Optimization of Hypnosis Depth in General Anesthesia Using a PID Controller

Abstract

Anesthesia is used during surgical procedures to avoid complications caused by patient consciousness. One way to measure the depth of hypnosis in general anesthesia is the bispectral index. Here, we present a PID controller and control system based on a paper by Padula et al., both parameterized by the bispectral index. The system is composed of a PK-PD system, a custom controller, and a nonlinear Hill function. After tuning controller gains and time constants, we found that the parameters $K_p = 4$, $T_d = 3.5$, $T_i = 0.001$, and $T_f = 0.15$ created a stable system that fulfilled design criteria such as exhibiting $> 5\%$ overshoot for 10% changes in input, negligible steady state errors for disturbances, and staying within an acceptable bispectral index range under steady state conditions.

I. Introduction

A. Background

General anesthesia is a treatment administered to patients undergoing surgery that puts them in a deep sleep. It is performed to avoid the patient experiencing pain, anxiety, or any breathing complications that could jeopardize the surgery [1]. General anesthesia's effects can be viewed as a combination of three processes: hypnosis, analgesia, and a neuromuscular blockade [2]; we will focus on hypnosis.

Depth of hypnosis is measured using the bispectral index (BIS), a dimensionless control variable ranging from 0 to 100 [2] that is measured through the collection and processing of electroencephalographic signals from the unconscious patient [3]. A value of 0 indicates no brain activity, while 100 indicates full consciousness; for general anesthesia, a BIS between 40 and 60 is required [3].

The administration of anesthesia can be broken into roughly three phases, each of which encodes important design goals. In the induction phase, the patient quickly transitions from conscious to a state with the appropriate depth of hypnosis, while avoiding hypotension due to overshoot [2]. It is important to consider that depth of hypnosis will vary considerably based on patient characteristics like age, height, weight, and sex [2]. In the maintenance phase, the BIS must be maintained within the desired 40-60 range in spite of disturbance from the surgery [2]. Lastly, in the emergence phase, the patient recovers consciousness as drug injection stops [2].

B. Purpose

The purpose of this project is to model the hypnosis administration as a biological control system equipped with a PID controller to provide negative feedback. The goal is to tune a controller that minimizes disturbance effects, has a low settling time, minimizes sensitivity to input changes, minimizes steady state error, and follows the setpoint range (BIS = 40-60) well.

Concretely put, we will optimize proportional gain and derivative and integral time constants to achieve the following goals:

1) For a 10% change in step input, percent overshoot should be less than 5%
2) For a 10% change in step input, settling time to within 2% error should be less than 5 minutes
3) For a change in step input or step disturbance (of amplitude 10-20), zero (or negligible) steady state error
4) Under steady-state conditions, the BIS should never fall out of the setpoint range of 40-60
5) Minimal sensitivity to an added step disturbance and Gaussian noise.

C. Hypothesis

We hypothesize that modification of the feedback mechanism, particularly controller gains and time constants, will allow these goals to be met without modification of other system parameters (such as PK-PD constants).

II. METHODS

A. Model

The hypnosis administration system is modelled as a closed loop, negative unity feedback control system. The design of this system, adapted from the work of Padula et al., is shown in the below schematic:

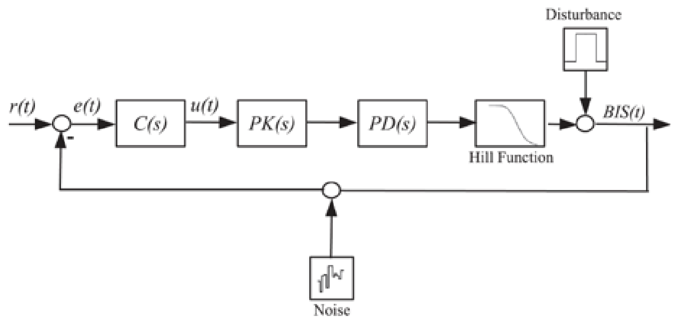

Fig. 1: Control system schematic as provided by Padula et al. [2]

Here, *r(t)* is the system input, *e(t)* is the error signal, *u(t)* is the drug infusion rate, and *C(s)* is the PID controller feedback signal. The other components of the system consist of a pharmacokinetic (PK) - pharmacodynamic (PD) model, which models the anesthetic infusion and diffusion in the body, along with a Hill function that represents the drug's affinity to body receptors [2].

In our project, the controller was a PID controller with a second-order filter from the paper, with a transfer function of [2]:

$$C(s) = K_p\left(1 + sT_d + \frac{T_i}{s}\right)\left(\frac{1}{(T_f s+1)^2}\right)$$

The PK-PD system was modelled as a system of first order differential equations in a three-compartment (blood, muscle, fat) environment, with the derived transfer functions taken from the paper as well [2]:

$$PK(s) = \frac{1}{V_1}\frac{(s+k_{21})(s+k_{31})}{(s+p_1)(s+p_2)(s+p_3)}$$
$$PD(s) = \frac{k_{e0}}{s+k_{e0}}$$

All variables used in the above two equations are defined by the paper and are dependent on the complex interplay of physiological properties of each individual patient. Since the the equations that define these constants were so complex, they will not be included in this report. Additionally, due to the difficulties of modelling the Hill function in Simulink, a sigmoidal approximation was used.

B. Tuning

The four tunable parameters, which will be modified to meet the design specifications outlined in the Hypothesis section are: proportional gain (K_p) and the integral (T_i), differential (T_d), and filter time (T_f) constants [2]. Average physiological values found in Padula et al. were used [2].

To derive the optimal parameters for the PID controller, the Closed-Loop Ziegler Nichols method was first used; however, it produced insufficient results as shown in the Appendix. Thus, three optimization steps for manual tuning were used instead. Each of these steps consisted of one or more sweeps to find the proper order of magnitude for each parameter, followed by sweeps to narrow down the parameters to around 2 significant digits. These sweeps are presented in the table below.

TABLE I: Summary of Optimization Steps

Tuned Parameter(s)	Other Parameters	Values Swept	Results
K_p (Step 1)	$T_d = 0, T_i = 0, T_f = 0$	Powers of 10 from 0.001 to 1000, 0	K_u localized between 1 and 10
		1 to 10 in intervals of 0.5	K_u determined to be around 3.5. Set $K_p = 1.75$
T_d, T_i (Step 2)	$K_p = 1.75$, $T_f = 0$	Powers of 10 from 0.001 to 1000 and 0 for both parameters	(T_d, T_i) localized to between $(0.1, 0)$ and $(10, 0.01)$
		[0.1, 0.3, 1, 3, 10] for T_d, [0, 0.0003, 0.001, 0.003, 0.1] for T_i	(T_d, T_i) localized to between $(1, 0)$ and $(10, 0.001)$. Set $T_i = 0.001$
		1 to 10 in intervals of 0.1	Set $T_d = 3.6$
T_f (Step 3)	$K_p = 1.75$, $T_d = 3.6$, $T_i = 0.001$	Powers of 10 from 0.001 to 1000, 0	T_f localized to between 0.01 and 1
		[0.01, 0.03, 0.1, 0.3, 1]	T_f localized to between 0.03 and 0.3
		0.03 to 0.3 in intervals of 0.03	Set $T_f = 0.15$
K_p, T_d (Step 4, re-tuning)	$T_i = 0.001$, $T_f = 0.15$	1 to 10 in intervals of 0.5 for both parameters	(K_p, T_d) localized to between $(3.5, 2.5)$ and $(6, 4)$
		3.5 to 6 in intervals of 0.1 for K_p, 2.5 to 4 in intervals of 0.1 for T_d	Set $K_p = 4$ and $T_d = 3.5$

First, as per the Closed-Loop Ziegler Nichols method, K_u (ultimate gain) was found, and K_p was set to $0.5K_u$. Then, T_i and T_d were set together, followed by setting T_f for noise. For each sweep, parameter values were evaluated based on the criteria listed in the Purpose section. As this original PID controller failed steady state error and settling time criteria, K_p and T_d were tuned again using another optimization step, leading to the final values presented in the results section.

III. Results

A. Final PID Model

K_u was found to be roughly 3.5 after a magnitude sweep from 0.001 to 1000 and a linear sweep between 1 and 10. The final values for the parameters were

$$K_p = 4.0, T_i = 0.001, T_d = 3.5, \text{ and } T_f = 0.15.$$

Graphs documenting the progress of the optimization steps, as well as testing on extreme patient models, can be found in the Appendix.

B. Evaluation of Design Criteria

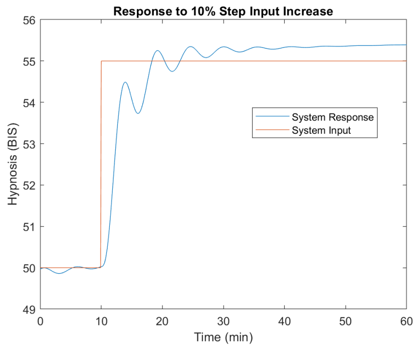

Fig. 2: System response for a 10% step input increase. Percent overshoot was 2.31% and settling time was 6.7 minutes.

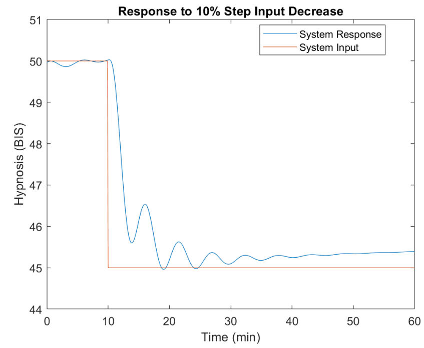

Fig. 3: System response for a 10% step input decrease. Percent overshoot was 3.42% and settling time was 7.3 minutes.

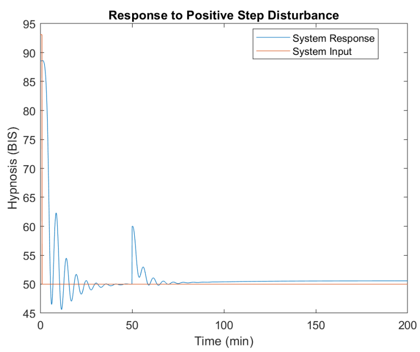

Fig. 4: System response for a 20% positive step disturbance.

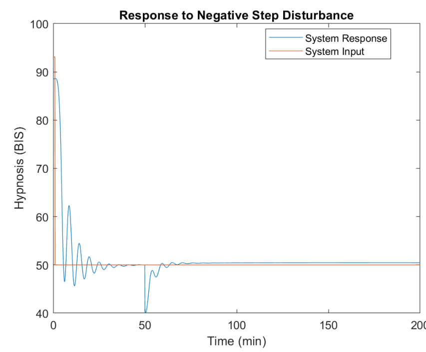

Fig. 5: System response for a 20% negative step disturbance.

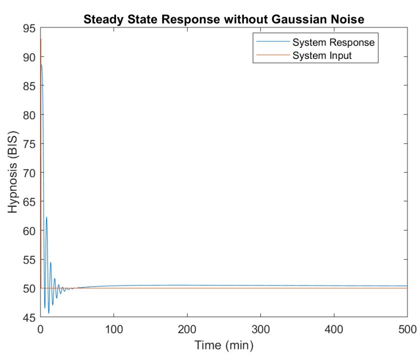

Fig. 6: Steady state operation of our controller without noise. Negligible steady state error occurs.

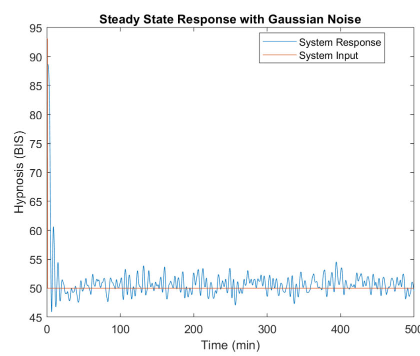

Fig. 7: Steady state operation of our controller with Gaussian noise. Values remain within the setpoint range of 40-60.

C. Bode Plot

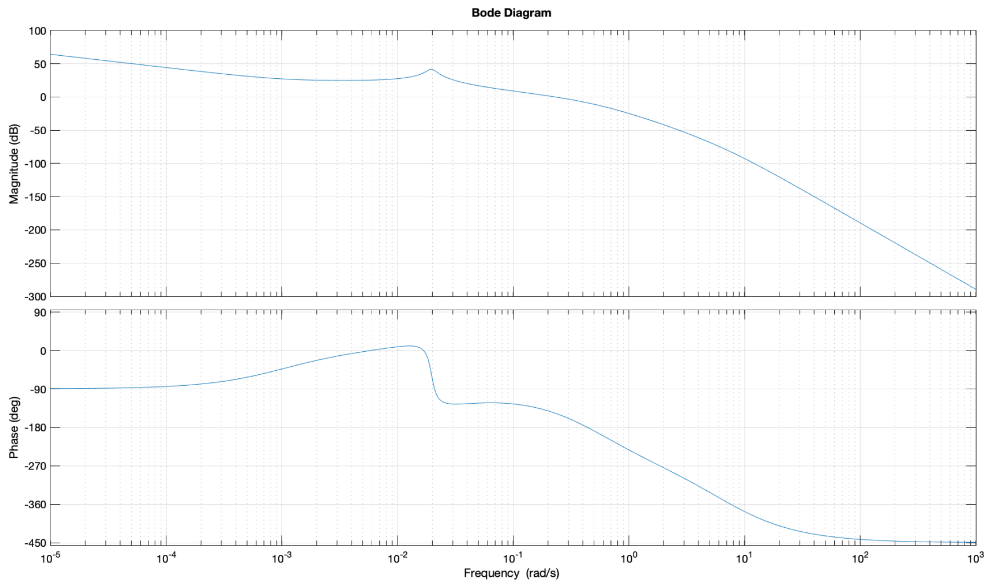

Fig. 8: Bode plot for the entire control system under our optimal PID parameters. The linearization of the input happens immediately. The system input is the step input used for parameter tuning.

D. Nyquist Plots

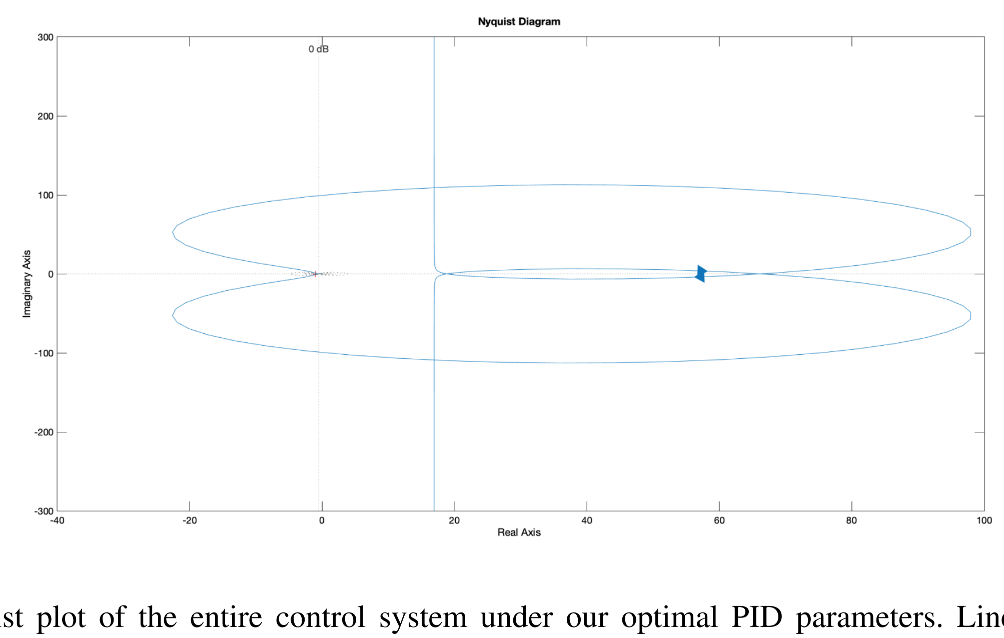

Fig. 9: Nyquist plot of the entire control system under our optimal PID parameters. Linearization of the input happens immediately. The system input is the step input used for parameter tuning.

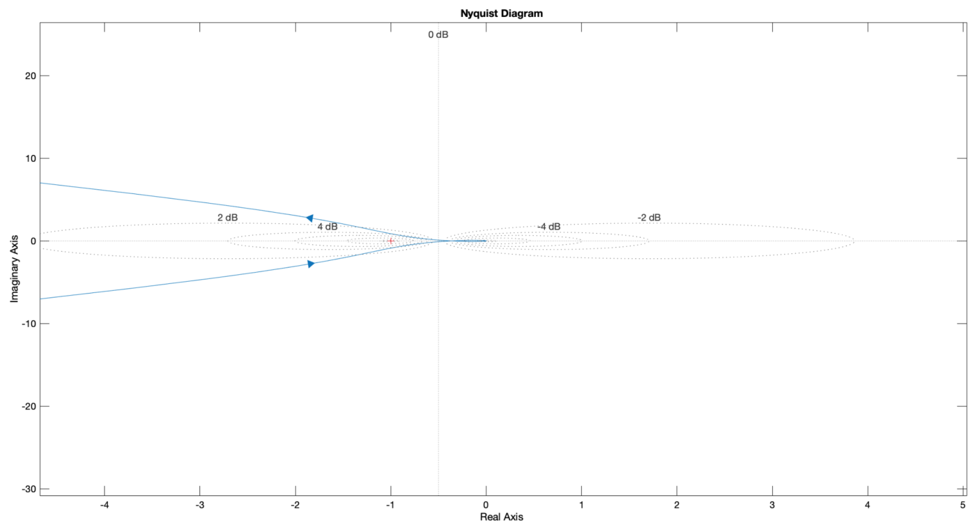

Fig. 10: Close-up of the Nyquist plot around the point (-1, 0), shown as a red +. Note that there are no encirclements of (-1, 0).

IV. Discussion

A. Extent of Achievement of Desired Goals

Ultimately, our tuning and analysis of PID controller gains and time constants was sufficient to meet most of the design criteria to some extent, though not the extent specified in the Purpose section. Our initial strategy employed the use of Closed-Loop Ziegler Nichols methods to tune the proportional gain and a parametric sweep to tune the time constants. However, this strategy produced poor steady state error, a high settling time, and a high percent overshoot. We then chose to manually retune the proportional gain and derivative time constants, which achieved better results.

The first two goals were to have a low 2% settling time (less than five minutes) and low percent overshoot (less than 5%) for a 10% change in step input. This goal was achieved, but only for the percent overshoot. For a 10% decrease in step input we obtained a 3.42% overshoot and a 7.3 minute settling time; while the former result is sufficient, the latter is worse than our intended goal of 5 minutes. For a 10% increase in step input, we obtained a settling time of 6.7 minutes and a percent overshoot of 2.31%.

The failure to reach goals for 2% settling time in both cases suggests that our system may be underdamped; this result coincides with the slow oscillations of the system about equilibrium at steady-state, which is characteristic of underdamped systems. Regarding percent overshoot, the excellent results for a 10% increase in step input are promising; this is a particularly important number to contain. An increase in step response corresponds to the induction phase of anesthesia, and overshoot here can result in potentially fatal hypotension [2], which our controller design avoids altogether. Similarly, a good overshoot for a decrease in step input suggests that our system sensitivity to changes in input is adequately low.

The other three goals were to have minimal steady state error for a change in step input or disturbance, to have BIS within 40-60 at steady state, and to minimize sensitivity to fluctuations in input. These goals were all successfully achieved. As Fig. 6 demonstrates, our optimal parameter set allows BIS to be maintained at around 50 with extremely small periodic deviations, which constitute a negligible steady state error. Similarly, Figs. 4-7, which illustrate the system's noise and disturbance responses, both suggest that sensitivity is not a major concern or detriment to the controller's usability.

B. Analysis of System Stability

For our optimal PID control parameters, the system is absolutely stable for relevant inputs. The system will undergo slow oscillations of negligible amplitude about equilibrium at steady-state (making it hard to visualize on a figure). Similar responses occur regardless of the initial and final amplitude of the step input across physiologically relevant ranges (initial BIS of 80-100; final BIS of 40-60).

The frequency response of the system is also absolutely stable, as indicated by the Bode (Fig. 8) and Nyquist (Fig. 9) plots. For the Bode plot, the gain margin is -8.86 dB, while the phase margin is (-180+147)º = -33º. Since both values are negative, this suggests that the system is indeed stable for a periodic input. This is confirmed by the Nyquist plot, in which all encirclements are to the right of (-1, 0), which indicates that the system satisfies the Nyquist criterion for stability (noting that there are no poles in the right hand plane).

C. Comparison to Literature Results

The paper referenced for our system design by Padula et al. contains identified controller gains for their own PID controller. The following values were assigned, in the case of optimizing following a variable homeostatic setpoint [2]:

$$K_p = 0.0622, T_i = 333.44, T_d = 34.37, T_f = 0.499$$

These are considerably different from the optimal parameters we identified:

$$K_p = 4.0, T_i = 0.001, T_d = 3.5, T_f = 0.15$$

Two reasons explain this divergence. Firstly, our criteria for optimality were considerably different. The paper utilized a global optimization algorithm specifically to minimize the integrated absolute error, with the intention of reducing rise time and percent overshoot. Compared to our criteria, there was also a much larger emphasis on disturbance rejection [2]. Moreover, the paper focused on the BIS value following changes in homeostatic set point, with less concern about steady-state error while our parameter choices were focused on minimizing deviation from a single set point.

The second reason for a discrepancy in results is that our control system model is not identical to the paper. One notable change is that we used a sigmoid instead of a Hill function, as this is more compatible with Simulink. Another change is that the paper considered parameters for a wide range of patients, while we instead focused on a single "average" patient identified in [2] and used their parameters for our system input. Both changes have a substantial impact on the problem being solved, and thus the optimal parameters that are obtained.

V. Conclusion

In this report, we designed and tuned a PID controller to optimize the depth of hypnosis in general anesthesia, with the goals of minimizing error, percent overshoot, settling time, and disturbance/noise responses. The optimal parameters we identified struggled to meet settling time goals, performed well for percent overshoot, and were successful in minimizing error and disturbance/noise responses. The chosen parameters granted the system absolute stability in both step and sinusoidal responses. Parameters differed from literature values due to a different model and different design criteria. Ultimately, we conclude that our hypothesis was mostly successful; we met most of our goals, but failed to meet the 2% settling time requirements while tuning only PID controller parameters.

REFERENCES

[1] "General anesthesia."

[2] F. Padula, C. Ionescu, N. Latronico, M. Paltenghi, A. Visioli, and G. Vivacqua, "Optimized pid control of depth of hypnosis in anesthesia," *Computer Methods and Programs in Biomedicine*, vol. 144, p. 21–35, 2017.

[3] S. Mathur, "Bispectral index," Sep 2021.

Appendix A
Attribution Table

Talha	**Kevin**
Wrote introduction (background, purpose, hypothesis)	Wrote abstract (all)
Wrote discussion (evaluation, comparison to literature, stability analysis)	Wrote methods(model, tuning)
Wrote conclusion (all)	Wrote results (all tables and plots except Bode/Nyquist)
Built model in Simulink	Built model in Simulink
Generated and formatted Bode and Nyquist plots	Did the parameter tuning
Edited the report	Formatted the report in LaTeX
Other miscellaneous things	Other miscellaneous things

APPENDIX B
ADDITIONAL FIGURES

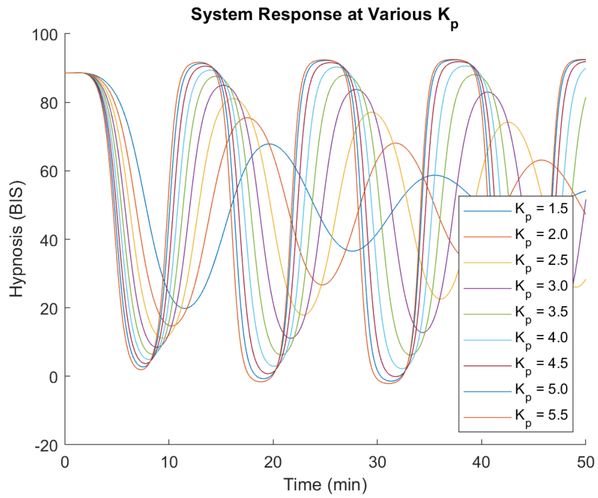

Fig. 11: Responses for various values of K_p while finding K_u. All other parameters are set to 0.

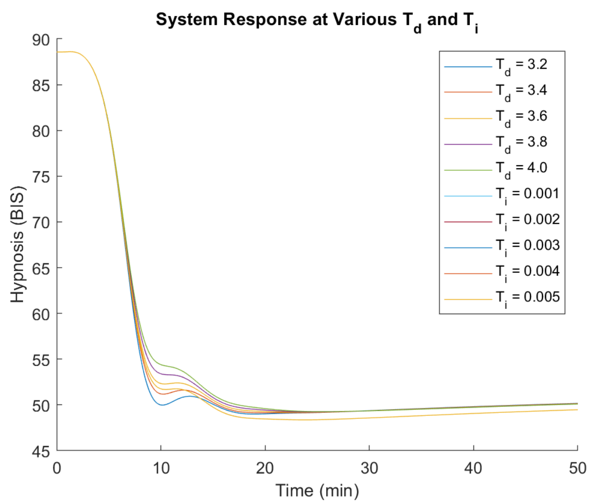

Fig. 12: Responses for various values of T_d and T_i found while tuning. K_p is set to 1.75 and T_f is set to 0. When not being varied, T_d is set to 3.6 and T_i is set to 0.001.

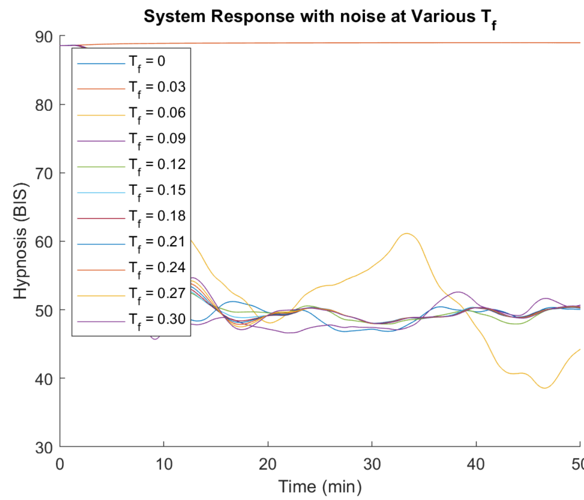

Fig. 13: The performance of T_f with Gaussian noise. All parameters are set to their Step 3 values.

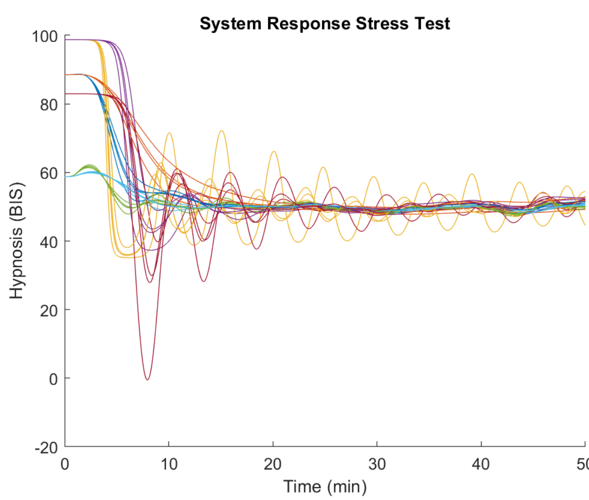

Fig. 14: A stress test conducted using the most extreme values for physiological parameters. Note that in most cases, the BIS is still kept within the required range of 40-60.

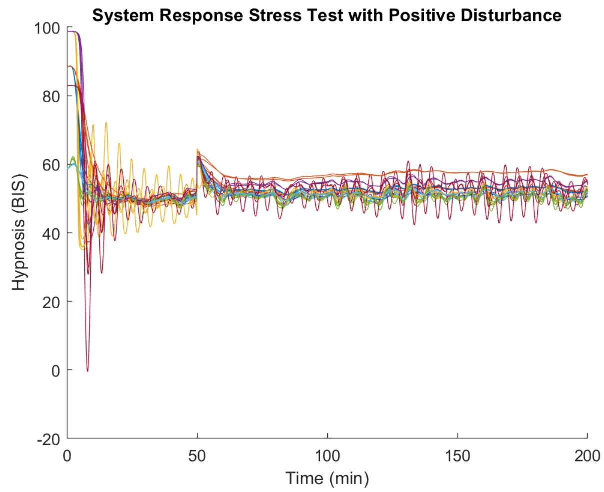

Fig. 15: The same stress test as above, but with a positive disturbance of 20 at t=50. Surprisingly, this actually seems to stabilize the system.

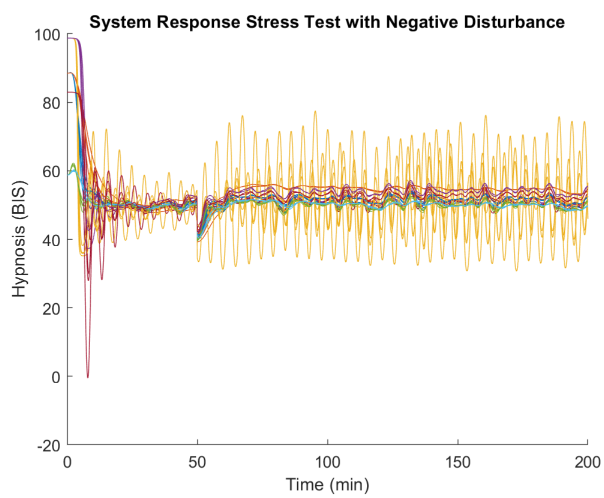

Fig. 16: The same stress test as above, but with a negative disturbance of 20 at t=50. This destabilizes the system, which shows that there may be some asymmetric effects occurring, and could be an area of investigation for the future.