Baroreflex sensitivity: estimated closed-loop versus true open-loop values, determined by a mathematical model

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1 Introduction

Noninvasive estimation of baroreflex sensitivity (BRS, the reflex-induced increase in the interval between heartbeats per mmHg arterial blood pressure rise) relies on the spontaneous fluctuations in blood pressure and heart rate. By using spectral analysis, i.e, computation of the systolic blood pressure (SBP) to interbeat interval (IBI) transfer function, the confounding influence of respiration can effectively be removed by applying high frequency, 0.25 Hz, metronome respiration, well above the frequency band of interest, namely, the low-frequency band (LF, 0.05-0.15 Hz). BRS is expressed as one number, representing the averaged modulus of the transfer function in this band [1,2].

Whether or not the modulus of the blood-pressure-to-interbeat-interval transfer function really represents baroreflex vigor is unclear. Baroreflex induced changes in heart rate, cardiac contractility and peripheral resistance are fed back to the baroreceptors in the form of blood pressure changes. Hence, all clinical measurements are inherently made in a closed-loop control system. If the open-loop transfer function represents true BRS, the closed-loop transfer function is basically an estimator of BRS.

Meaningful clinical applicability of noninvasive closed-loop estimation of BRS depends on the error thus made. To our knowledge, only two groups have investigated this topic [3,4], with different results. Our study aims to contribute to this unresolved issue by means of simulations with a mathematical model, in open-loop and closed-loop conditions, for low and high baroreflex gains in the baroreflex feedback loop to the heart and to the peripheral vasculature, and for physiological and pathological hemodynamic and autonomic conditions.

2 Methods

For our study we elaborated a simulation model on the basis of the TenVoorde model as recently published by TenVoorde and Kingma [5].The used model is outlined in Figure 1, and will henceforth be called the “modified TenVoorde model”. Like the original model, the modified

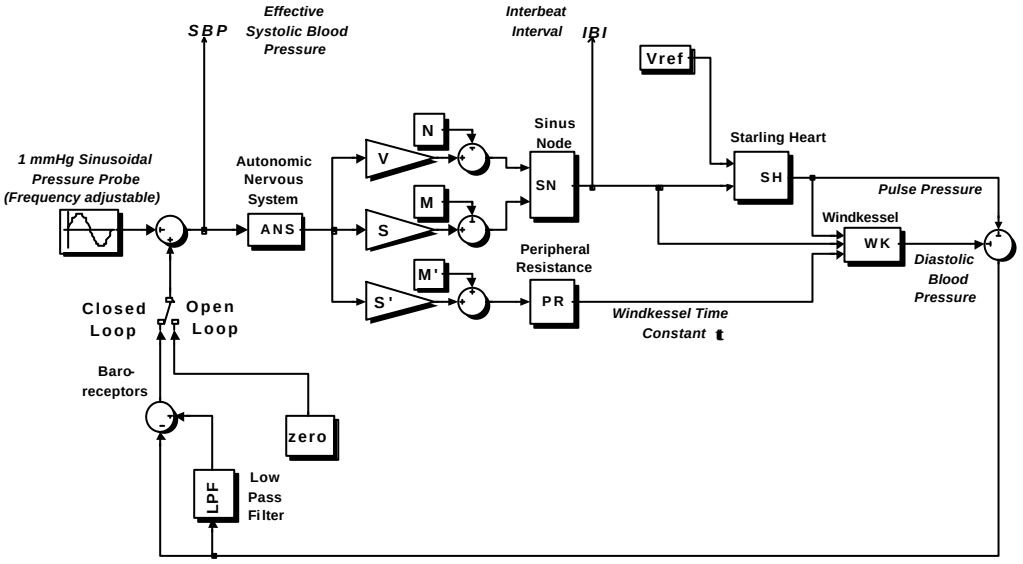

Figure 1: The modified TenVoorde model
The following parameters are adjustable: M = sympathetic tone to the heart according to Rosenblueth and Simeone; M’ = sympathetic tone to the peripheral resistance; N = vagal tone according to Rosenblueth and Simeone; S = sympathetic baroreflex gain to the heart; S’ = sympathetic baroreflex gain to the peripheral resistance; V = vagal baroreflex gain to the heart; V_{ref} = stroke volume at 1000 ms filling time.

TenVoorde model of the human cardiovascular control system consists of a beat-to-beat hemodynamic part — Starling heart, Windkessel — and a continuous neural control part with different dynamics for the sympathetic and vagal branches. For a complete description of TenVoorde model, we refer to [5].

We removed respiration from the original model because this can in practise be moved away from the LF band by high frequency metronome respiration. A pressure probe signal at the baroreceptors was added.This sinusoid signal with a 1 mmHg amplitude that is superimposed on SBP allows for generation of IBI and SBP variability at different frequencies. The quotient of the IBI and SBP amplitudes constitutes the transfer function.

To simulate different physiological and pathological conditions, we made baroreflex gains (V, S and S') and autonomic tones (N, M, M') explicit and adjustable. Finally, a switch was incorporated to open or close the feedback loop, thus facilitating the measurement of true, open-loop, BRS and estimated, closed-loop, BRS values.

The three autonomic tone parameters M, N, M' and cardiac stroke volume V_{ref} were set as two fixed combinations to represent either normal, physiological, or abnormal, pathological, resting conditions. The three baroreflex gains V, S and S' were set at nine different combinations that may be associated with real-life circumstances (see Table 1).

3 Results

Table 1 shows the estimated closed-loop and true open-loop BRS for all simulated combinations, under physiological conditions. The estimated BRS is almost equal to true BRS: the largest difference was 5.1%. In pathological conditions (results not shown), the largest difference was 5.2%

Condition (nine different settings of V, S and S')	**Estim. BRS** [ms/mmHg]	**True BRS** [ms/mmHg]
partial β-adrenergic blockade:	7.75	7.80
partial cholinergic blockade:	2.08	2.09
partial α-adrenergic blockade:	7.21	7.22
weak baroreflex:	2.56	2.70
normal baroreflex:	7.16	7.22
strong baroreflex:	21.02	21.15
strong symp. gain to heart:	5.76	5.83
strong vagal gain:	23.28	22.99
strong symp. gain to the peripheral resistance:	6.98	7.22

Table 1: Simulation results under physiological conditions

4 Discussion

Barbieri and colleagues [3] reported much larger differences between the closed-loop and open-loop values than we have found. Admittedly, their analysis by model identification was based on human real-life data. However, during the actual measurements, respiratory intervals were set through a random-interval breathing technique, which may have introduced mechanical and direct central, rather than baroreflex mediated heart rate variability in the LF band.

Kawada and colleagues [4] were able to measure open-loop transfer functions in rabbits, and found little difference with closed-loop transfer functions. Whether or not this supports our results is not clear, because in these experimental studies the animals were surgically prepared, heavily instrumented, artificially ventilated, and under anaesthesia. Furthermore, rodents are predominantly sympathetic, while humans are predominantly vagal in rest, which renders neurophysiological information obtained by rodent experiments of limited value for the human subject.

5 Conclusion

In conclusion, our study suggests that closed-loop BRS estimation does not introduce relevant measurement errors.

References

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