33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Sequential versus Concurrent Computation of Complex Model Systems for Medical Decision Support

Joern Kretschmer, Knut Moeller

Abstract—**Medical Decision Support Systems employ mathematical models to optimize therapy settings. The mathematical models are used to predict patient reactions towards alteration in the therapy regime. This prediction should not be limited to one detail but should feature a broad picture. A previously proposed framework is able to dynamically combine submodels of three model families (respiratory mechanics, gas exchange and cardiovascular dynamics) to form a complex, interacting model system.**

When concurrent computation of the combined submodels is employed, tests exhibited high computing costs. Therefore, a sequential computing approach is introduced. Thereby, direct interaction between the submodels is not applicable as all submodels are computed individually. To simulate submodel interaction, interface signals that are normally present in the concurrent approach were precalculated using reduced models of respiratory mechanics and cardiovascular dynamics.

Evaluation of the new approach showed that results feature a discrepancy lower than 2.5% compared to the results computed by the concurrent approach. Simulation error could be decreased to 2% by improving the precalculation of the interface signals. Computing costs have been decreased by a factor of 17.

I. Introduction

MEDICAL Decision Support Systems (MDSS) can aid doctors in optimizing therapy settings, e.g. ventilation regime in artificially ventilated patients to prevent ventilator induced lung injury. In order to find the optimal setting for each patient individually, the MDSS needs to compute forecasts of the patients' reactions towards changes in the therapy settings. This might be accomplished through employing mathematical models that reproduce the patient's physiological behavior. However, this forecast should not be exclusive to one organ or physiological detail. It is pertinent to not omit interactions between physiological processes.

A previously presented framework [1-2] is able to dynamically combine models of three different model families: respiratory mechanics, gas exchange and cardiovascular dynamics. To enable interaction between the model families several interfaces allowing the submodels to exchange parameters values were introduced. This enables the MDSS to optimize therapy settings based on a broader picture.

Manuscript received March 25, 2011. This work was supported by the Bundesministerium für Bildung und Forschung (WiMVenT, Grant 01IB10002D).

J. Kretschmer and K. Moeller are with the Institute for Technical Medicine, Furtwangen University, 78054 Villingen-Schwenningen, Germany (phone: 0049-7720-307-4370; fax: 0049-7720-307-4210; e-mail: krj@hs-furtwangen.de).

However, simulations showed to be computationally costly, especially if overall system complexity is increased, i.e. the number of differential equations describing the system. MDSSs need to present the optimized therapy settings in a reasonable time and simulations must be performed faster than real time. Thus, the existing method of computing the complex model system compromises the applicability in MDSSs.

In the present framework all submodels were computed concurrently to avoid temporal inaccuracies. Thereby, all submodels need to be computed with a step size fitting the submodel with highest system dynamics. Therefore, parts of the complex model system are computed with a step size much smaller than necessary, leading to a waste of computing time. Sequential computation should neutralize the disadvantage as long as synchronization of model interaction is ensured. Below, an approach towards sequential computation of the complex model system will be proposed.

II. Methods

A. Interfaces and parameters

The present framework comprises three internal interfaces. Using these interfaces, four parameters values are exchanged between the models (cardiac output CO, intrathoracic pressure P_{th}, air flow $\dot{V}_A$ and alveolar volume V_A) to enable model interaction. Interfaces to the overall model system are provided by the ventilator settings, i.e. inspiratory air flow $\dot{V}_{in}$, respiratory frequency f_R and gas fractions of oxygen $F_{i,O2}$ and carbon dioxide $F_{i,CO2}$. Figure 1 shows the interfaces and exchanged parameter values of the overall simulation.

B. Sequential Computation

In order to lower computing costs by reducing the number of calculation steps per submodel, every model has to be computed solely with an integration step size fitting its dynamic behavior. However, applying a fixed step size for this computation would again lead to wasting precious computing time in moments of low model dynamics. Thus, solver algorithms with automatic step size control have to be employed. The sequential computation lacks direct interaction between the submodels, as they are computed individually. Interface signals typically exchanged in concurrent computation must be precalculated to retain the submodels reaction due to influences from neighboring physiological processes.

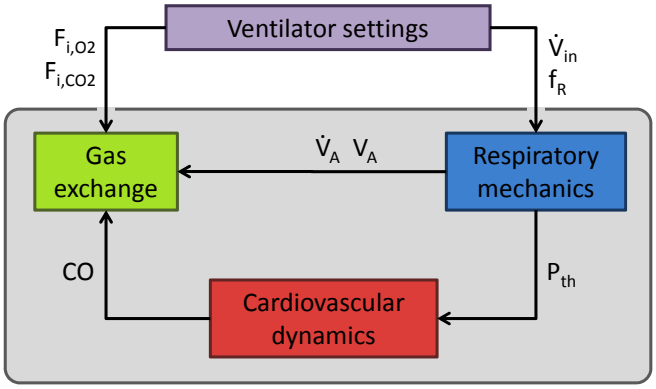

Fig. 1. Model interactions and parameter interfaces used by the framework. Three interfaces between the model families enable model interaction. An additional interface provides the complex model with inputs applied by the ventilator.

To this end, hierarchical model families, i.e. groups of models that are directly descended, have been built. These families comprise models of different complexity but with equal outputs concerning exchanged parameter values for model interaction. In detail, the 19 compartment cardiovascular model by Leaning et al. [3] used in the concurrent simulation has been reduced to an 8 compartment model which shows the same arterial blood pressure and cardiac output. Discrepancy of these values compared to the original model showed to be lower than 0.2%. Also the applied 2nd order viscoelastic RC-Model of respiratory mechanics [4] has a hierarchical descendent by the 1st order RC-Model.

The reduced models were used to precalculate pseudo interface signals for cardiac output, intrathoracic pressure, air flow and alveolar volume. These values were interpolated to feature 20000 data points per second, minimizing errors caused by an excessive data grid, i.e. the solver algorithms cannot be fixed to a predefined set of time steps, so the provided interface data always has to be as close as possible to the actual time step. The interpolated signals were then applied as interfaces to the complex models. Thus, there is no direct interaction between the models, but interaction is simulated through the interface signals computed by the reduced models before. Figure 2 shows the sequential computation procedure.

C. Evaluation

Evaluation of the sequential approach was done by comparing simulation results of concurrent computation with the results computed by the sequential approach. Results evaluated were arterial blood pressure, cardiac output and alveolar oxygen and carbon dioxide partial pressures.

Additionally, the difference of parameter values that were exchanged by model interaction (cardiac output, air flow, alveolar volume and intrathoracic pressure) in concurrent computation compared to the precalculated interface signals in sequential computation was evaluated.

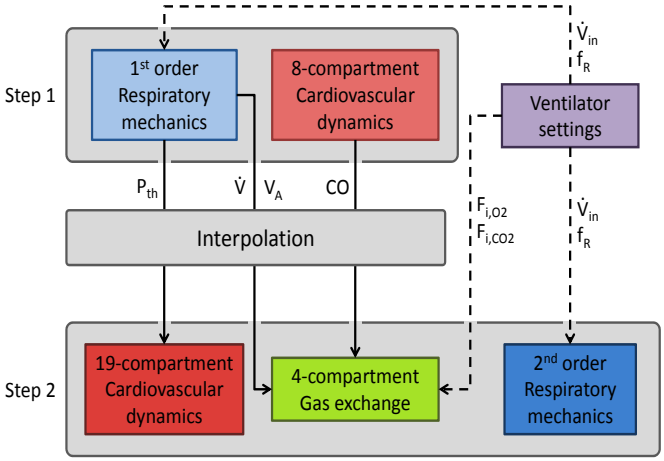

Fig. 2. Sequential computation procedure. Parameters that are exchanged in concurrent computation are precalculated by reduced models of cardiovascular dynamics and respiratory mechanics. After interpolation, these pseudo signals are applied as interfaces to the complex model system to simulate model interaction. Thus, in contrast to concurrent computation, no direct interaction between the submodels is present.

Both concurrent and Step 2 of sequential computation employed 2nd order respiratory mechanics [4], a 4-compartment gas exchange model [5-6] as well as a 19-compartment model of cardiovascular dynamics [3]. Preliminary test showed major simulation error in the gas exchange model. The reasons for these errors were integration steps chosen too large by the solver algorithm. Thereby, changes in the interface signal of cardiac output were mostly ignored. Thus, maximum step size for simulation of the gas exchange model was set to 0.005 seconds.

The model system was simulated for an interval of 50 seconds. Initial values were chosen from an equilibrium system state. Employing these initial values simulation results were reproducible. The simulation was conducted on a standard PC (Q8200, 4x2,33Ghz, 4GB RAM) while the computing times for the concurrent computation and sequential computation were recorded. All models and algorithms were coded in MATLAB (R2008a, The MathWorks Inc., Natick, MA, USA).

I. Results

A. Initial Approach

Results for alveolar oxygen partial pressure are shown in Figure 3. The graph displays reactions of the partial pressure level to alterations in blood flow and alveolar volume. The observed oscillations of partial pressure feature the same frequency as applied for ventilation. Moreover, plateau phases with a frequency equal to the employed heart rate show a reaction to cardiac ejection phases.

Table 1 shows the percentaged simulation error in sequential computation compared to concurrent computation. Computing times for both approaches are shown in Figure 4.

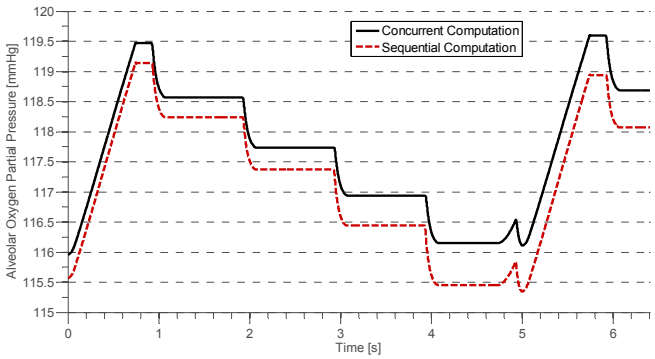

Fig. 3. Comparison of results for alveolar oxygen partial pressure in concurrent and sequential computation. Reactions to alterations in blood flow and alveolar volume can be observed in the graph.

TABLE I
PERCENTAGED ERROR OF SIMULATION RESULTS

Measured Signal	Error
Arterial blood pressure	0.33%
Cardiac output	2.36%
Alveolar oxygen partial pressure	0.41%
Alveolar carbon dioxide partial pressure	2.19%

Percentaged errors of sequential computation compared to results of concurrent computation.

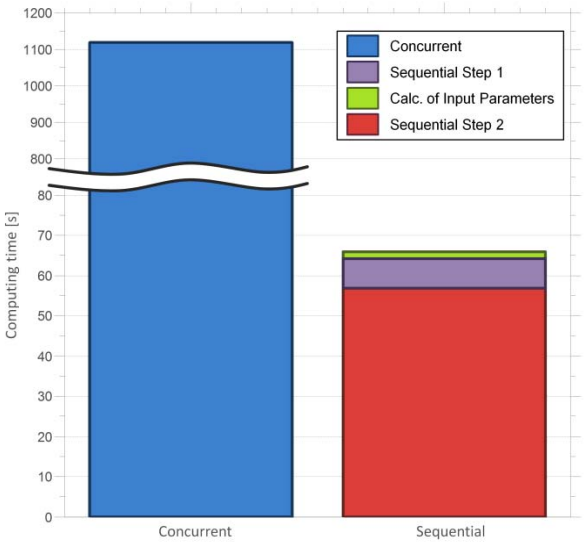

Fig. 4. Comparison of computing times for concurrent and sequential computation. Computing times in sequential approach were recorded for each step (Computation of reduced models, calculation and interpolation of interface parameters to complex model system, simulation of complex model system) individually.

Computing time decreases from 1118 to 66 seconds if sequential approach is employed. Computation of the reduced models ("Step1") and subsequent calculation of interface parameters for the complex model system causes only a small portion of the overall computing costs. Highest simulation error is present in cardiac output (2.36%).

Simulation errors were found to be mostly caused by interface signals differing from the values being present for interaction in the concurrent computation. In sequential approach reduced models were used to calculate interface signals to the complex model system. Despite them featuring model behavior close to the advanced models employed in the concurrent approach, still small discrepancies can be observed in the simulation output. Additionally, no interaction between the reduced models is included in the first step of the sequential approach. In contrast to the model employed in concurrent computation, the 8-compartment model of cardiovascular dynamics does not feature reaction to intrathoracic pressure alterations. This leads to a high discrepancy in the cardiac output parameter signal for the gas exchange model. The interface error generated by the aforementioned factors then affects simulation results in the second computing step. Figure 5 shows simulation results for cardiac output used to influence gas exchange. The graph shows cardiac output that is present in concurrent approach compared to the precalculated interface signal employed in sequential computation. Table 2 presents discrepancies of all precalculated interface signals compared to interaction signals in concurrent approach.

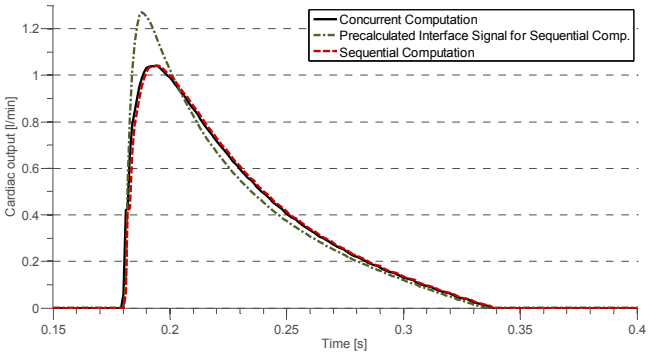

Fig. 5. Cardiac output interface signal in concurrent computation compared to the precalculated signal and the final result in sequential approach. The discrepancy between final results in concurrent and sequential approach compared to the precalculated signal seen in the graph is caused by the lack of interaction in the reduced model employed in step 1 of the sequential computation procedure. The signal discrepancy leads to simulation errors in the gas exchange submodel.

TABLE 2
PERCENTAGED ERROR OF INTERFACE SIGNALS

Interface Signal	Error
Cardiac output	30.81%
Alveolar volume	0.46%
Air flow	17.95%
Intrathoracic pressure	22.57%

Percentaged errors of precalculated interface signals for sequential computation compared to interface signals in concurrent computation.

A. Improved approach

Simulation errors shown in Table 1 have been decreased significantly when 2nd order respiratory mechanics were employed to precacalculate interface signals for sequential computation. Table 3 shows the simulation results of this improved approach.

TABLE 3
PERCENTAGED ERROR OF SIMULATION RESULTS

Measured Signal	Error
Arterial blood pressure	0.05%
Cardiac output	2.01%
Alveolar oxygen partial pressure	0.25%
Alveolar carbon dioxide partial pressure	1.42%

Percentaged errors of sequential computation compared to results of concurrent computation if 2nd order respiratory mechanics are employed to precalculate the interface signal.

B. Additional error causes

In order to test for additional causes of error apart from the ones named above, interface signals computed in the concurrent approach were recorded and applied as input signals to the sequential computation procedure. These signals served as an input for the second step of the procedure instead of the previously used precalculated pseudo signals. This in turn eliminates all errors caused by differing input signals. Results still show noticeable discrepancies, especially in cardiac output. Table 4 shows simulation errors of sequential compared to concurrent approach.

TABLE 4
PERCENTAGED ERROR OF SIMULATION RESULTS

Measured Signal	Error
Arterial blood pressure	0.01%
Cardiac output	2.07%
Alveolar oxygen partial pressure	0.15%
Alveolar carbon dioxide partial pressure	0.31%

Percentaged errors of sequential computation compared to results of concurrent computation if interface signals recorded from concurrent approach are applied to sequential approach.

To test the impact of numerical error of the applied solver algorithms, both the concurrent and sequential approaches were computed with a simple explicit algorithm based on Euler's method using the same integration step size. Results showed simulation error of 0% for all results in the sequential approach.

II. CONCLUSION

The presented approach is capable of computing complex model systems comprising different model families. Direct interaction of the submodels is not applicable due to the employed sequential computation. Thus, interaction is simulated by precalculation of interface signals by reduced models with hierarchical dependency to the employed complex submodels. Simulation error compared to concurrent approach is below 2.5% for all significant simulation results and can be decreased to 2% when 2nd order respiratory mechanics are already employed in the interface signal precalculation.

Additional tests demonstrated that remaining simulation errors are caused by differing interface signals in sequential and concurrent computation as well as numerical errors evoked by using different solver algorithms in these approaches. The achieved simulation errors of at most 2% already allow implementation of the presented approach in medical decision support. Although, discrepancies in input signals could be decreased by improvements in the signal calculation employed in Step 1 of the sequential procedure. One approach would be introducing a third step using the same complex models as employed in Step 2 and exploiting the simulation results of Step 2 as input signals to Step 3.

However, the goal of this work was to decrease computing costs by altering the computing approach. Computing costs were successfully decreased by a factor of 17 which marks a big step towards applicability of combined interacting model families in medical decision support. The presented framework employed physically plausible models, i.e. compartmental description of physiological processes. Utilizing beat-to-beat or breath-to-breath model would naturally lead to a further decrease in computing time; however synchronization of model interaction would be more challenging. Nevertheless, this approach is planned for future investigations. Further decrease in computing time could also be achieved by employment of parallel computing which is already offered by MATLAB.

REFERENCES

[1] J. Kretschmer, A. Wahl, J. Guttmann, and K. Möller, "Dynamic generation of physiological model systems", in *IFMBE Proceedings 2009*, O. Dössel and W. Schlegel, Eds., (Springer Verlag, Munich, 2009), vol. 25/4, pp. 334-7.

[2] J. Kretschmer, A. Wahl, and K. Möller, "Dynamically generated models for medical decision support systems," *Comput Biol Med,* submitted for publication

[3] M. S. Leaning, H. E. Pullen, E. R. Carson, and L. Finkelstein, "Modelling a complex biological system: the human cardiovascular system - 1. Methodology and model description," *T I Meas Control,* vol. 5pp. 71-86, 1983.

[4] L. E. Mount, "The ventilation flow-resistance and compliance of rat lungs," *J Physiol,* vol. 127 (1), pp. 157-67, Jan 28 1955.

[5] H. Benallal, C. Denis, F. Prieur, and T. Busso, "Modeling of end-tidal and arterial PCO2 gradient: comparison with experimental data," *Med Sci Sports Exerc,* vol. 34 (4), pp. 622-9, 2002.

[6] L. Chiari, G. Avanzolini, and M. Ursino, "A comprehensive simulator of the human respiratory system: validation with experimental and simulated data," *Ann Biomed Eng,* vol. 25 (6), pp. 985-99, 1997.