Visualization and Classification of Physiological Failure Modes in Ensemble Hemorrhage Simulation
Song Zhang\textsuperscript{a}, William Andrew Pruett\textsuperscript{b}, Robert Hester\textsuperscript{b}
\textsuperscript{a}Computer Science and Engineering, Mississippi State University, Mississippi State, MS, USA 39762-9637; \textsuperscript{b}University of Mississippi Medical Center, Jackson MS, USA

ABSTRACT

In an emergency situation such as hemorrhage, doctors need to predict which patients need immediate treatment and care. This task is difficult because of the diverse response to hemorrhage in human population. Ensemble physiological simulations provide a means to sample a diverse range of subjects and may have a better chance of containing the correct solution. However, to reveal the patterns and trends from the ensemble simulation results is a challenging task. We have developed a visualization framework for ensemble physiological simulations. The visualization helps users identify trends among ensemble members, classify ensemble member into subpopulations for analysis, and provide prediction to future events by matching a new patient’s data to existing ensembles. We demonstrated the effectiveness of the visualization on simulated physiological data. The lessons learned here can be applied to clinically-collected physiological data in the future.

Keywords: Physiology, ensemble, simulation, prediction, failure, visualization

1. INTRODUCTION

Hemorrhage is a common cause of medical emergency. Cardiovascular compensation for hypovolemia (loss of blood) is a complex process synthesizing responses from multiple subsystems: cardiac, vascular, autonomic, hormonal, and more, to ensure the protection of vital tissues in a preferential order. Clinically, it is vital to know an individual’s state of shock as quickly and as precisely as possible; this knowledge is even more vital in the context of triage. Because the body excels at protecting vital functions from the effects of hypovolemia, the most clinically important measures of hypovolemic shock (cerebral perfusion pressure and the preservation of tissue perfusion as determined by intact cardiovascular function) are the last physiological components to show failure, complicating the evaluation of a patient.

One challenge in identifying the patients in the state of shock is the diverse response to blood loss in humans. Any single prediction is certain to be inaccurate for a portion of the population. Therefore ensemble simulations that cover all possible outcome of a population are more likely to contain the correct prediction for a new patient. However, revealing patterns from the ensemble simulations and using the ensemble for prediction are challenging, especially when the number of ensembles are in the hundreds or thousands.

In this paper, we aim to reveal patterns in ensemble physiological simulations of hemorrhage patients, classify the patients into subpopulations, and predict the imminent failure of new patients hence helping doctors prioritize the treatment of patients. We achieve our objectives by collecting hemorrhage simulation data from an ensemble of virtual patients, visualize the outcome with image plot, cluster the patients into subpopulations based on their simulated physiological outcome during hemorrhage, and partially matching a new patient’s data to the ensemble data for prediction. Our work is based on HumMod physiological simulations \cite{1} because it is easy to control the experiment and observe the results. However, the methods developed in this paper can be easily applied to clinically-collected physiological data in the future.

Specifically, we created an ensemble of 395 patients and subjected them to virtual bleeding. We recorded a number of physiological variables over a period of 60 minutes. We then selected three vital variables for further processing: heart rate, respiration rate, and diastolic blood pressure. We visualized these variables using image plots with preprocessing steps including alignment and sorting. The variables were visualized individually with a single channel color map and also visualized together with a three channel color map. Then, for each variable, a similarity matrix between the patients was calculated and unsupervised clustering was performed to separate the patients into subpopulations based on their responses to hemorrhage. The user can then examine the consistent trends and patterns in a subpopulation. For a new
patient, the up-to-date response data can then be partially matched to the ensemble. This matching allows a user to make a visual prediction of possible cardiovascular failure in the new patient based on its closely matched ensemble members.

Our results show that the patients can be grouped into subpopulations with consistent patterns of response within a subpopulation and distinct patterns across subpopulations in a hemorrhage situation. Partially matching a new patient’s data provides guidance on the possibility and timing of cardiovascular failure, hence helping prioritize the patient treatment.

The contributions of this paper include the application of image plot and several improvements to improve the visualization of ensemble physiological simulations of hemorrhage response, the application of clustering methods to the ensemble physiological simulations to classify subpopulations of the patients, and the comparison of clustering methods and distance metrics for the physiological simulation data, and a novel predictive plot based on matching a new patient’s data to existing ensemble data.

2. BACKGROUND AND RELATED WORK

2.1 Hemorrhage prediction

As humans hemorrhage, they progress through three distinct phases of the relationship between heart rate and blood pressure. The phases correspond to differing control mechanisms exerted by the body to maintain pressure (tachycardic normotensive phase), preserve cardiac and brain function (bradycardic hypotensive phase), and a last ditch effort to preserve life (final tachycardic phase). In the tachycardic normotensive phase, the primary impulse of the body is to compensate for fluid deficit by increasing heart rate to sustain pressure. This keeps the whole body well-perfused, but puts metabolic strain on the heart. As the blood volume shrinks, by-products of metabolism build up in cardiac tissue, resulting in a relaxing signal to the brain which then reduces heart rate and directs blood preferentially to the most important tissues. As the brain becomes hypoxic, this relaxing signal is overridden by a last ditch effort to preserve flow by increasing heart rate. This puts enormous metabolic strain on the heart, resulting in ischemia and inefficient pumping. At this point in the progression, re-infusion of blood into the system is unlikely to change the outcome of the hemorrhage because the heart is unable to pump against a higher systemic pressure due to acute damage from the previous hypovolemia. For this reason, this phase is referred to as irreversible decompensation.

Early efforts to predict cardiovascular collapse have focused on indirectly measuring blood volume in hemorrhaged patients. Convertino et al. 2-5 detailed a method using the lower body negative pressure (LBNP) model of hemorrhage on live humans while noninvasively monitoring standard variables: blood pressure (BP), heart rate (HR) and HR variability (HRV). This technique has allowed ethical experimentation on humans, from which Convertino’s group has produced two machine-learning algorithms whose purpose is to evaluate volume status in hemorrhaged patients. Glass’s group used wavelet analysis on EKG data (R-R and R-S intervals, and QRS magnitude) to predict blood volume in hemorrhaged pigs to great effect, noting 91% predictive accuracy using a training set comprising of three animals. 6 One problem with this approach is that the spectrum of response to blood loss in humans is surprisingly wide, 7, and is believed to be predicated on variables that are difficult to observe in an experimental setting, much less a clinical or triage setting.

Convertino’s group has proposed an alternative method, and has experienced some success. 5 Their method uses derived measures, assembled by considering simultaneously multiple indicators of cardiovascular function, to predict a patient’s likelihood of CV collapse. They used nonlinear regression analysis to calculate a scoring mechanism from a database of trauma patients, and validated their methods utilizing their LBNP model of hemorrhage. They reported that 21% of patients classified as “normal” by their methods required a life-saving intervention in practice.

The lack of a complete understanding of the physiological response mechanism to hemorrhage in humans, combined with the known diversity in human responses, prompted us to design a better visualization method to tap into an expert’s ability to recognize visual patterns in patients’ response and act accordingly.

2.2 Ensemble data visualization

Ensemble simulations have been increasingly common in scientific fields like numerical weather simulation or hydrology simulation. The most commonly used method for ensemble 1D data is the overlapping curve plot similar to Figure 1. Similarly, spaghetti plot has been used to visualize contours in 2D ensemble data. Current efforts have extended to 2D or 3D data ensemble visualizations. User studies have been done on visualization methods for
ensemble data and their uncertainties. However, empirical knowledge indicates that without careful design, patterns and trends may well be hidden in the ensembles even for 1D data (see Figure 1). In this paper, we apply 1D ensemble visualization to physiological simulation data and improve the visibility of useful patterns in several ways.

One of the improvements is in the classification of the ensemble patients. Unsupervised clustering is a commonly used method for identifying groups and patterns in data. It is especially useful for identifying patterns when prior knowledge is rare or the patterns are not fully understood. In this paper, we utilized unsupervised learning for identifying patterns in physiological simulations among ensemble patients. It is beyond the scope of this paper to fully survey a diverse range of clustering methods. However, we have experimented with two widely used clustering methods: k-means and hierarchical clustering, and two difference distance metrics for time series data: Euclidean distance and dynamic time warping distance. The results demonstrated the pros and cons of each method.

3. METHODS

3.1 Data simulation

The simulations were performed in HumMod, a well-established interactive physiological simulator comprising some 7000 variables (Guyton/Coleman model) developed over the past 30 years. HumMod’s focus is on integrating all facets of cardiovascular control (neural, hormonal, fluid-dynamic) to produce a robust model of circulatory physiology, with auxiliary endocrine, metabolic, and respiratory models fleshing out the simulator. Precursors of this model have been used in numerous studies whose intent was to provide a more detailed understanding of the physiologic mechanisms at play in common clinical conditions. The model is composed of mathematical expressions of the relationships between physiological variables based upon well-understood cell/tissue/organ physiology. The model incorporates the cardiovascular and neurogenic physiologic responses to changes in pressures and flows that occur throughout an acute hypovolemic event. The details of model structure are beyond the scope of this article, and have been described previously.

A population is generated from HumMod by incorporating variance into each model parameter (independent variable). Explicitly, we allow parameters to vary uniformly in a ±10% band around the best-fit values, treating the models that are so constructed as individual subjects. Approximately 85% of these individuals are physiologically viable, with cardiovascular outputs that resemble normal humans (Table 1). Only these individuals are retained for this study. We did not attempt to calibrate HumMod to match a particular population, preferring instead to use this study as proof-of-principle that effective classification/prediction could be generated. 395 individuals remained after sampling and steadying. Subjects were brought to steady state by simulating three days. The hemorrhage was conducted at three fixed rates of 37.5, 75, and 150 mL/min over 40 minutes, time sufficient to extract between 1.5 and 6 L of blood. The variables observed are detailed in Table 1. Observations were recorded at the beginning of each minute. The raw data was then used to assemble the space of sequential observations by combining three consecutive observations. It should be noted that the rate of hemorrhage was not observed; clinically quantifying a hemorrhage rate is a difficult process with large uncertainty.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diastolic Blood Pressure</td>
<td>83±8.3</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>11.6±0.14</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>74±2.1</td>
</tr>
</tbody>
</table>

3.2 Initial visualization

A simple plot along the timeline of the simulation shows the complete trace of a single variable. Figure 1 shows the plots of three variables from a single patient’s simulation. From Figure 1, it is clear that the patient went into shock around 10 minutes into the simulation and died at around 20 minutes. Ensembles can be overlaid in one plot for comparison. The visualization of ensemble plots for variables heart rate, respiration rate, and diastolic blood pressure are shown in Figure 2. Color is randomly chosen for each ensemble. In these plots, we can see the initial distributions of the variables, the progressive diverging ensemble outcome over time, and the physiological failure of a group of patients where their heart rates went to zero.
The primary characteristic of human hemorrhage to irreversible decompensation is the progression through tachycardic normotensive, bradycardic hypotensive, and final tachycardic phases. This progression is shown in the case of a single individual in Figure 1 (a). The curve shown is typical; note the presence of two tachycardic events. The first restores system balance momentarily, while the second signifies the initiation of irreversible decompensation. This profile illustrates one of the difficulties in predicting patient performance: nonlinearities in the system can lead to events that resemble a sentinel event. The visualization in this paper helps to identify imminent physiological failure of the patient.

![Figure 1: Plots of a single patient’s heart rate (a), respiration rate (b), and diastolic blood pressure (c) over time.](image1)

While ensemble curve plots show the progression of physiological outcome over time, they are also challenging for interpretation and prediction. The sheer amount of information from hundreds of ensembles in one plot obscures the trends and patterns. It is difficult to identify the abnormal patterns in heart rate in Figure 2 (a) among 395 ensembles. For example, the answers to the following questions are not immediately clear:

1) How many distinct groups of response patterns do these patients form?
2) Which patients show the similar pattern to the patient in Figure 1 (a)?

In the following sections, we improve the visualization of the ensemble data through preprocessing, image plot, and clustering.

### 3.3 Image plot

The curve plot in the above section visualizes the data with the shape of the curve. While effective for single patient, the overlay of multiple curve plots in a single plotting canvas creates clutters since multiple curves can go through a single pixel. This problem exacerbates quickly as the number of ensembles grow.

A simple yet effective alternative to curve plot is the image plot that converts data to colors. The image plot of a single patient and a single variable is a stripe of colored pixels. Figure 3 (a) shows the image plot of the heart rate of two patients as two color stripes. The color here is selected to be black to white (mapped from the minimum to the maximum values of the data). There are several advantages of using an image plot over a curve plot. (1) A single patient’s data are confined in a stripe of pixels and visualized by color. This removes overlapping in curve plots, making them more...
scalable to the number of ensembles. (2) Compared to a curve plot, it is easier to trace a single patient’s data in an image plot over time in an ensemble, since the path of the data is always a horizontal straight line. (3) It is also easier to compare ensemble members in an image plot since they are regularly laid out in the 2D plotting space, lined up along the timeline, and easily tracked individually.

Figure 3: (a) shows an image plot of two patients’ respiration rate during a simulation. (b,c,d) show ensembles of heart rate (b), respiration rate (c), and diastolic blood pressure (d) of the simulation with image plots.

Figure 4: (a) The randomly ordered image plot of heart rate. (b) After alignment according to the failure point. (c) After sorting according to the failure point.
For these reasons we visualize the three physiological variables in the simulation results with image plots. Figure 3 (b,c,d) show the image plots of heart rate, respiration rate, and diastolic blood pressure of the 395 ensembles.

From Figure 3 we can clearly identify each ensemble member’s pattern of response and compare two neighboring ensemble members easily, especially when zooming in on individual ensemble members. However, when patients showing similar patterns are not located close to each other, it is difficult to identify consistent trends in a subset of patients. Furthermore, some patterns might not have the same time interval but are still considered similar patterns, only with time lags. For example, in Figure 1 (a), the time interval between the three phases (tachycardic normotensive phase, bradycardic hypotensive phase, and the final tachycardic phase) might change from patients to patients, but the patterns are still considered similar. For these reasons, several improvements are designed and implemented to better reveal patterns and facilitate ensemble comparisons.

**Critical-time based alignment** The image plot provides a natural cross-patients comparison at the same location of the horizontal axis, i.e., at the same time point of the simulation. However, the similar patterns in patients might not be aligned at the same simulation time. Therefore we seek to realign the data based on our needs and the nature of the data. In this simulation, one time point, the time of cardiovascular failure, is especially important for doctors. The short time period before the time of failure may offer clues to whether imminent failure will occur. However, the implicit and environmental differences between patients lead to different responses to hemorrhage. This means that even if we start the hemorrhage from the same time, the point of failure will differ among patients, which creates difficulty in visually comparing ensemble members for the change of their physiological variables before the time of failure. Therefore we right align all ensemble members to the point of failure. Figure 4 (a,b) show the ensemble heart rate image plot of heart rate before and after the alignment. The data after the failure point (zero heart rate) were shifted around to fill the void at the beginning. From the shifted image we can clearly see that some patients show a high spike of heart rate right before failure and some patients do not show this spike.

![Figure 5: The color image plot of three variables: heart rate (red), respiration rate (green), and diastolic pressure (blue).](image)

**Ensemble sorting** The original order of the patients is assumed to be random and usually not very meaningful, as is often the case in a clinical setting. As a result, patterns might be hidden under the randomness of the ensemble order. Sorting the ensemble members according to a physiological value or a derived quantity may reveal hidden patterns in the ensemble data. For example, Figure 4 (c) is a sorted image plot of Figure 4 (b). The sorting here is done over the time of failure. The patient with the shortest time to failure is placed on the top of the image while the bottom part of the image contains the patients who did not fail at all during the simulation time. In this sorted image plot, the patterns of heart rate before the time of failure is much clearer than in Figure 4 (a,b). Namely, many patients who eventually died experienced
tachycardic normotensive, bradycardic hypotensive, and final tachycardic phases, similar to the patient in Figure 1 (in the middle to top portion of the Figure 4 (c)).

Figure 6: Clustering results of heart rate with k-means (a,b), and hierarchical clustering with Euclidean (c,d) and dynamic time warping (e,f) metrics. The number of clusters is selected at 4. The rightmost column of pixels in each picture shows the spans of the four clusters by different shades of gray. Right column pictures show the same clustering results as their left neighbors but with ensemble members in each cluster sorted by the time of failure.

Multi-variable image plot There are thousands of output variables from HumMod simulation. While observing all is neither feasible nor necessary, it is often helpful to observe two or three variables from the outcome in the same space in the decision making process. Therefore we generated a multi-variable image plot with color blending. Specifically, we selected three variables for observation, e.g., heart rate, diastolic blood pressure, and respiration rate. We normalize these variables to the range of [0,1]. We then selected the same number of colors as target variables and made color ramps
from black to the fully saturated colors and mapped the data value of the variables to their colors with the color ramps. We then created a single image by blending the three colors. Figure 5 shows a three-variable image plot. Heart rate, respiration rate, and diastolic blood pressure are mapped to red, green, and blue. All three variables are aligned and sorted the same way as in Figure 4 (c).

Specific phenomena can be inferred by the blended color, e.g., the purple color indicates the time when heart rate and respiration are high and blood pressure is low (tachycardic hypotensive). From Figure 5, we observe that a general trend just before death is that the heart rate and respiration rate go up while blood pressure goes down. Recall that this combination is indicative of a patient going into irreversible shock. In general, we observe the interdependency between all variables in this multi-color plot.

3.4 Clustering

With some preliminary transformation of the data, e.g. alignment and sorting mentioned above, ensembles are visualized with stronger order and patterns are better revealed. In addition, the results are easy to interpret since all transformations are relatively simple and straightforward. A disadvantage is that the revealed patterns depend on the choices of the transformations. The combination of all the transformations is a large number, and the search for a revealing data transformation takes time and often requires experience from the users. Furthermore, more complex task like the classification of patients into similarly behaved subpopulations may not be accomplished by simple transformations. Alternatively, we can reveal classification of the data with either supervised learning or unsupervised learning. Today, the mechanism of the human physiological responses to hemorrhage is still not well understood. Hence not many patterns can be predefined for training. As such, we focus on unsupervised learning, i.e., clustering to help us reveal the data patterns without prior knowledge of the clusters.

Two important factors in unsupervised clustering are the similarity matrix and the clustering method. Most clustering methods operate on a predefined similarity matrix that gives the distance between any pair of data points in the group. The clustering method then tries to assign data into clusters based on predefined objectives, i.e., to minimize in-cluster distance and maximize between-cluster distance. We experimented with both similarity metrics and clustering algorithms.

Specifically, we experimented with k-means algorithm and hierarchical clustering algorithm. Briefly, k-means algorithm aims to partition n observations into k clusters in which each observation belongs to the cluster with the nearest mean. K-means algorithm works well when observations are grouped around k centroids. Hierarchical clustering aims to build a hierarchy of clustering results. The hierarchical clustering itself comes with different flavors, including single link, complete link, Ward’s method, etc., depending on the objective function for the clusters. We choose to use Ward’s minimum variance method for hierarchical clustering which minimizes the total within-cluster variance. For hierarchical clustering algorithm, we also experimented with the widely used Euclidean distance between 1D ensemble data and the alternative dynamic time warping distance. Briefly, dynamic time warping measures the similarity between two time series while allowing them to be “stretched”. For example, if two patients experienced the same up and down pattern of heart rate during the simulation, but differed in the timing and interval of the pattern, then dynamic time warping will assign a much lower distance than Euclidean distance, which tries to match up the pair aligned at each time point.

The clustering results are shown in Figure 6. These results are right aligned to the time of failure for better viewing. However, the clustering was done with the original data without alignment. The results are shown without (left column) and with (right column) sorting within each cluster. For example, Figure 6 (b) shows the same clustering result as 6 (a) with ensemble members within each cluster sorted according to the failure time. The number of clusters is set to 4 based on empirical evaluations. Figure 6 (a,b) shows the results of a k-mean clustering. Figure 6 (c,d) show the results of hierarchical clustering with Ward’s method and Euclidean distance. Figure 6 (e,f) show the results of hierarchical clustering with Ward’s method and dynamic time warping distance.

We observed that hierarchical clustering results accurately identify two groups of the virtual patients who did not die during the simulation (Figure 6 (c,d,e,f)). The top cluster in these results contains patients whose heart rate kept normal during the simulation. The bottom cluster in these results contains patients whose heart rate decreased then increased during the simulation. This is caused by the hemorrhage. However, these patients were able to compensate for the hemorrhage during the simulation. K-means clustering, on the other hand, was not able to pick out these two groups of virtual patients in the 4-cluster result (Figure 6 (a,b)).
For the virtual patients who died, the result of hierarchical clustering with Euclidean distance (Figure 6 (c,d)) grouped them into two groups mainly according to the time of failure which is a good indicator of how well the response curves lined up to each other. This is evident by the nicely increasing times to failure in the middle two clusters in Figure 6 (c,d). Hierarchical clustering with dynamic time warping (Figure 6 (e,f)), on the other hand, classified the two groups of virtual patients who died based on their heart rate patterns before the failure. Namely, while both groups experienced the tachycardic normotensive, bradycardic hypotensive, and final tachycardic phases, one group of patients experienced a spike of heart rate right before the failure (see the 3rd cluster in Figure 6 (f)) much higher than the other group of patients. These different patterns are potentially very helpful for doctors in both analysis and prediction tasks in hemorrhage patients. We conclude that the combination of dynamic time warping distance and hierarchical clustering is effective in identifying subpopulations with similar patterns among patients.

3.5 Ensemble matching and prediction

![Figure 7](image)

Figure 7: Part of a new patient’s data is matched to all ensemble members and the result is used to sort these members. The sorted ensemble members are shown with the new patient’s data at the bottom. The closer matched members are placed closer to the bottom. We show the entire 395 ensemble members and the closest 4 members. And we recorded the results by using the new patient’s data from the beginning to 1-6 minutes from failure. (a,b,c): all members matched to new data cut at 1 to 3 minutes from failure. (d,e,f): the closest 4 ensemble members cut from (a,b,c). (g,h,i): all members matched to new data cut at 4 to 6 minutes from failure. (j,k,l): the closest 4 ensemble members cut from (g,h,i).

While clustering helps analyzing the results of ensemble simulation, we are also interested in predicting imminent failure in a real time situation. Although machine learning algorithms can be used for prediction, we are more interested in a direct visualization of the possible progressions of the patient. The direct visualization is easy to interpret and contains details from data often unavailable in machine learning approach, hence providing a complementary analysis to learning approaches. Our key idea is to find the best matches to the current patient from existing patients and use the closely matched ensemble members to predict what will happen next. Specifically, the dynamic time warping distance is calculated from the new data to each ensemble member. The ensemble members are then sorted according to the
distance. An image plot can then be generated for the closely matched ensemble members. Our reasoning is that if there is a clear pattern leading up to the failure of the patient, this pattern will be matched to similar patients whose recorded progress past the time of the new patient’s data can be used for prediction. Figure 7 shows the results of this approach. In this figure, dynamic time warping distance is calculated between the new patient’s data and all 395 ensemble members. The closest 4 ensemble members are also shown. We performed this experiment with a new patient’s data cut at 1-6 minutes from failure time to emulate a clinical setting. In the results, we can see that when we can observe this new patient within 5 minutes to failure, the closest 4 ensemble members predict imminent failure fairly effectively. However, if we only have the data up to 6 minutes from failure, the closest ensemble members may not predict failure.

4. DISCUSSION AND CONCLUSION

We generated ensemble simulations of hemorrhage with HumMod. We chose to use hemorrhage because it integrates well understood processes into a complex dynamic setting. The dynamics of hemorrhage are very challenging to predict due to inter-subject variability, though the progress of hemorrhage has been classified into three distinct and easily distinguished phases. This combination of simple processes and complex dynamics yields a unique vantage from which classification and prediction algorithms can be proposed and interpreted. While the problem we addressed is hemorrhage, we believe that similar methods could be used to understand other progressive pathologies such as heart failure.

Our goal was to reveal the patterns in the simulation results, compare similarity and differences among ensemble members, and help predict imminent failures. For this purpose, we began by using image plots to show all ensemble members in a regular layout. These plots were improved with alignment and sorting. Multiple variables were combined into a single plot with multiple color channels. We employed unsupervised clustering to ensemble members in order to classify these members to meaningful subpopulations. We experimented with different clustering methods and metrics and found that hierarchical clustering and dynamic time warping provided good clustering results.

Finally, we matched new patient’s data to the ensemble members for prediction. The process of comparing two profiles with dynamic time warping for the purpose of prediction is novel. Most algorithms have considered the problem of quantifying blood loss rather than physiological state. We feel that these approaches are doomed to failure due to the wide variability in human responses to hemorrhage. Previous efforts have shown that many of these differences are intrinsic to the individuals observed. In smaller models, the impact of parameter variability on the human hemorrhage response has been tested and found to be significant, but that study required prior information about virtual patients including baseline pre-hemorrhage measurements. Still, these studies suggested that a predictive metric that could be applied during a simulation or clinical hemorrhage may be obtained.

The metric used here concentrates on comparing the time series of new individuals to clusters of time series of existing virtual patients. Considering individuals as dynamical systems with slightly different parameters, it is intuitively clear that different individuals will express a range of values in the observed variables. However the trajectories of different individuals may express more similarities than the individual values themselves. Hence classifying an individual into a cluster gives an expectation for future behavior which can be used as a benchmark for future observations. Because information on patients pre-hemorrhage is rarely available, this comparison is of greater clinical utility than the previous efforts on classification. It is still not certain how or if parameter variability can be tied to variability in the time-series defined clusters. Intuitively, such a link exists but it may be obfuscated by noise from less specific parameters. Further investigations are planned to investigate this relationship.

The results show the following conclusions. 1) Rudimentary preprocessing of ensemble data including alignment and sorting helps user better visualize the patterns within and between ensemble members. 2) Some clustering methods are effective in classifying virtual patients into meaningful groups based on their physiological response to hemorrhage. In particular, hierarchical clustering with Ward’s method and dynamic time warping distance shows promising results for classifying patients’ responses during hemorrhage. 3) Partially matching a new patient’s data to existing ensembles provides a qualitative evaluation and prediction of the new patient’s risk of going to imminent shock.
REFERENCES


