Can this new glycemia metric tell me if my critical care patients are going to live or die?

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INTRODUCTION

Critically ill patients often exhibit abnormal glycemia due to the severity of their illness. High blood glucose levels and high glycemic variability have both been independently associated with increased mortality in these patients. More recently, it was hypothesized that glucose complexity may also be associated with increased mortality.

Two studies have used Detrended Fluctuation Analysis (DFA) to investigate glucose complexity in continuous glucose monitoring (CGM) data from critically ill patients (Lundelin 2010, Brunner 2012). Both studies reported an association between glucose complexity and mortality in critically ill patients. The aim of this study was to extend the knowledge of glucose complexity in critically ill adults by investigating the effects of CGM device type/calibration and CGM sensor location on DFA results.

Patients

Table 1: Cohort Demographics

Patients	10
Age (years)	51 [39 - 64]
Sex (M/F)	5/5
APACHE II	24 [17 - 27]
APACHE III	85 [52 - 99]
SAPS II	52 [30 - 59]
LOS (days)	20 [10 - 33]
Outcome (L/D)	6/4
Diabetes (None/T1/T2)	10/0/0

This study used CGM data from 10 patients admitted to the Christchurch Hospital ICU. Patients wore Medtronic Guardian and Medtronic iPro2 devices on their abdomen, and a second iPro2 device on their thigh. This configuration allowed the effects of CGM device type and sensor location to be investigated, for each participant.

METHODS

Monofractal Detrended Fluctuation Analysis (DFA)

"The monofractal structure of biomedical signals are defined by a single power law exponent, and assumes that scale invariance is independent on time and space" Ihlen 2012

Monofractal DFA results in an exponent, H - the Hurst coefficient, which describes the scaling properties of a time series

$$X(ct) = c^{H}X(t)$$

The larger the H, the less 'complex' the signal is

Failing regulatory system → **Lower Glucose complexity =** Higher Hurst coefficient → Mortality?

Multifractal Detrended Fluctuation Analysis (MFDFA)

If scaling properties of the signal are not independent on time and space, multifractal DFA should be used to analyze the signal. For multifractal signals, H is dependent on q-order statistical moments and the complexity of the signal is better described by the 'Multifractal Spectrum'

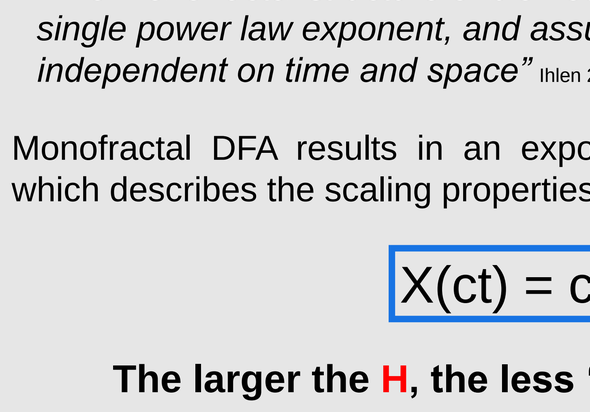

Figure 1: CGM signal displaying multifractal properties with a Hurst coefficient that varies with q order statistical moments

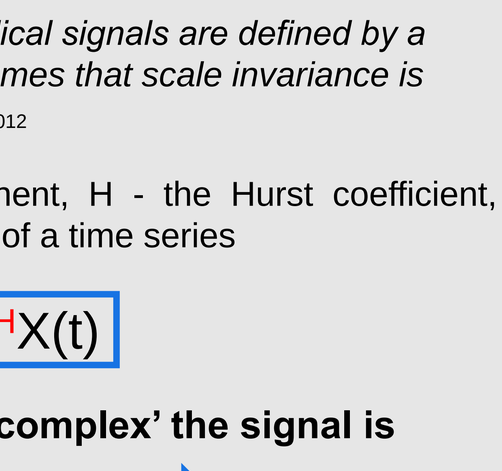

Figure 2: Multifractal spectrum of a mono and multifractal signal, data supplied by Ihlen 2012

RESULTS

DFA

Table 2: Monofractal DFA cohort results

Analysing calibrated SG data			
CGM device type (both in abdomen)			
	Guardian	**iPro2**	**P value**
Number of data sets	9	8	
Scaling exponent (H)	1.43 [1.37 - 1.48]	1.56 [1.46 - 1.60]	
Difference in H (iPro2 - Guardian)	0.10 [0.03 - 0.20]		0.08
Sensor location (both iPro2)			
	Abdomen	**Thigh**	**P value**
Number of data sets	8	9	
Scaling exponent (H)	1.56 [1.46 - 1.60]	1.52 [1.50 - 1.61]	
Difference in H (Thigh - Abdomen)	0.04 [-0.06 - 0.11]		0.64
Outcome mortality			
	Lived	**Died**	**P value**
Number of data sets	17	9	
Scaling exponent (H)	1.51 [1.46 - 1.57]	1.47 [1.39 - 1.59]	0.50

Consistently higher H values from iPro2 data compared to Guardian data.

No significant difference in sensor location or mortality results

MFDFA

There was no clear associations between any of the CGM parameters tested and the shape, width or location of the multifractal spectrums (Figure 3). Furthermore, on several occasions Monofractal and Multifractal DFA gave contradictory results and indicate that future DFA results should be interpreted with care (Figure 4).

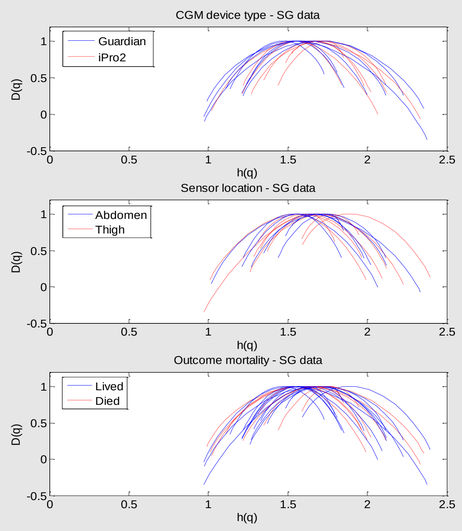

Figure 3: Multifractal spectrums comparing CGM device types, sensor locations and outcome mortality

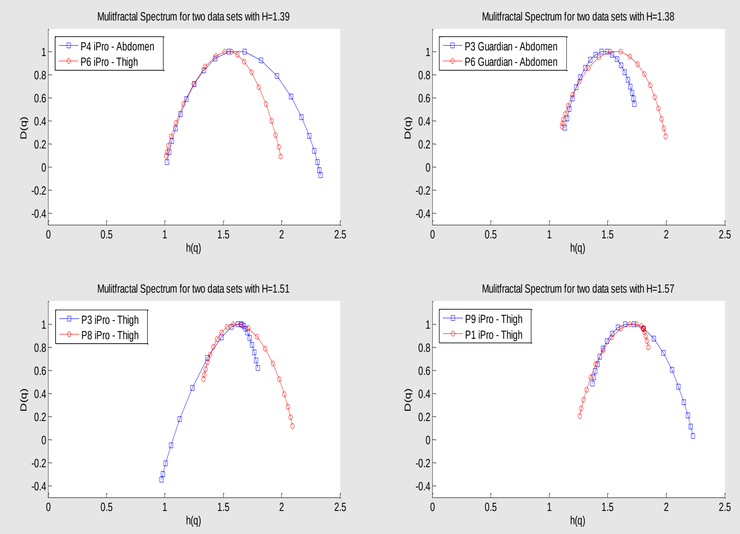

Figure 4: Multifractal Spectrum comparison for data sets that had the same scaling exponent from monofractal DFA

The CGM traces obtained by multiple devices in a single patient can be very similar but produce very different multifractal spectrums

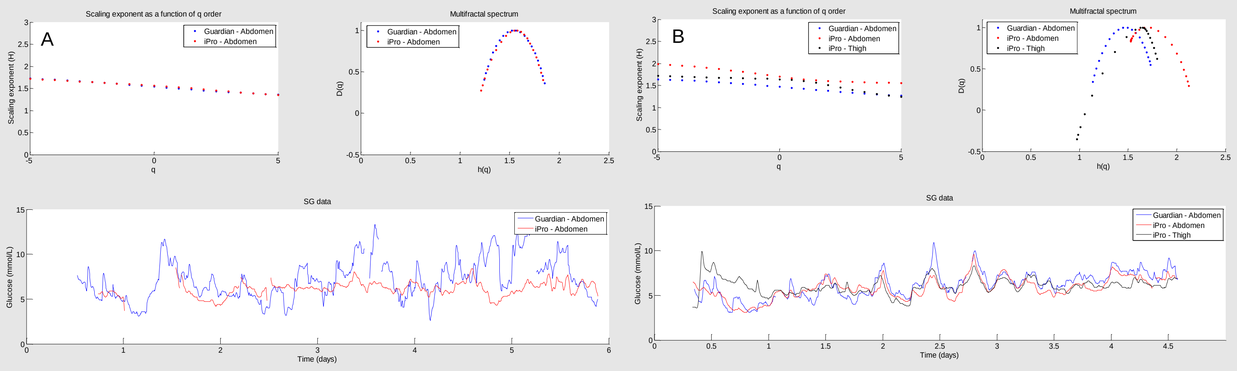

Figure 5: A)This example shows average agreement between SG data for two CGMs, but the multifractal spectrums for each data set overlap. B) his example shows good agreement between SG data for each of the three CGMs, but the multifractal spectrums for each data set are quite different.

CONCLUSION

This study clearly highlights where care should be taken in future DFA studies. Monofractal DFA results were sensitive to the type of CGM device used to collect the glucose data. Multifractal DFA results were not always consistent with monofractal DFA results. The width of the multifractal spectrums suggests that multifractal DFA is more appropriate for this type of data. Finally, an association between DFA results and mortality could not be detected in this limited data set.

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