fitting the AR model to the data, the employed constrained least squares method also limits the curvature (i.e., the norm of the second derivative) of the AR coefficients. This is illustrated in FIG. **4**, where the shape of the model coefficients can be loosely described as a dampened sine wave, also reflecting the periodic nature of the glucose signal and that model coefficients that are further apart have weaker correlations than closer ones. This behavior of the AR model coefficients is correct, as the glucose data gradually loses inter-sample correlations as a function of time lag between samples. However, if the curvature constraint is not imposed, unconstrained least squares produces AR model coefficients that exhibit unphysiologic behavior, with model coefficients corresponding to further apart (and less correlated) glucose samples contributing more to the predictions than more correlated, closer ones.

[0113] FIG. **7** shows that although the models are portable, their performance, in terms of RMSE, may vary from subject to subject. For example, the RMSE for subject #9 in scenario I is 0.09 mmol/l, whereas for subject #2 the RMSE is 0.30 mmol/l. This difference in prediction error for specific subjects is due to the different amounts of noise present in different subjects' data. However, as can be seen from FIGS. **6-8**, for a given subject, the models' performance is practically identical.

[0114] FIGS. **6** and **7** also reveal that sometimes a small time lag is introduced in the cross-subject and the cross-study scenarios. This small time lag is likely due to small differences in glucose dynamics across different individuals. AR models exhibit prediction lags if they failed to account for some frequency component present in the test signal. Such small differences in frequency components exist in the datasets and are the likely reason for the small prediction time lags. The introduction of a 5-minute lag for iSense subject #1 in scenario I (FIG. **6**) is likely due to small frequency differences between this subject's training and testing data.

[0115] The results on model portability are valid for AR-type models. As discussed above, AR models capture the signal's frequency information and are invariant to the signal's phase and amplitude. The latter property is not shared by other modeling approaches, such as those based on ordinary differential equations or harmonic regression, which prevents their portability.

[0116] Accordingly, at least one embodiment of the invention develops stable, universal glucose models that capture the correlations in glucose time-series signals of diabetic patients. Given continuous glucose signals from a patient, such universal models are readily usable to make near-future glucose concentration predictions for other patients without any need for model customization.

[0117] The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting of the invention. As used herein, the singular forms "a", "an" and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise. It will be further understood that the root terms "include" and/or "have," when used in this specification, specify the presence of stated features, integers, steps, operations, elements, and/or components, but do not preclude the presence or addition of one or more other features, integers, steps, operations, elements, components, and/or groups thereof.

[0118] The corresponding structures, materials, acts, and equivalents of all means plus function elements in the claims below are intended to include any structure, or material, for performing the function in combination with other claimed elements as specifically claimed. The description of the present invention has been presented for purposes of illustration and description, but is not intended to be exhaustive or limited to the invention in the form disclosed. Many modifications and variations will be apparent to those of ordinary skill in the art without departing from the scope and spirit of the invention. The embodiment was chosen and described in order to best explain the principles of the invention and the practical application, and to enable others of ordinary skill in the art to understand the invention for various embodiments with various modifications as are suited to the particular use contemplated.

[0119] The invention can take the form of an entirely hardware embodiment or an embodiment containing both hardware and software elements. In at least one exemplary embodiment, the invention is implemented in a processor (or other computing device) loaded with software, which includes but is not limited to firmware, resident software, microcode, etc.

[0120] Computer program code for carrying out operations of the present invention may be written in a variety of computer programming languages. The program code may be executed entirely on at least one computing device (or processor), as a stand-alone software package, or it may be executed partly on one computing device and partly on a remote computer. In the latter scenario, the remote computer may be connected directly to the one computing device via a LAN or a WAN (for example, Intranet), or the connection may be made indirectly through an external computer (for example, through the Internet, a secure network, a sneaker net, or some combination of these).

[0121] It will be understood that each block of the flowchart illustrations and block diagrams and combinations of those blocks can be implemented by computer program instructions and/or means. These computer program instructions may be provided to a processor of a general purpose computer, special purpose computer, application specific integrated circuit (ASIC), or other programmable data processing apparatus to produce a machine, such that the instructions, which execute via the processor of the computer or other programmable data processing apparatus, create means for implementing the functions specified in the flowcharts or block diagrams.

[0122] The invention has industrial applicability to predict future glucose levels in diabetic patients. The invention utilizes the predicted glucose levels to alter or improve the patient's lifestyle, to tighten their glycemic control, or to adjust therapy in a proactive manner. The universal AR models of the invention predict future glycemic states, which can be used to avoid undesired hypoglycemic or hyperglycemic episodes.

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