

# PREVENTION OF DIABETIC AUTONOMIC NEUROPATHY THROUGH EARLY MATHEMATICAL EVALUATION

M. Fevre-Genoulaz\* MJ. Lafitte\* SS. Srikanta\*  
L. Punitha\* S. Vidyand\*

\* DyAnslys, Inc., USA  
\* Samatvam, Endocrinology Diabetes Center, India

## INTRODUCTION

A new mathematical method was proposed previously to assess the sympathovagal balance on a beat-to-beat basis. Based on Scale Covariance Physics, this method can extract information on the state of the respective subsystems of the Autonomic Nervous System (ANS), the Sympathetic and Parasympathetic, from the sole time-intervals between R waves of the ECG.

The measure given is that of a trajectory of a point particle whose position describes the overall state of the ANS, whereas indices can be calculated as degrees of activity of both subsystems locally. This latter measure enables one to better investigate the interaction of the ANS' two major components, while the former describes the dynamics and the outcome of the systems' interaction.

## PURPOSE OF THE STUDY

- Application of this measurement to the evaluation of Autonomic Dysfunction, in particular that of Diabetic Autonomic Neuropathy (DAN).
- First validation of this DAN measurement through:
  - Test of non-ambiguity of measure
  - Stability over time of the evaluation
  - Comparison with existing autonomic scoring
  - Coherence with clinical observations
- Further description of the Valsalva manoeuvre and its role in the evaluation of DAN

## METHOD

The ANSscope™ was used for this new measurement, the above mentioned indices being here the ANSindices™, and the trajectorial representation, the balANS™, both bounded by -50 and +50 in index values and coordinates. Autonomic scoring was performed as detailed by Bellavere et al. All recordings were performed according to conditions detailed below, as a preliminary study executed by Clinigene, Biocon. The degree of Autonomic Dysfunction is obtained and defined by the ANSscope™ as the amount of lack of coupling of the sympathetic and parasympathetic indices, the persistence of disassociation in the time evolution of these indices.

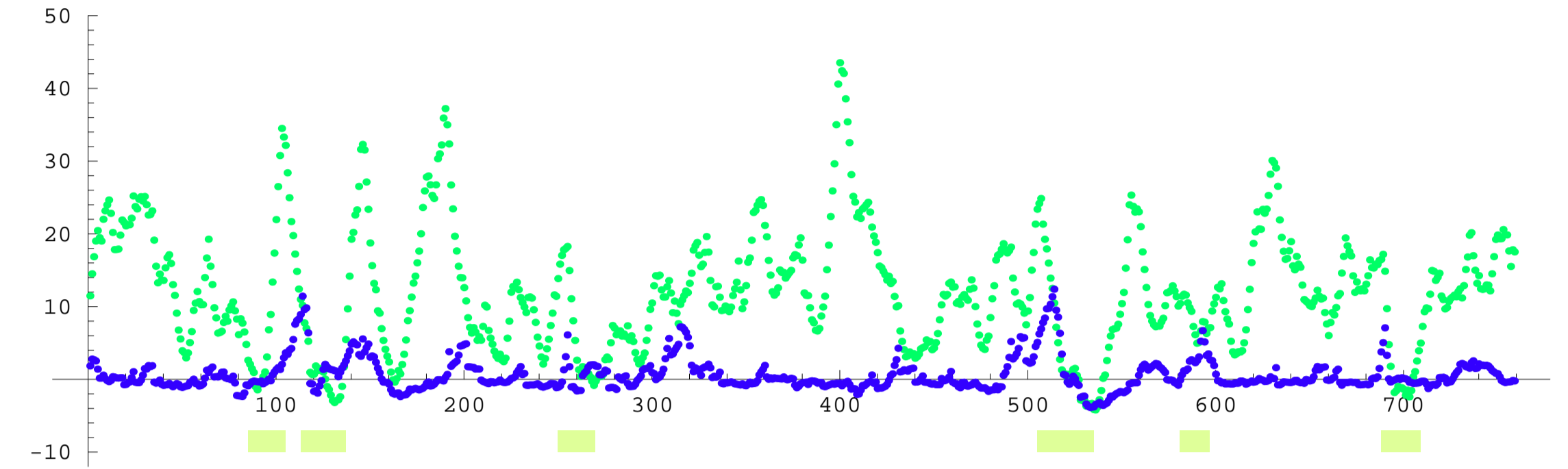


Figure 1: Graphical tentative to define Autonomic Dysfunction. (markers indicate detected association of green and blue indices, respectively corresponding to sympathetic and parasympathetic activities.)

30 patients (mean age: 47(+/- 10) years) recruited on a prospective basis; screening visit to determine presence of diabetes; all with recorded enlightened consent. Continuous recording of RR-intervals throughout the entire procedure. Recording in supine position for 500 RR intervals unless otherwise stated. Autonomic scoring consisted of 3 tests: RSA (respiratory sinus arrhythmia), Valsalva manoeuvre and the 30:15 ratio, drawdown of blood pressure during a tilt test.

## RESULTS

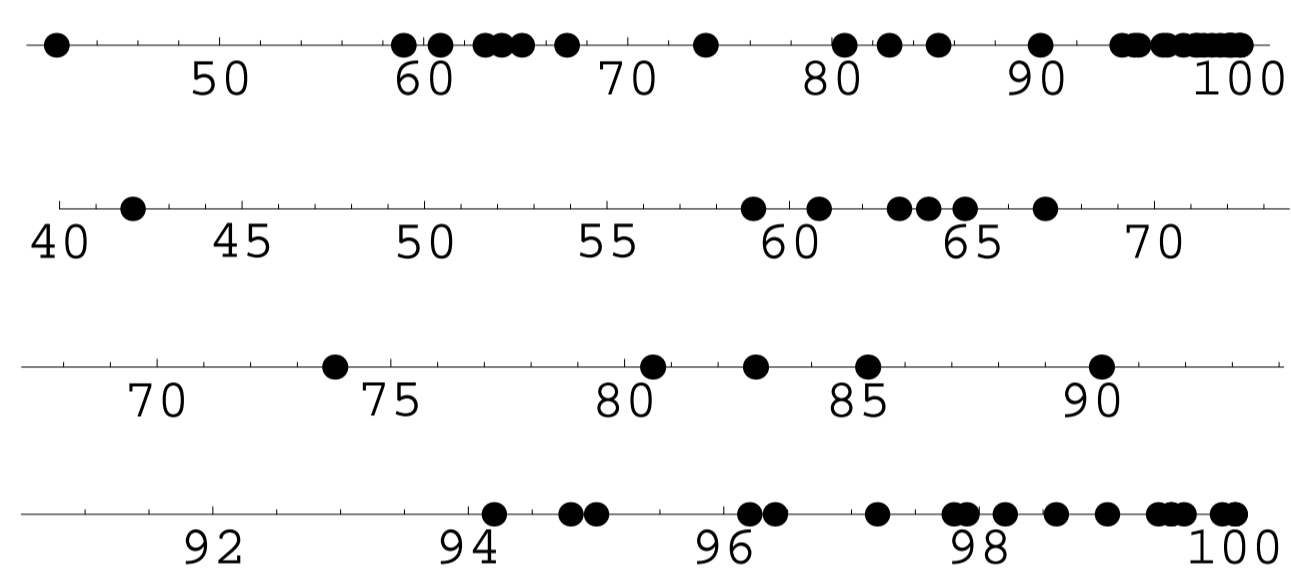


Figure 2: Aggregation of Autonomic Dysfunction percentage values in clearly cut groups.

Figure 3: Invariance of groups of patients (according to aggregates as illustrated in figure 2) under change of measurement time-frame. (Order of arrival of patients; order induced by dysautonomia measurement during 500 RR intervals; order induced during 10 minutes of recording.)

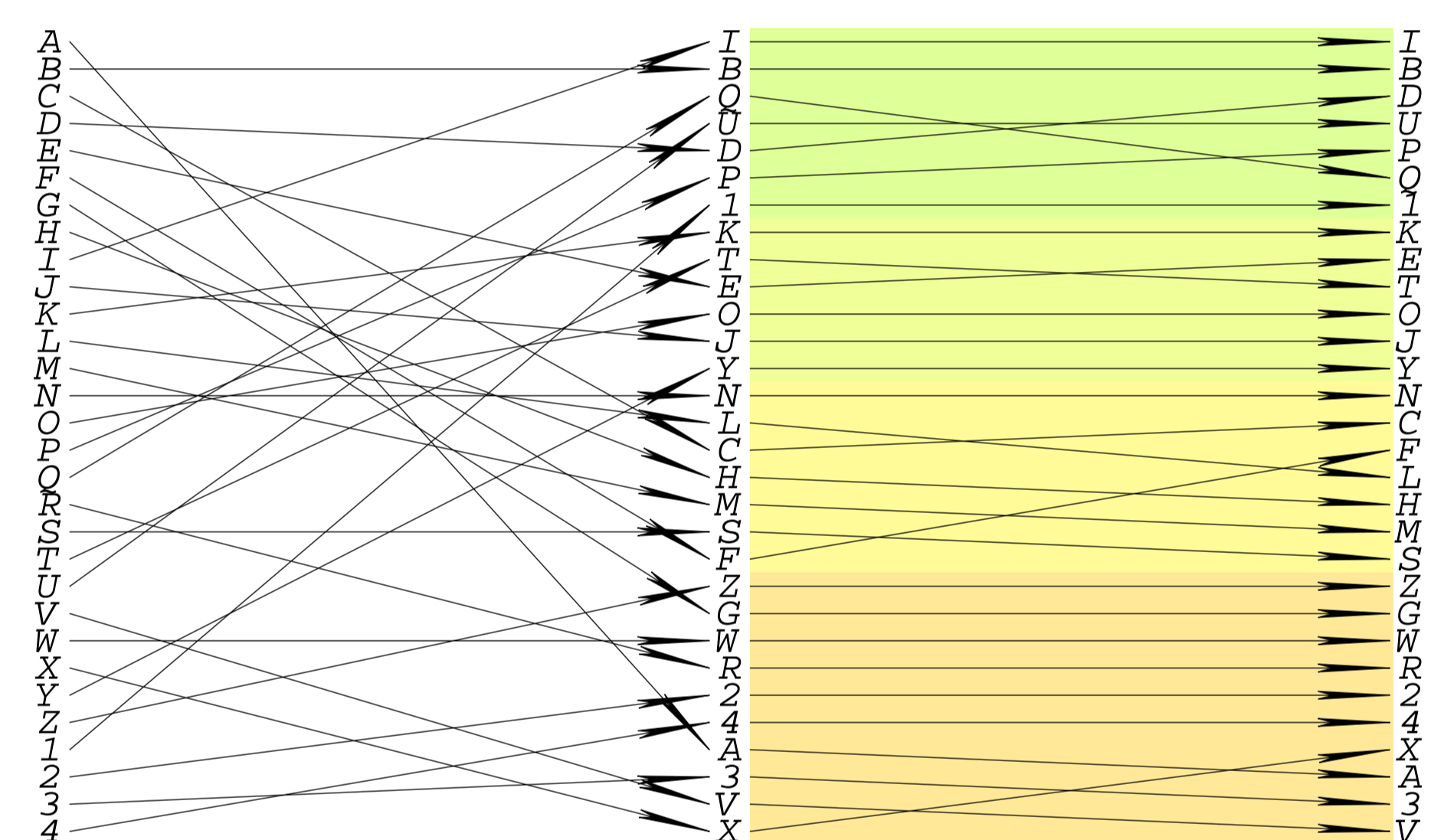


Figure 4: Comparison with autonomic scoring and its contradictions. (Order of arrival of patients, to 3 groups intimated by scoring, to the complete order induced by the dysautonomia measurement; red and green arrows resp. indicate violation of the scoring group and coherence of scoring group with ultimate meas.)

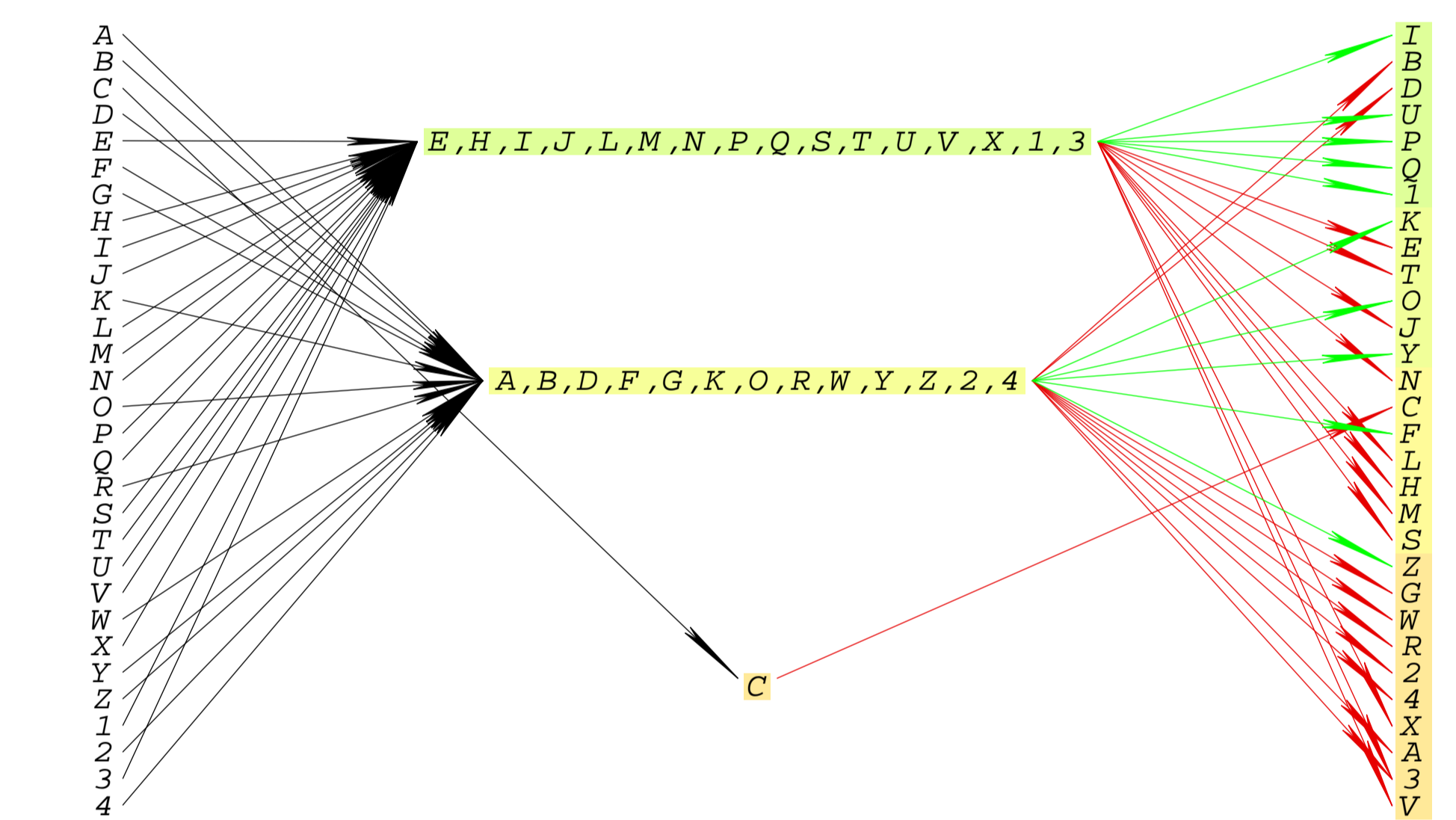
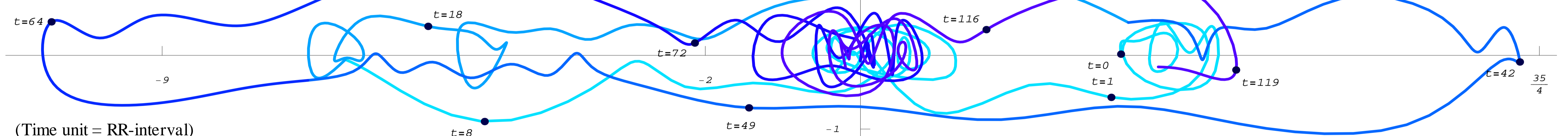


Figure 5a: Theoretical Valsalva manoeuvre as observed by combination of all valsalva manoeuvres for healthy and early DAN cases.



(Time unit = RR-interval)

Figure 5b: Theoretical indices of independent sympathetic and parasympathetic activities (resp. green and blue graphs) for the valsalva manoeuvre as caused by the theoretical balANS™ trajectory observed in figure 5a.

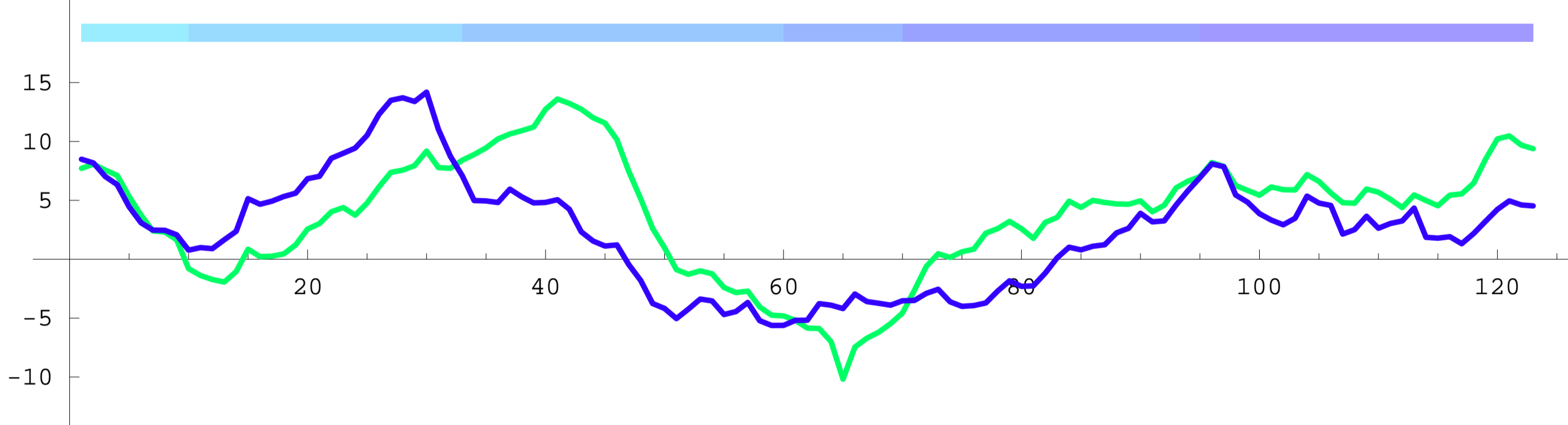
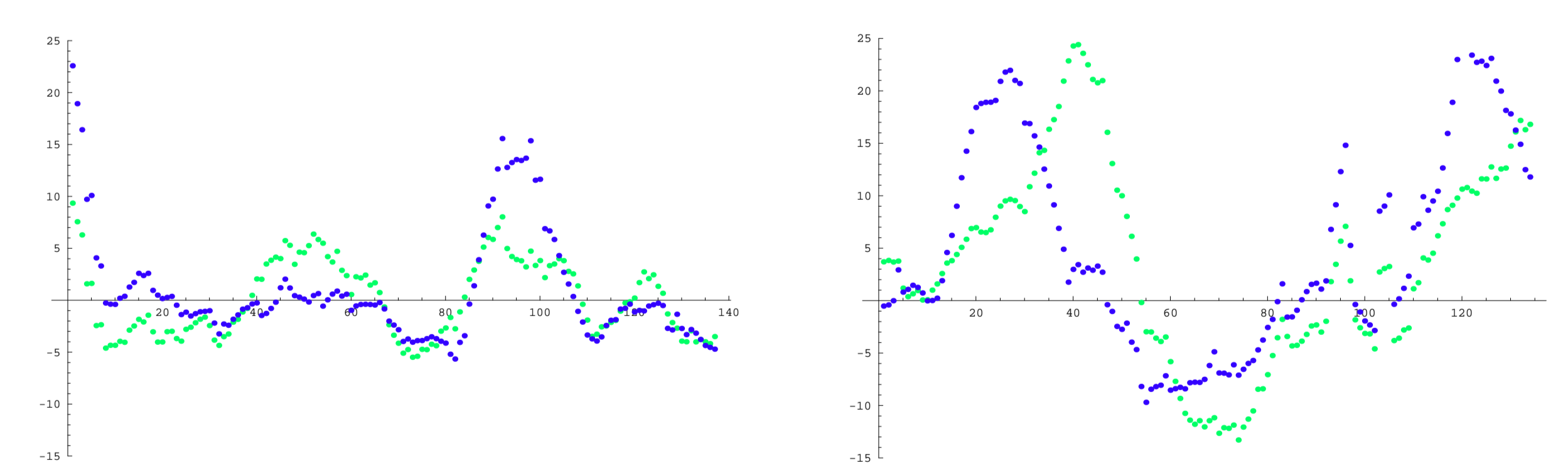


Figure 6: Examples of nonconclusive valsalva manoeuvres for a healthy patient (left) and a patient with early DAN (right): latter being closer to theoretical valsalva indices than the former.



## CONCLUSION

The definition of Autonomic Dysfunction, in evaluating DAN, as a lack of coupling of ANSindices proves sound in light of results which suggest that for such a measurement, no overlap would exist between absence and presence of DAN. Patients are ordered with clear groups, obtained by measure in what appears to be a natural separation. These groups stay stable under change of the observation window. Rest conditions during 500 RR intervals allowed here evaluation and detection of DAN. Moreover, no contradictions were found with the clinical observations. None of this was previously possible with autonomic scoring. Furthermore, a new portrayal of the valsalva manoeuvre was obtained as the theoretical behaviour of the sympathetic and parasympathetic systems under such a manoeuvre. Indications were sought and found that isolated manoeuvres would incorrectly distinguish in their alterations the cases of presence or absence of DAN. Such contradictions did not arise from the new measurement of autonomic dysfunction during supine conditions.

Results infer a pure discrimination between healthy and DAN cases. Such a discrimination allows here for the definition of early DAN, early in its detection and presence. The transition from one case to the other should be studied and is believed to be at the heart of the prevention of DAN.