Reviewer's report

Title: On integrative cancer biology approaches to therapeutic gain

Version: 1 Date: 22 October 2005

Reviewer: William Hazelton

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The manuscript contains several points of interest. However, it needs serious re-writing in simple explanatory language, eliminating all of the jargon and generalities. The abstract begins by introducing a number of acronyms that are not defined until later. Worse, it is full of phrases that have meaning to the author, but that are not readily understood without trying to decipher the full manuscript.

Examples of jargon include phrases such as "solved cancer counterpart guide", "cell death surrogates", "fractionated patients", "models which connect anti-cancer agents to a critical, capable of reversing, determinant of treatment failure". The paper is full of these needlessly obscure phrases, and needs re-writing. There are also many general statements with no substance, or that are obvious, such as the statement "Control system concepts may carry over directly, however." when talking about moving from linear to non-linear systems. But the example that follows is not correct.

The assertion "For example, because process controllability always increases as the number of inputs increases ..." is not necessarily true. New inputs may not span a larger basis in the model so they may make no difference at all in process controllability. (Furthermore, adding inputs may be detrimental to control even if they do increase the degrees of freedom for control in a model. Imagine trying to control a car with the usual steering wheel, brakes, and gas pedal. Now increase inputs by adding a steering wheel, brakes, and gas pedal that control each wheel separately. Technically there may be more controllability, but just trying driving the car - it will be totally uncontrollable.) The point is that the author does not address some important issues in control theory or modeling such as over parameterization, approaches to parameter estimation, or objective measures for improving parameter estimates such as likelihood methods. However, I think the author's discussion of two approaches for incorporating control theory to influence cancer treatment is interesting, and may prove useful if it can be presented through simple exposition.

Organizational suggestions: What is the thesis? How do the methods address the thesis. The thesis appears to be that there are two methods for using control theory in cancer treatment. However, more thought needs to go into how to explain these approaches clearly. The methods as stated in the abstract do not address the thesis. It should be stated at the beginning and in the abstract that the purpose of this paper is not to solve control problems in cancer therapy, but to formulate them. Given this, a clear presentation is required.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the
author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No