

# A Class of Simple Biomolecular Antithetic Proportional-Integral-Derivative Controllers

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The Manuscript Microscope Sentence Audit is a research paper introspection system that parses the text of your manuscript into minimal sentence components for faster, more accurate, enhanced proofreading.

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**Manuscript Source:** <https://www.biorxiv.org/content/10.1101/2021.03.21.436342v1>

**Manuscript Authors:** Maurice Filo & Mustafa Khammash

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### Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title      **A Class of Simple Biomolecular Antithetic  
Proportional-Integral-Derivative Controllers**

**S1 [001]      Abstract**

**S1 [002]**      Proportional-Integral-Derivative (PID) feedback controllers have been the most widely used controllers in the industry for almost a century.

Proportional-Integral-Derivative ...  
... (PID) ...  
... feedback controllers have been the most widely used controllers ...  
... in the industry ...  
... for almost a century.

**S1 [003]**      This is mainly due to their simplicity and intuitive operation.

This is mainly ...  
... due to their simplicity ...  
... and intuitive operation.

**S1 [004]**      Recently, motivated by their success in various engineering disciplines, PID controllers found their way into molecular biology.

Recently, ...  
... motivated ...  
... by their success ...  
... in various engineering disciplines, ...  
... PID controllers found their way ...  
... into molecular biology.

**S1 [005]**      In this paper, we consider the mathematical realization of (nonlinear) PID controllers via biomolecular interactions in both the deterministic and stochastic settings.

In this paper, ...  
... we consider the mathematical realization ...  
... of ...  
... (nonlinear) ...  
... PID controllers ...  
... via biomolecular interactions ...  
... in both the deterministic ...  
... and stochastic settings.

**S1 [006]**      We propose several simple biomolecular PID control architectures that take into consideration the biological implementation aspect.

We propose several simple biomolecular PID control architectures ...  
... that take ...  
... into consideration the biological implementation aspect.

**S1 [007]** We verify the underlying PID control structures by performing a linear perturbation analysis and examine their effects on the (deterministic and stochastic) performance and stability.

We verify the underlying PID control structures ...  
... by performing a linear perturbation analysis ...  
... and examine their effects ...  
... on the ...  
... (deterministic ...  
... and stochastic) ...  
... performance ...  
... and stability.

**S1 [008]** In fact, we demonstrate that different proportional controllers exhibit different capabilities of enhancing the dynamics and reducing variance (cell-to-cell variability).

In fact, ...  
... we demonstrate ...  
... that different proportional controllers exhibit different capabilities ...  
... of enhancing the dynamics ...  
... and reducing variance ...  
... (cell-to-cell variability).

**S1 [009]** Furthermore, we propose a simple derivative controller that is mathematically realized by cascading the antithetic integral controller with an incoherent feedforward loop without adding any additional species.

Furthermore, ...  
... we propose a simple derivative controller ...  
... that is mathematically realized ...  
... by cascading the antithetic integral controller ...  
... with an incoherent feedforward loop ...  
... without adding any additional species.

**S1 [010]** We demonstrate that the derivative component is capable of enhancing the transient dynamics at the cost of boosting the variance, which agrees with the well known vulnerability of the derivative controller to noise.

We demonstrate ...  
... that the derivative component is capable ...  
... of enhancing the transient dynamics ...  
... at the cost ...  
... of boosting the variance, ...  
... which agrees ...  
... with the well known vulnerability ...  
... of the derivative controller ...  
... to noise.

**S1 [011]** We also show that this can be mitigated by carefully designing the inhibition pathway of the incoherent feedforward loop.

We also show ...  
... that this can be mitigated ...  
... by carefully designing the inhibition pathway ...

... of the incoherent feedforward loop.

**S1 [012]** Throughout the paper, the stochastic analysis is carried out based on a tailored moment-closure technique and is also backed up by simulations.

Throughout the paper, ...  
... the stochastic analysis is carried out based ...  
... on a tailored moment-closure technique ...  
... and is also backed up ...  
... by simulations.

## **S2 [013] 1 Introduction**

**S2 [014]** One of the most salient features of biological systems is their ability to adapt to their noisy environments.

One ...  
... of the most salient features ...  
... of biological systems is their ability ...  
... to adapt ...  
... to their noisy environments.

**S2 [015]** For example, cells often regulate gene expression to counteract all sorts of intrinsic and extrinsic noise in order to maintain a desirable behavior in a precise and timely fashion.

For example, ...  
... cells often regulate gene expression ...  
... to counteract all sorts ...  
... of intrinsic ...  
... and extrinsic noise ...  
... in order ...  
... to maintain a desirable behavior ...  
... in a precise ...  
... and timely fashion.

**S2 [016]** This resilience toward undesired disturbances is often achieved via feedback control that has proved to be ubiquitous in both natural (e.g. [1–3]) and engineered systems (e.g. [4,5]).

This resilience toward undesired disturbances is often achieved ...  
... via feedback control ...  
... that has proved ...  
... to be ubiquitous ...  
... in both natural ...  
... (e.g. ...  
... [1–3]) ...  
... and engineered systems ...  
... (e.g. ...  
... [4,5]).

**S2 [017]** In fact, synthetically engineering biomolecular controllers is gaining a wide attention from biologists and engineers (e.g. [6–14]).

In fact, ...  
... synthetically engineering biomolecular controllers is gaining a wide attention ...  
... from biologists ...  
... and engineers ...  
... (e.g. ...  
... [6–14]).

**S2 [018]** A standard general setup for feedback controllers is depicted as a block diagram (refer to Box 1: A Primer on Block Diagrams) in Panel A of Figure 1. The “Plant” block represents the process to be controlled.

A standard general setup ...  
... for feedback controllers is depicted ...  
... as a block diagram ...  
... (refer ...  
... to Box 1: ...  
... A Primer ...  
... on Block Diagrams) ...  
... in Panel A ...  
... of Figure 1. The “Plant” ...  
... block represents the process ...  
... to be controlled.

**S2 [019]** It can be actuated through its input, denoted here by  $u$ , to dynamically manipulate its output of interest, denoted here by  $y$ .

It can be actuated ...  
... through its input, ...  
... denoted here ...  
... by  $u$ , ...  
... to dynamically manipulate its output ...  
... of interest, ...  
... denoted here ...  
... by  $y$ .

**S2 [020]** The objective of such control systems is to design a feedback controller that automatically actuates the plant in a smart autonomous fashion and guarantees that the output  $y$  meets certain performance goals despite the presence of disturbances in the plant.

The objective ...  
... of such control systems is ...  
... to design a feedback controller ...  
... that automatically actuates the plant ...  
... in a smart autonomous fashion ...  
... and guarantees ...  
... that the output  $y$  meets certain performance goals ...  
... despite the presence ...  
... of disturbances ...  
... in the plant.

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