

Mathematical Description of Diabetic Autonomic Neuropathy Development

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Background: Based on scale covariance physics, a new mathematical method, implemented in the ANSiscope™ device, extracts beat-by-beat information on the sympathetic and parasympathetic subsystems of the Autonomic Nervous System, from the R-R time-intervals of the ECG. Calculated indices give activity-degrees of subsystems locally. The lack of coupling of these indices then defines autonomic dysfunction as a percentage over the time period considered.

Aim: Patterns, in the autonomic dysfunction measurements over a population, are sought for evidence of a discrete chronological development of Diabetic Autonomic Neuropathy (DAN).

Material and Methods: 21 diabetic patients and 9 non-diabetic volunteers (mean age: 47+/-10 years) with enlightened consent were enrolled in the study. Demarcating groups of values, obtained by the new measurement (5 to 7 minutes in supine condition) on a population of 30 diabetic patients is a first step towards identifying common ground between the ascending order of measurement values and the chronicity of DAN. Homogeneity of DAN's development pace is expected within groups.

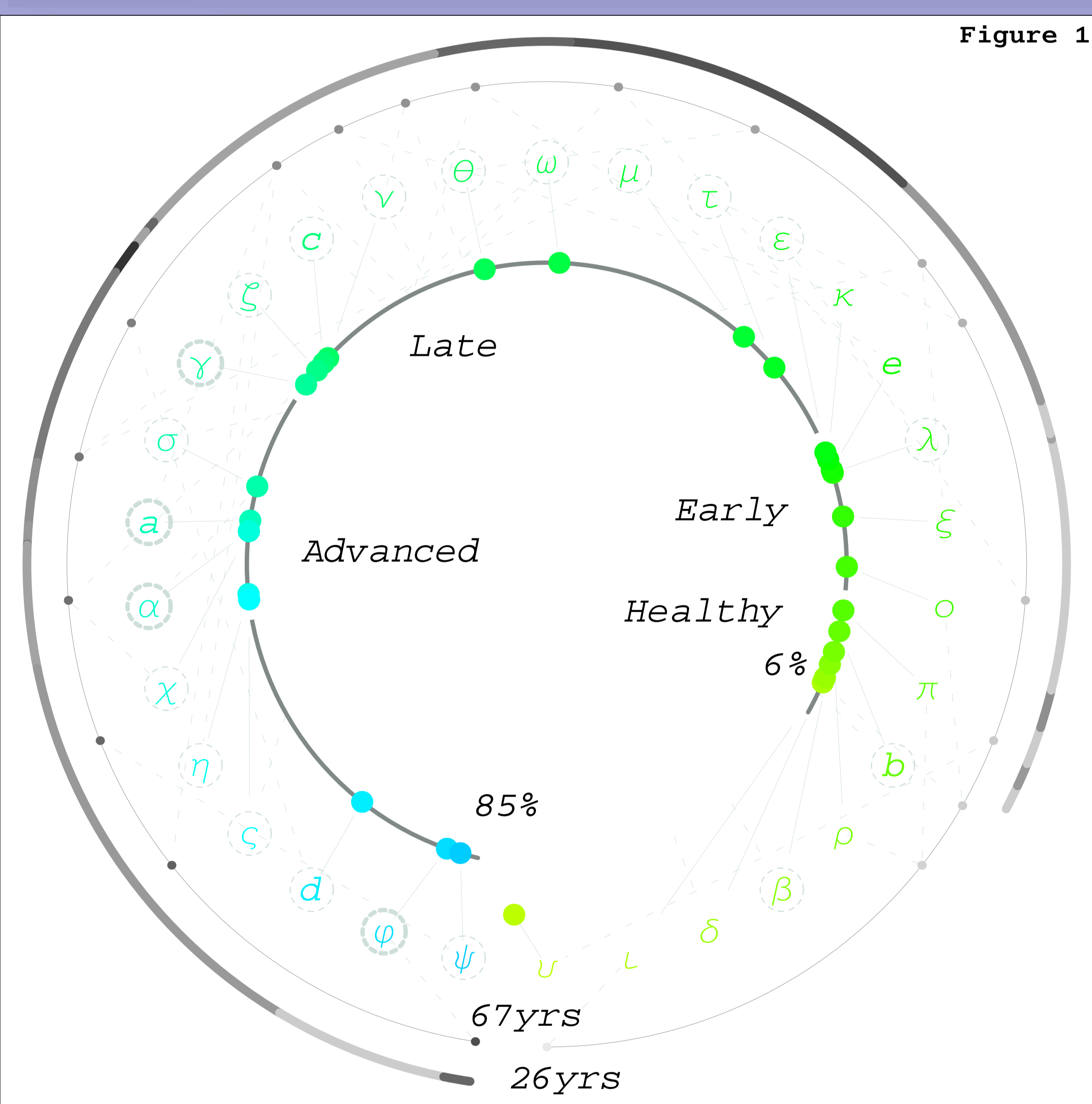


Figure 1

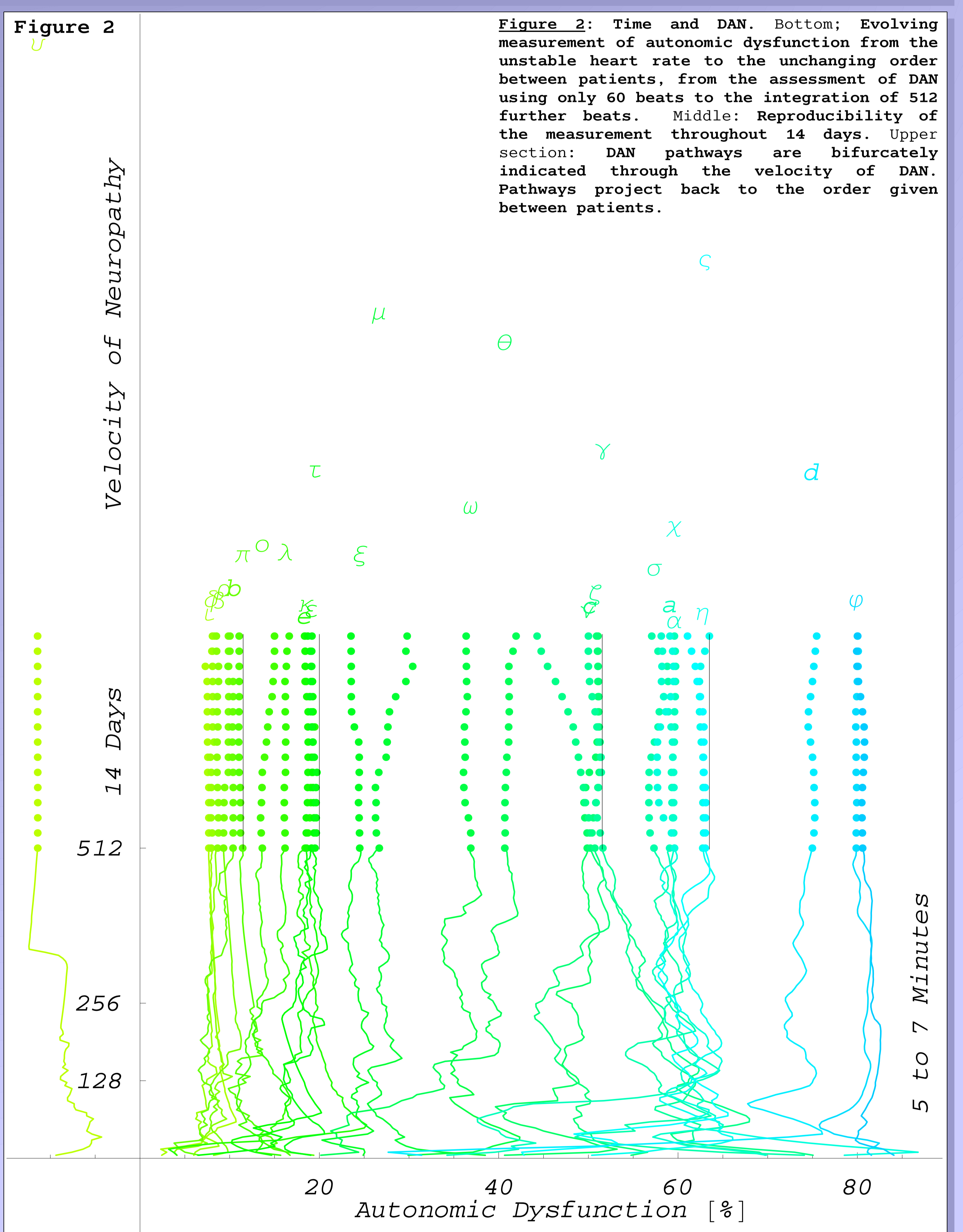


Figure 2

Figure 2: Time and DAN. Bottom; Evolving measurement of autonomic dysfunction from the unstable heart rate to the unchanging order between patients, from the assessment of DAN using only 60 beats to the integration of 512 further beats. Middle: Reproducibility of the measurement throughout 14 days. Upper section: DAN pathways are bifurcately indicated through the velocity of DAN. Pathways project back to the order given between patients.

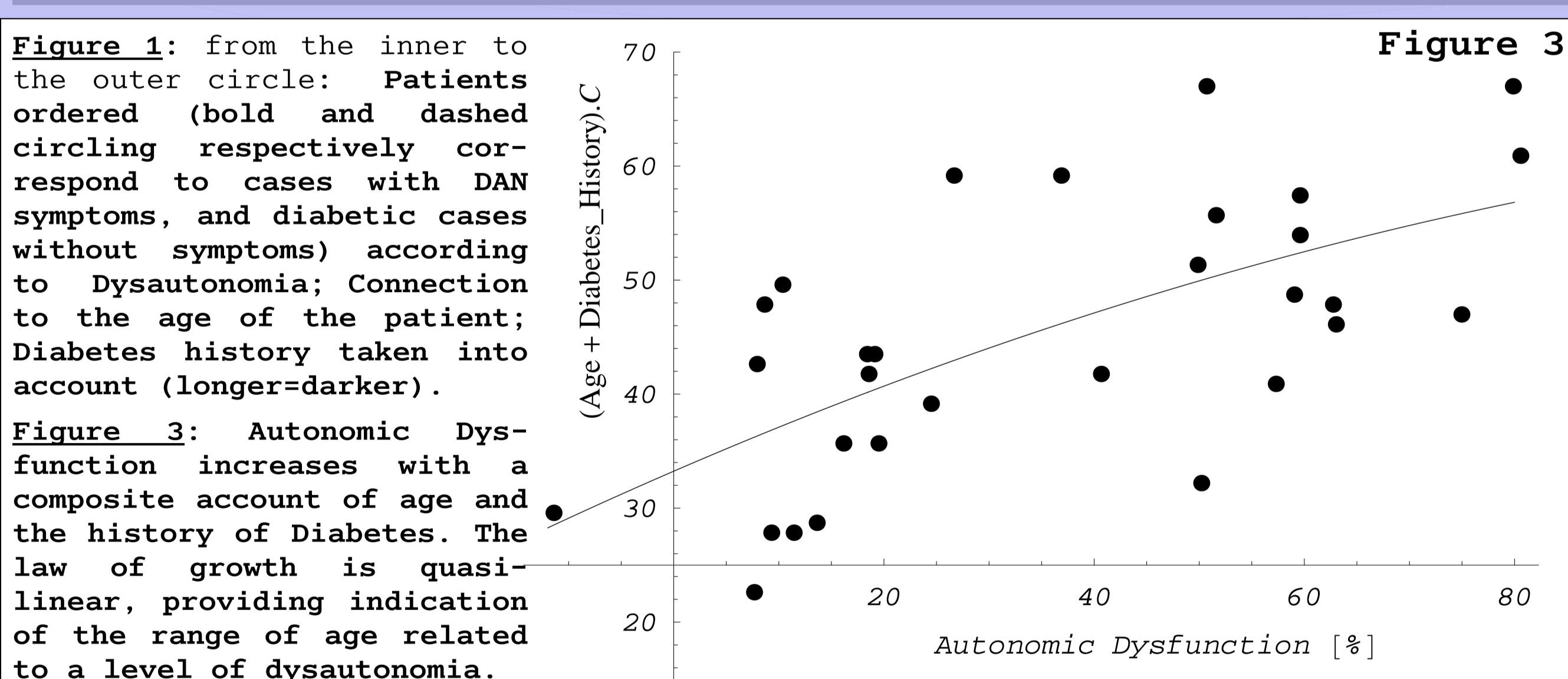


Figure 3

Figure 1: from the inner to the outer circle: Patients ordered (bold and dashed circling respectively correspond to cases with DAN symptoms, and diabetic cases without symptoms) according to Dysautonomia; Connection to the age of the patient; Diabetes history taken into account (longer=darker).

Figure 3: Autonomic Dysfunction increases with a composite account of age and the history of Diabetes. The law of growth is quasi-linear, providing indication of the range of age related to a level of dysautonomia.

Results: Five groups made of four main classes (Healthy (H): -8->11.5, Early (E): 13.5->20, Late (L):23->51 and Advanced (A): 51.5->80) are found to respect their demarcations under a change of the measurement-time window. They are also found to possess higher demarcations which act as accumulation limits for the preceding values (except for the last group, the ending values admit convergence of autonomic dysfunction values as sequences leading to them). The four classes form an order of progression and so do the elements within each group. Both orders are stable over time. The fifth group arises from the distinction of complete failure/abnormality of the parasympathetic and sympathetic systems in the fourth class. DAN symptoms were observed only in the L and A DAN classes, leaving the E DAN group at the onset of autonomic dysfunction before the time where regulated organs would be affected. Estimating the velocity of neuropathy enabled us to find descriptive pathways between conditions of DAN. Naturally, aging is a factor in the development of DAN, but the sole history of diabetes cannot be associated with this development; in fact, long history of diabetes is most associated with a transition (without belonging) to the later groups.

Conclusion: DAN is the first example of a chronic disease with discrete progression. The stability of the demarcated groups under a change of measurement conditions hints to the universality of such discontinuities. Additionally, the convergence properties in this progression's structure suggests that the patient stratification is natural and the sole product of DAN. DAN's state, progression or regression as a consequence of diabetes, may now be studied with this new measurement and the evolving description it provides. Further studies are required in a larger population of patients. in order to confirm these novel conclusions.