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# Is it Prostate Cancer ?

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**Given a set of PSA values, we answer the question: "Is its information content typical for the existence of a prostate cancer, or not ?" Our findings support PSA screening.**

Prostate cells, benign or malignant or both together, cause the blood to contain the Prostate-Specific Antigen (PSA), whose concentration may be regularly measured. We describe how to extract parameter values which are characteristic for specific properties of the producing cells, but otherwise independent of environmental influences, as long as these are approximatlely constant in time.
It is important to note that the Least Squares analysis we are using, does not only allow for the determination of the cell-parameter values of interest, but also for a quantitative appreciation ("goodness of fit") of the empirical validity of the assumptions made. Inadequate conjectures are likely to be unveiled.
Our basic assumption is that the measured PSA concentration is caused by one or two growing cell populations which develop, at least for some initial time span, uninfluenced and independently from each other with characteristic, constant cell reproduction times, the doubling times, *DT1* and *DT2*. Since such populations grow, each, according to an exponential law, our measured PSA concentration, PSA(t), is thus a superposition of two exponentials

$$PSA(t) = a \cdot 2^{t/DT1} + b \cdot 2^{t/DT2} \quad . \qquad (1)$$

The task is two-fold. First: Given a set of measured PSA(t) values. Find the constants *DT1* and *DT2* without any (previous) knowledge of the values of *a* and *b*, and give a quantitative estimate (standard deviation, std) of the reliability of the results. This is a purely mathematical application, independent of any medical considerations, see [1, 2].
Second: Show that formula (1) represents real patient data, calibrate *DT2* versus diagnostic findings, and apply the method to early diagnosis of prostate cancer.

Figure 1 (top) shows the agreement of 10 measured PSA data points with the curve calculated from the formula (1). It establishes the action of a second, faster growth mechanism, and demonstrates, that the method is capable to predict this mechanism already 20 months earlier, on the basis of the first 7 data points, as represented in the bottom of *Fig.* 1.

Out of a random collection[3] of measured PSA data, 36 sets have been chosen, and analyzed with formula (1).
The reader is invited to consult the corresponding graphs which show the reductions of the various PSA time-evolutions to their exponential components. They are available from www.psadynamics.com (→ "Wissenschaftliche Grundlagen", in english)

The resulting frequencies of the components' doubling times are displayed in *Fig*. 2; *DT1* in green, *DT2* in red.

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For the data of a single person, it is natural (and true) that $0 < DT2 < DT1$ for $DT1 > 0$. However, for a collection of doubling times from different persons, this is no more applicable. It is thus a non-trivial finding, that there is a region of short doubling times, as displayed in the bottom part of *Fig*. 2, where the red and green events (the *DT2* and *DT1* values) are entirely separated. This is the first and main message of this paper.

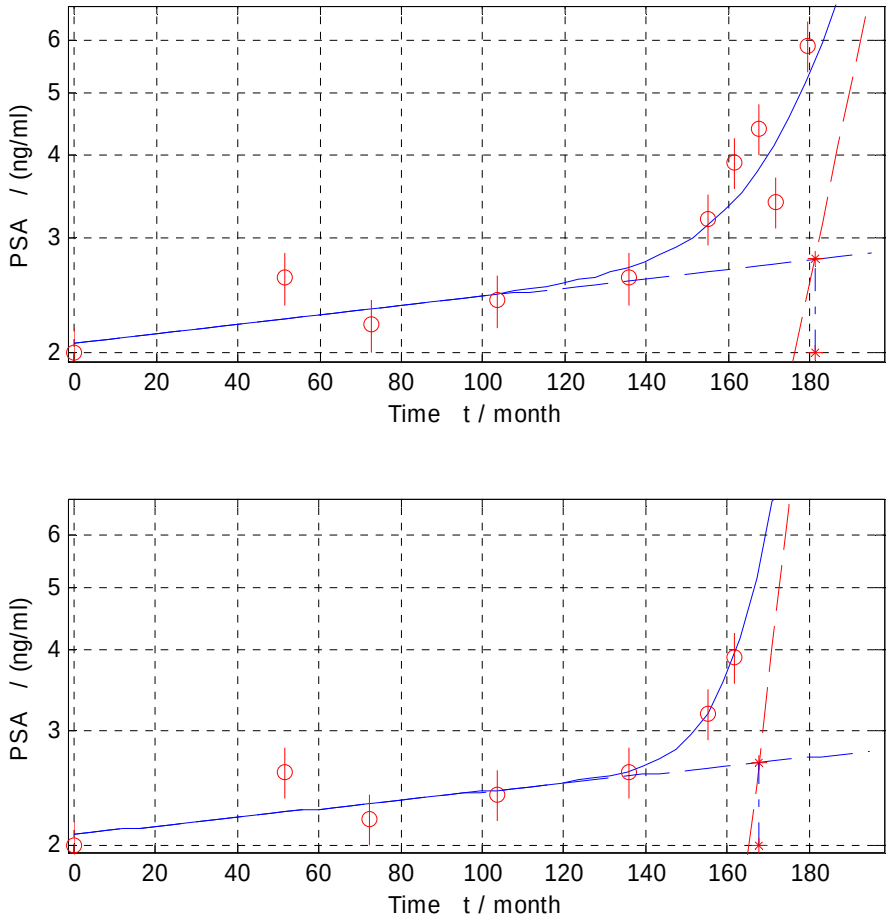


*Fig. 1. Agreement and prediction.*
*Top:* Measured PSA values show good statistical agreement with the blue curve, calculated from formula (1). (Points ± 9 % std assumed, resulting $\chi^2$ /d = 2.6).
In the (semi-log) plot, the exponential components are represented by the straight, dashed lines. Evidence for the existence of a second growth processs comes from the value found for *DT2* = 10 ± 4 months, which is incompatible with the value found for *DT1* = 430 months.
*Bottom:* This conclusion could have been reached 20 months earlier ! The analysis, based on the first 7 PSA values, would have predicted *DT2* = 6 ± 5 months (in perfect statistical agreement), and would have led to the same conclusion.
The patient is 49 years old. Note that all of the PSA values, in this part of the figure, are below (the widely used reference value of) 4 *ng/ml*. (Figure: $\chi^2$ /d = 0.95).

We note in passing, that only an adequate mathematical procedure is able to produce this clean separation.

In order to arm this formal result with diagnostic power, we have calibrated *DT* against a new and independent PSA data set[3] with a total of 411 patients, having a diagnosis of a Benign Prostatic Hyperplasia (BPH), and no prostate cancer. None of the doubling times was shorter than 27 months. The second main result of this paper thus is, that the "DT1-free" region of *Fig*. 2 is also "BPH free".

To conclude, we answer the question, posed in the abstract, with reference to the set of PSA values in *Fig. 1*: Its information content, expressed by the value of $DT2 = 10 \pm 4$ months, which falls well into the "DT1-free region", is typical for a cell-reproduction process other than BPH, even though the PSA values are low.

Early PSA screening helps by providing early data points as needed by the algorithm to disentangle the processes.

COMPETING INTERESTS STATEMENT
The authors D.D and H.-J.G are consultants of Praxis für Prävention, D-Freising.
Besides this, the authors declare to have no competing final interests.

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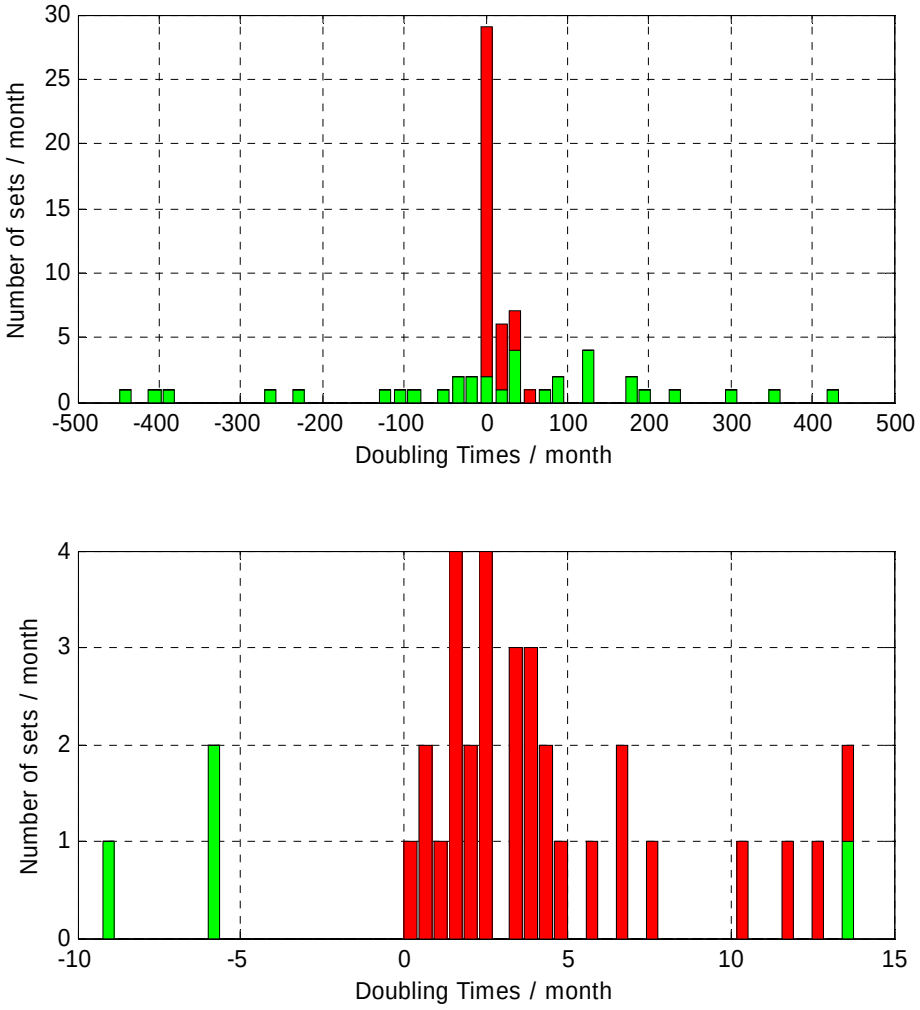


*Fig. 2. The first main finding of this work. Separation of the cell population's properties.*
*Top:* Measured PSA doubling times *DT1* due to the first cell population are distributed over a wide range (34 cases of 36 reach from -500 to +500 months), whereas those from the unveiled second population (*DT2*) cluster around small values.
*Bottom:* Zoom of the top subpicture. Clustering of the *DT2* values.
In the range from 0 to 13 months, 30 (of 36) values of *DT2* are located, in contrast to none (of 36) of *DT1*. With high probability, they are not BPH events.