capabilities. The intent is not to suggest that an agent-based framework is "the" format for an executable ontology layer; the experience with classic ontologies suggests that it is impossible to produce a definitive knowledge representation tool. It is fully expected that other researches will develop similar types of tools, using different modeling paradigms. However, we believe that an ABMF demonstrates a robust, evolvable approach and will provide an essential translational step toward the goal of having as many steps as possible of the discovery process be automated. Eventually, this type of architecture would allow the automated generation of models that can be picked through by the researcher, providing a truly evolutionary solution to the synthetic aspect of biomedical research.

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### Fluctuation-dissipation theorem provides a simple analytical relationship between post-stress heart rate recovery and heart rate variability during the stress

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**Objectives:** The autonomic nervous system modulates both the dynamics of heart rate (HR) recovery (HRR) after a cardiac stress test (eg, treadmill exercise test) and the HR variability (HRV) under steady-state ("free-running") conditions. Also, both reduced HRV and prolonged HRR are believed to be predictors of mortality. Thus, we hypothesized that there is a relationship between post-stress HRR time constant ($T_{\mathrm{off}}$) and an HRV measure.
**Methods:** Although all previous studies have used conventional statistical tools (such as correlation coefficients) to explore empirical correlations between HRR time constant and different HRV indices during the exercise, we adopted an alternative strategy, deriving such a relationship theoretically rather than empirically (statistically) inferring it from the data. We applied the fluctuation-dissipation theorem (FDT), which relates the system response to a relatively small perturbation to the fluctuations in the stationary state of the system.

We test our theoretical results with 20 HR data sets recorded during and after the spontaneous breathing trial (SBT), considered as a stressor, from 16 mechanically ventilated critically ill patients in an intensive care unit.
**Results:** The FDT predicts the exponential shape of HRR and provides a simple analytical relationship linking post-stress HRR time constant with a standard HRV measure, namely, the correlation coefficient of the Poincare plot of the HR dynamics during the stress (SBT). For 17 of 20 data sets, FDT correctly predicts the values of post-SBT HRR time constant using HRV during the SBT. The cases when the FDT-based relationship fails correspond to nonexponential shapes of HRR.
**Conclusion:** The relationship between the *microscopic fluctuations* (HRV) during the stress and the *macroscopic response* (HRR) after the stress was terminated can be interpreted as an example of FDT or, equivalently, Onsager Regression Hypothesis, which states that the same time constant characterizes both the decay of *spontaneous microscopic fluctuations* (HRV) at steady state and the *macroscopic relaxation* (HRR) to a new steady state after a relatively small external perturbation (stress) was withdrawn.

The approach is specific neither to cardiac physiology nor to transitions between mechanical and spontaneous ventilation as a specific stress. It may therefore have wider applicability (both in intensive care unit and elsewhere) to many physiologic systems subjected to modest stresses.

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### Dynamic information improves discharge prediction after cardiac surgery

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**Objectives:** To predict the probability of ICU discharge the day after scheduled cardiac surgery and to examine the independent contributions of data available upon ICU admission and dynamic data of the first 4 hours of ICU stay.
**Methods:** All 461 adult patients who were admitted to our 56-bed surgical ICU after scheduled cardiac surgery between the January 18 and December 4, 2007, were selected as development cohort. All data in this study were available in the computerized medical chart of the patient (Metavision, iMD-Soft). We used the following ICU admission data: age, sex, body mass index, weekday and hour of admission, APACHE II score, history of diabetes, use of temporary epicardiac pacing, presence of endocarditis, preoperative lung function, heart rate, blood pressure, baseline serum creatinine, type of surgery, and intraoperative blood loss. Three signals with a sample interval of one measurement per minute were selected for time series analysis: heart rate, systolic arterial blood pressure, and oxygen saturation measured by pulse oximetry ($SpO_2$). The dynamic features of these signals were calculated using multivariate autoregressive models, cepstral coefficients, detrended fluctuation analysis results, and approximate entropy values. We used 4 hours of data of each of these signals. Models were built using a Gaussian process classifier to predict the probability of ICU discharge on the day after surgery. Three separate models were developed: a first model used only the ICU admission data, a second model used only the coefficients from the dynamic data analysis, and a third model was based on a combination of both admission data and dynamic coefficients. Models were validated in a previously unseen validation cohort of 116 patients. Area under the receiver operating characteristic curve (aROC) was used

**Table 1** The aROC values and Brier scores of the different experiments

| Input | aROC | BS |
|---|---|---|
| Admission | 0.650 | 0.226 |
| Dynamic coefficients | 0.721 | 0.182 |
| Combined model | 0.720 | 0.187 |
| Nurses | 0.724 | 0.241 |
| Doctors | 0.788 | 0.212 |