about patients' homeostatic capacities. To achieve this, we will consider tools from graph theory [Ortega et al., 2018, Alippi and Zambon, 2023] to characterize the features of the structural and/or functional network shared between clusters, or distinguishing them. The relevance of the developed indicator will be evaluated in terms of three variables indirectly reflecting the evolution of the patient's condition: the time between exercise tests and death, the number of hospitalizations since the tests, and the generated medical expenses. If found promising, a prospective study will be initiated.

In addition to the supervising team, the PhD candidate will work in close collaboration with a junior hospital doctor.

3 Candidate Profile:

We are looking for a candidate with both an appeal to work on precise and effective medical problems, and a strong theoretical background in one of the following:

- System and control theory
- Signal/Image/Graph processing
- Computer science
- Machine learning/Artificial intelligence

Good coding skills are also required, preferably in Python

Application

The application process is in two steps. First by mail to the supervision team, who will shortlist three candidates. Then Laennec's scientific board will interview and rank the candidates. The application must include

- Resume
- Application letter
- Grade transcripts (at least for both years of master's degree)

Important note: Due to the nature of the funding, the candidate must **NOT** be enrolled at AMU.

4 Location and Supervision:

Location: LIS and C2VN laboratories in Marseille

Starting Date: September-October 2024

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