Introduction: Context Of This Submission

- Only a “sticky note” in the space of ideas that might help to optimize the wellbeing of children with RASopathies

- A hint of a trace of a concept* for a category of application that would help to predict the time course of wellbeing, based on discrete inputs and estimates of the wellbeing of a child with RASopathies over time

- Based on machine learning techniques to elucidate the correlations and interactions between physiological system impulse response functions and wellbeing outcomes

- Submitted as a solo project (not eligible for awards), in the spirit of brainstorming and community

- Due an unexpected event related to a chronic, but unpredictably acute medical condition, coinciding with the Hack4Rare timeline, this submission is purely conceptual due to the resultant time constraints

- All techniques outlined in the proposed system are ones I’ve relied on heavily, some extending over decades, in systems that I’ve personally developed to solve machine learning problems in signal and image processing applications (many of these of a mission critical nature, requiring both accuracy and robustness)

- Further development would require close cooperation with families with children with RASopathies in order to collect data that would be used to develop a prototype, validate the overall system concept and level of accuracy, and ultimately, it’s utility for optimization of wellbeing of children (and potentially adults) with RASopathies

- If this submission does nothing more than stimulate interest on the part of other system developers to pursue this overall concept, using any competing techniques or system designs, it will have served it’s purpose

*A phrase plagiarized, but further mangled, originally from a Woody Allen film

Introduction: Context Of This Submission v2

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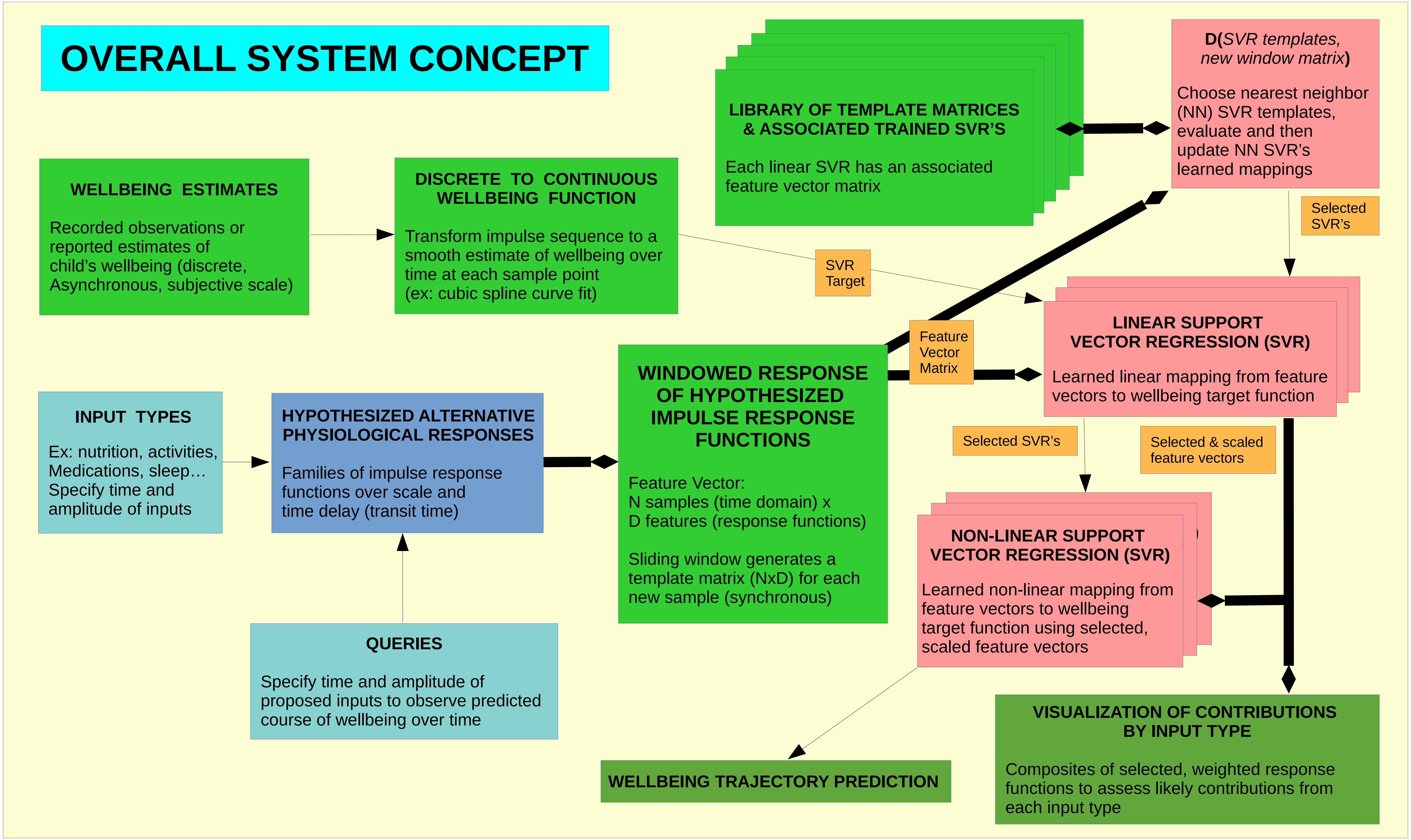
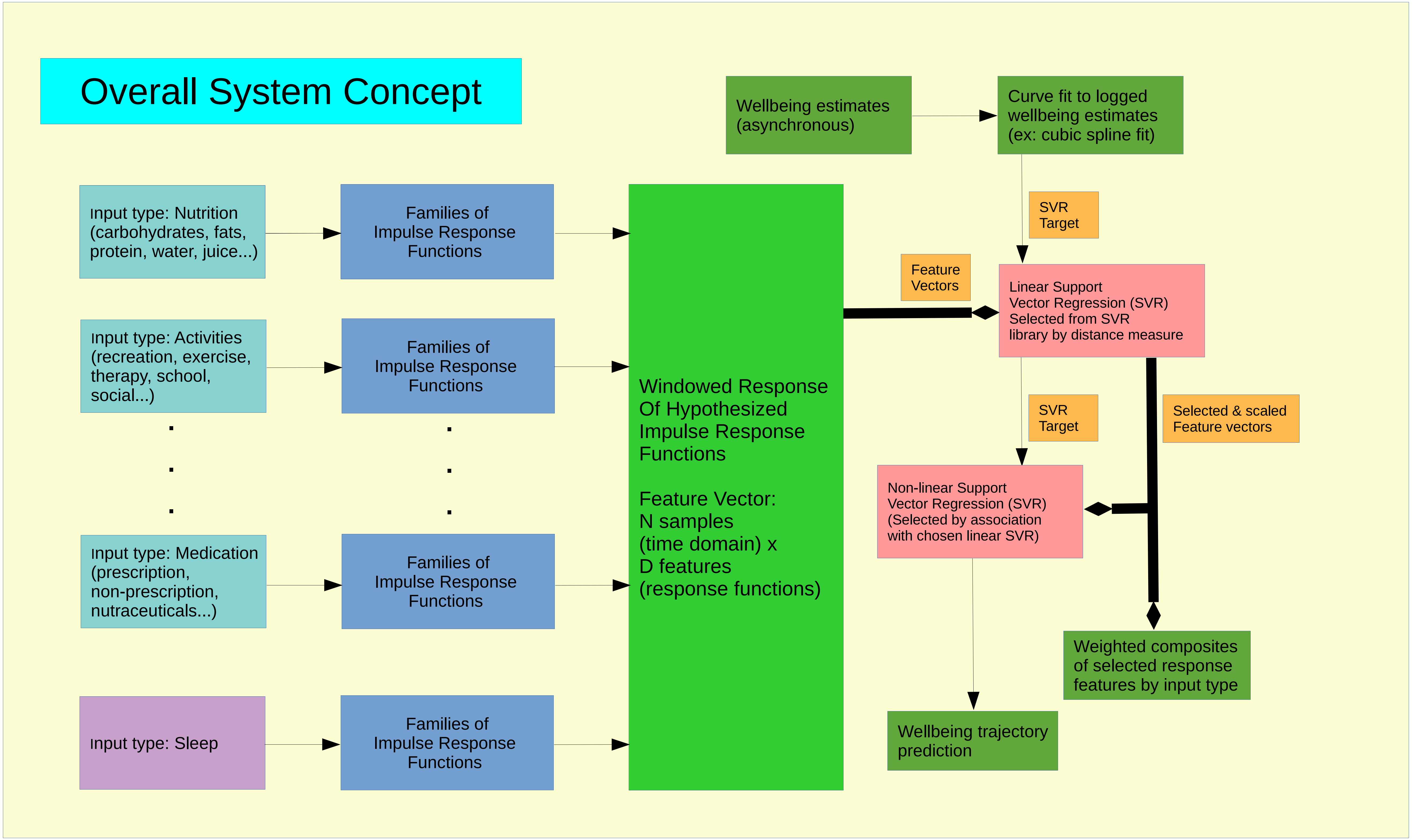

OVERALL SYSTEM CONCEPT
LIBRARY OF TEMPLATE MATRICES & ASSOCIATED TRAINED SVR'S
Each linear SVR has an associated feature vector matrix
D(SVR templates, new window matrix)
Choose nearest neighbor (NN) SVR templates, evaluate and then update NN SVR's learned mappings
Selected SVR's
WELLBEING ESTIMATES
Recorded observations or reported estimates of child's wellbeing (discrete, Asynchronous, subjective scale)
DISCRETE TO CONTINUOUS WELLBEING FUNCTION
Transform impulse sequence to a smooth estimate of wellbeing over time at each sample point (ex: cubic spline curve fit)
SVR Target
LINEAR SUPPORT VECTOR REGRESSION (SVR)
Learned linear mapping from feature vectors to wellbeing target function
Feature Vector Matrix
INPUT TYPES
Ex: nutrition, activities, Medications, sleep… Specify time and amplitude of inputs
HYPOTHESIZED ALTERNATIVE PHYSIOLOGICAL RESPONSES
Families of impulse response functions over scale and time delay (transit time)
WINDOWED RESPONSE OF HYPOTHESIZED IMPULSE RESPONSE FUNCTIONS
Feature Vector: N samples (time domain) x D features (response functions)
Sliding window generates a template matrix (NxD) for each new sample (synchronous)
Selected SVR's
Selected & scaled feature vectors
NON-LINEAR SUPPORT VECTOR REGRESSION (SVR)
Learned non-linear mapping from feature vectors to wellbeing target function using selected, scaled feature vectors
QUERIES
Specify time and amplitude of proposed inputs to observe predicted course of wellbeing over time
WELLBEING TRAJECTORY PREDICTION
VISUALIZATION OF CONTRIBUTIONS BY INPUT TYPE
Composites of selected, weighted response functions to assess likely contributions from each input type



Overall System Concept
Wellbeing estimates (asynchronous)
Curve fit to logged wellbeing estimates (ex: cubic spline fit)
Input type: Nutrition (carbohydrates, fats, protein, water, juice...)
Input type: Activities (recreation, exercise, therapy, school, social...)
Input type: Medication (prescription, non-prescription, nutraceuticals...)
Input type: Sleep
Families of Impulse Response Functions
Families of Impulse Response Functions
Families of Impulse Response Functions
Families of Impulse Response Functions
Windowed Response Of Hypothesized Impulse Response Functions
Feature Vector: N samples (time domain) x D features (response functions)
SVR Target
Feature Vectors
Linear Support Vector Regression (SVR) Selected from SVR library by distance measure
SVR Target
Selected & scaled Feature vectors
Non-linear Support Vector Regression (SVR) (Selected by association with chosen linear SVR)
Weighted composites of selected response features by input type
Wellbeing trajectory prediction

Overall System Concept

Use only “inputs” and observations of wellbeing to attempt to learn the correlations and interactions between input types, and timing, with the “wellbeing quotient” of a child with RASopathies:

- Inputs:
  > Input types can be any type of external influence that has been observed to have an effect on a child’s wellbeing
  > Inputs should also include basic factors such as nutrition, medications, and sleep
  > Input types can be sub-divided if more detailed analysis would be anticipated to be useful (ex: nutrition = [carbohydrates, protein, fats, water, juices, favorites (like ice cream)…]
  > Since distinct inputs like favorite foods, movies, games, etc., have psychological effects which feed back into physiology, they can be isolated as separate factors for analysis

- Modeling physiological responses to inputs:
  > Potential effects of inputs on physiological sub-systems are “predicted” using families of physiologically plausible impulse response functions, simulating the time domain response of organs and sub-systems to relevant inputs. These families of impulse response functions are then combined with a range of delays to simulate organ or sub-system and input specific transit times.
  > Families of pre-defined impulse response functions are used as crude models over a range of physiologically plausible responses to “impulsive” (Dirac delta functions) inputs. (Most inputs are modeled as amplitude modulated impulses, input by the user (parent) at any point in time (asynchronous inputs), while some inputs, such as sleep, will be modeled as pulsed inputs (pulse width = time duration of sleep, for example).

Overall System Concept

- Modeling physiological responses to inputs (cont'd):

> The initial list of function types considered for use in this system are a set of wavelet kernels (FIR filters) over scale (both symmetric and asymmetric: Gaussian, Mexican hat, Morlet, symlets, Daubechies…), IIR filters: exponential decays (RC filter impulse response) and exponentially decaying sinusoids (damped sinusoids) over frequency and scale), and a “bias” (constant) term. These filters can, of course, be used with either impulsive inputs (most inputs), or inputs like sleep (pulse inputs). Again, all functions will also be synthesized using a range of delays, to allow modeling of physiological transit or delay times. There are undoubtedly other applicable families of both FIR and IIR filters to explore for this application in what is essentially physiological signal modeling (after extraction of selected responses based on the SVR functions). [1]

> The selection and relative weighting of specific impulse response functions are made using two forms of support vector regression.

* using both the technique of recursive feature selection as a wrapper around the linear support vector regression (each specific response function is treated as a feature) in concert with the feature weighting functions provided by linear support vector regression after convergence on the optimal feature set.

Overall System Concept

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Overall System Concept

Use only “inputs” and observations of wellbeing to attempt to learn the correlations and interactions between input types, and timing, with the “wellbeing quotient” of a child with RASopathies:

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  > Input types can be any type of external influence that has been observed to have an effect on a child’s wellbeing
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  > Input types can be sub-divided if more detailed analysis would be anticipated to be useful
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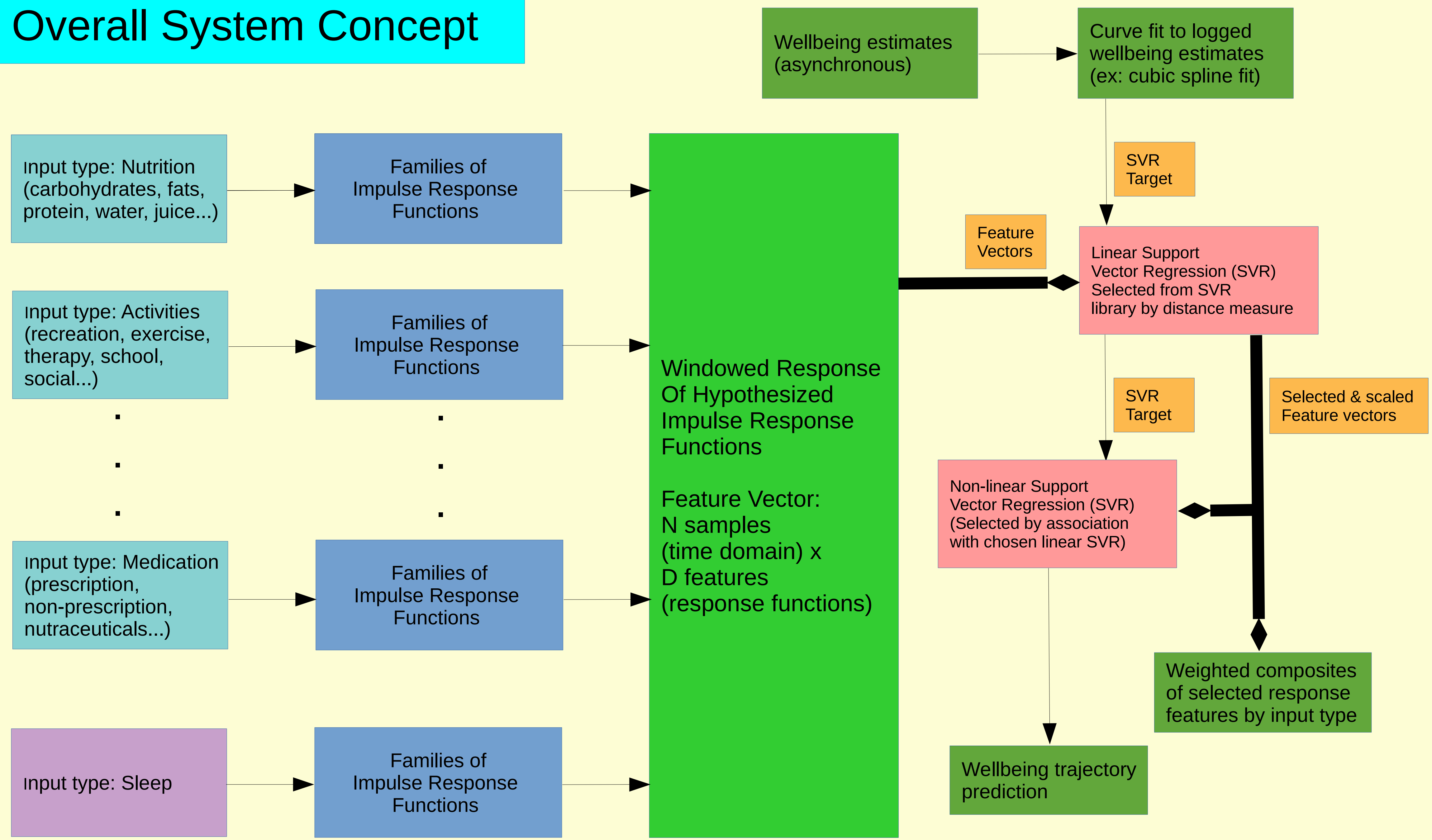
  >
  > The choice and relative weighting of specific impulse response functions are made using two forms of support vector regression, using both the technique of recursive feature selection as a wrapper around the linear support vector regression (each specific response function is treated as a feature) in concert with the feature weighting functions provided by linear support vector regression after convergence on the optimal feature set.

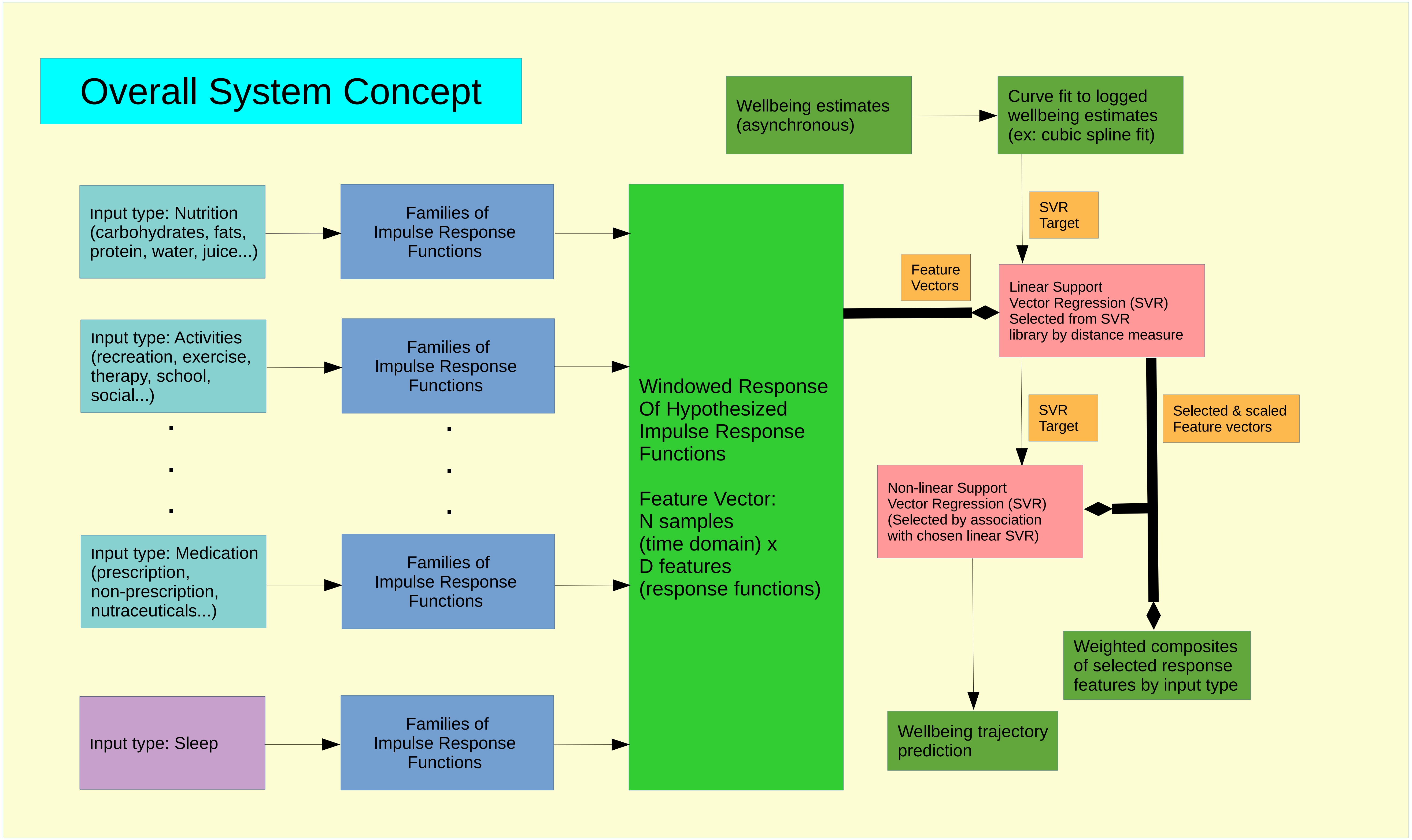
- Use these learned correlations to attempt to predict a child’s wellbeing trajectory in response to either chosen, or hypothesized inputs

References

1) “SIMULATION OF PHYSIOLOGICAL SIGNALS USING WAVELETS”, Soniya Naresh Bhojwani (U Akron MS Thesis,

Overall System Concept

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Weighted composites of selected response features by input type
Input type: Sleep
Families of Impulse Response Functions
Wellbeing trajectory prediction

Families of Hypothesized Impulse Response Functions
For Prediction of Physiological Subsystem Responses to Inputs

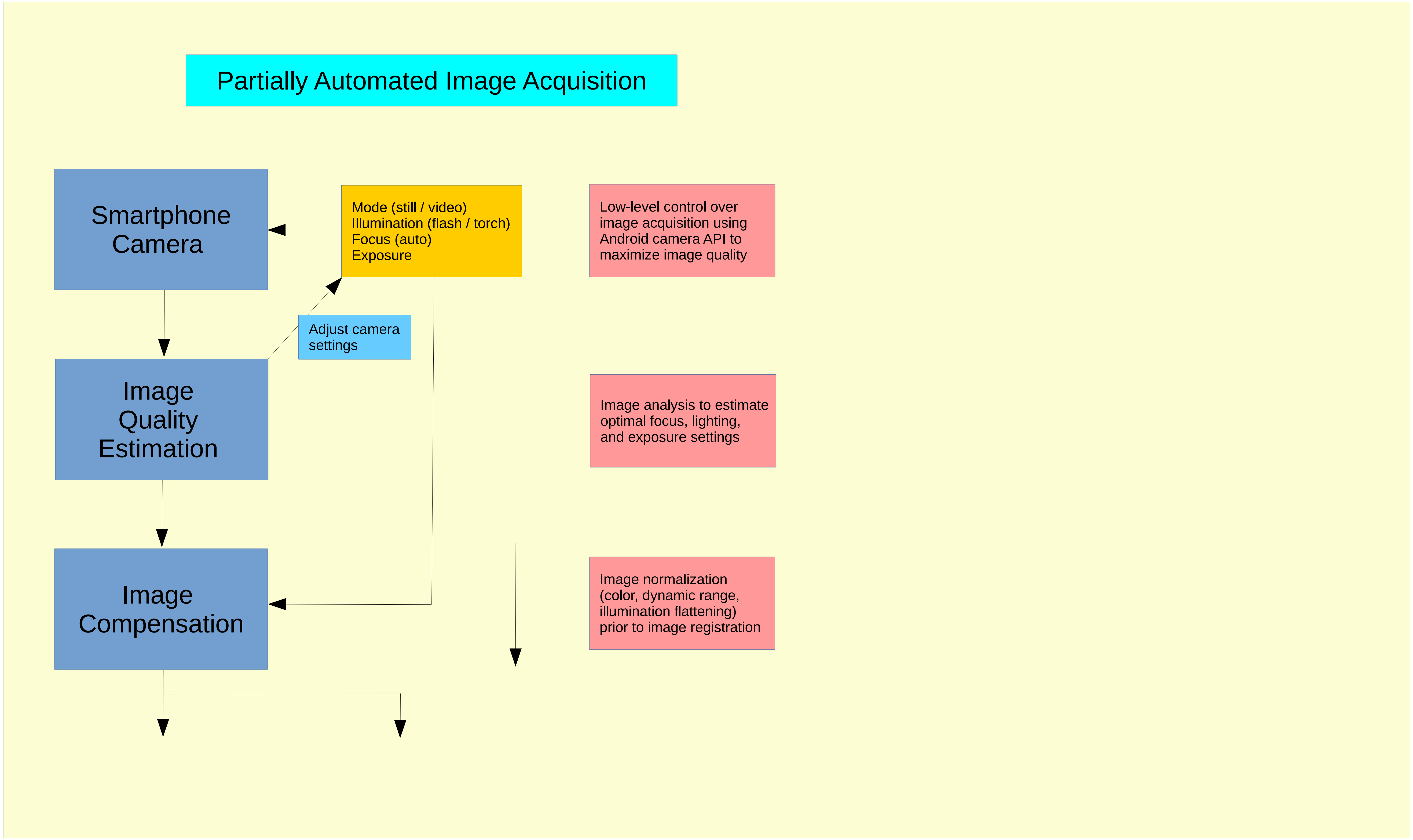
Smartphone Camera

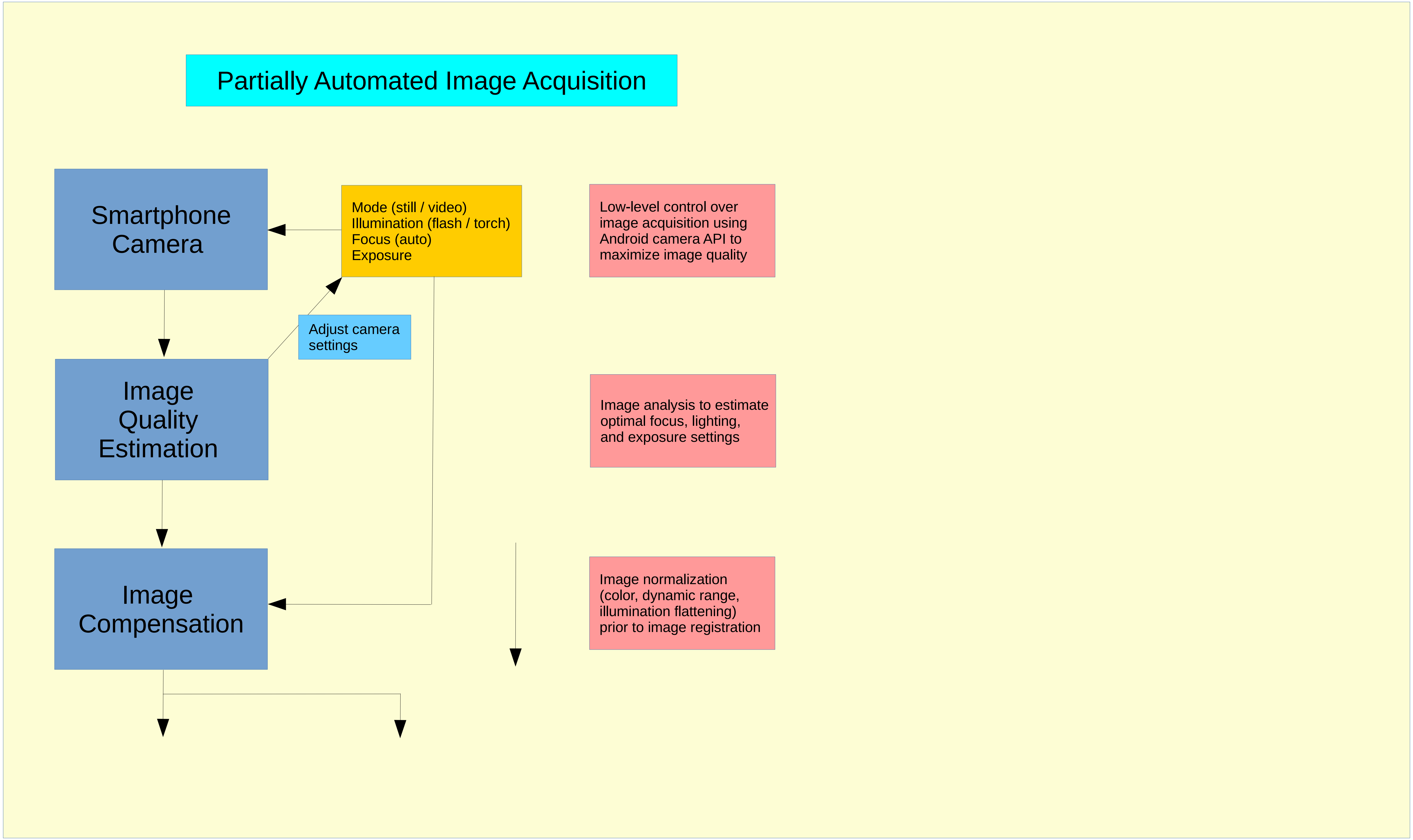
Mode (still / video)
Illumination (flash / torch)
Focus (auto)
Exposure

Low-level control over image acquisition using Android camera API to maximize image quality

Image analysis to estimate optimal focus, lighting, and exposure settings

Image normalization (color, dynamic range, illumination flattening) prior to image registration


Partially Automated Image Acquisition
Smartphone Camera
Mode (still / video)
Illumination (flash / torch)
Focus (auto)
Exposure
Low-level control over image acquisition using Android camera API to maximize image quality
Adjust camera settings
Image Quality Estimation
Image analysis to estimate optimal focus, lighting, and exposure settings
Image Compensation
Image normalization (color, dynamic range, illumination flattening) prior to image registration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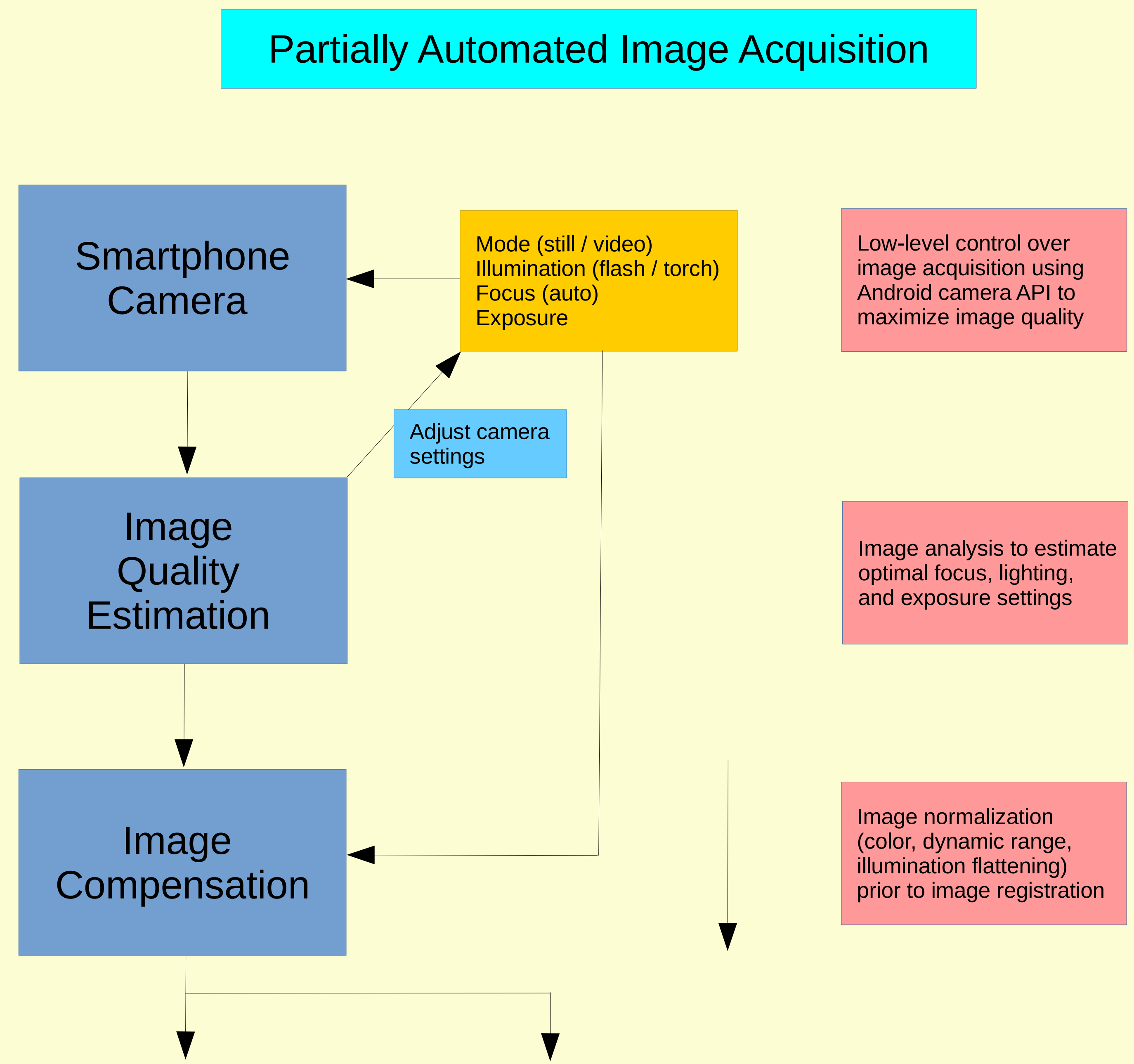
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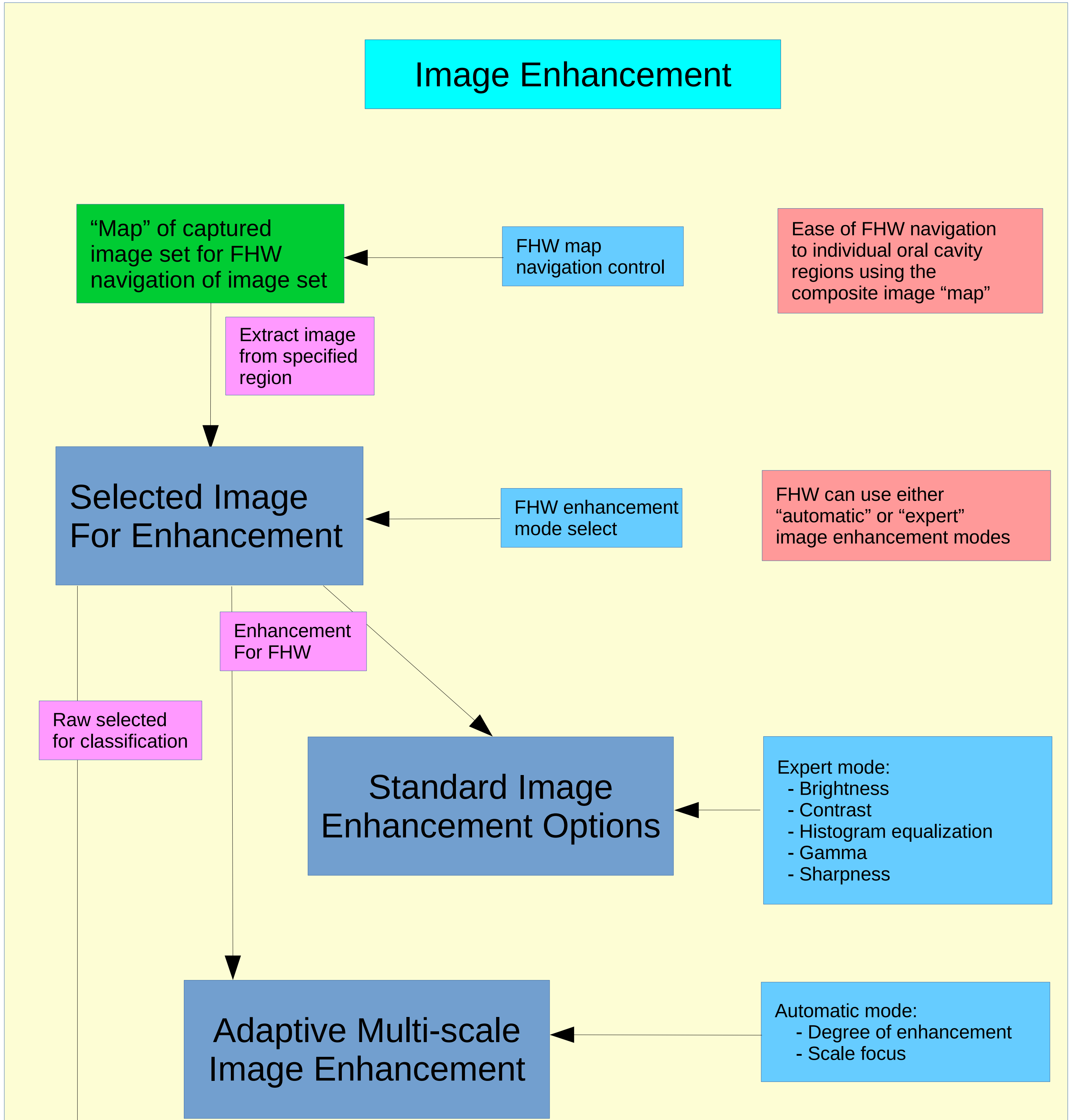
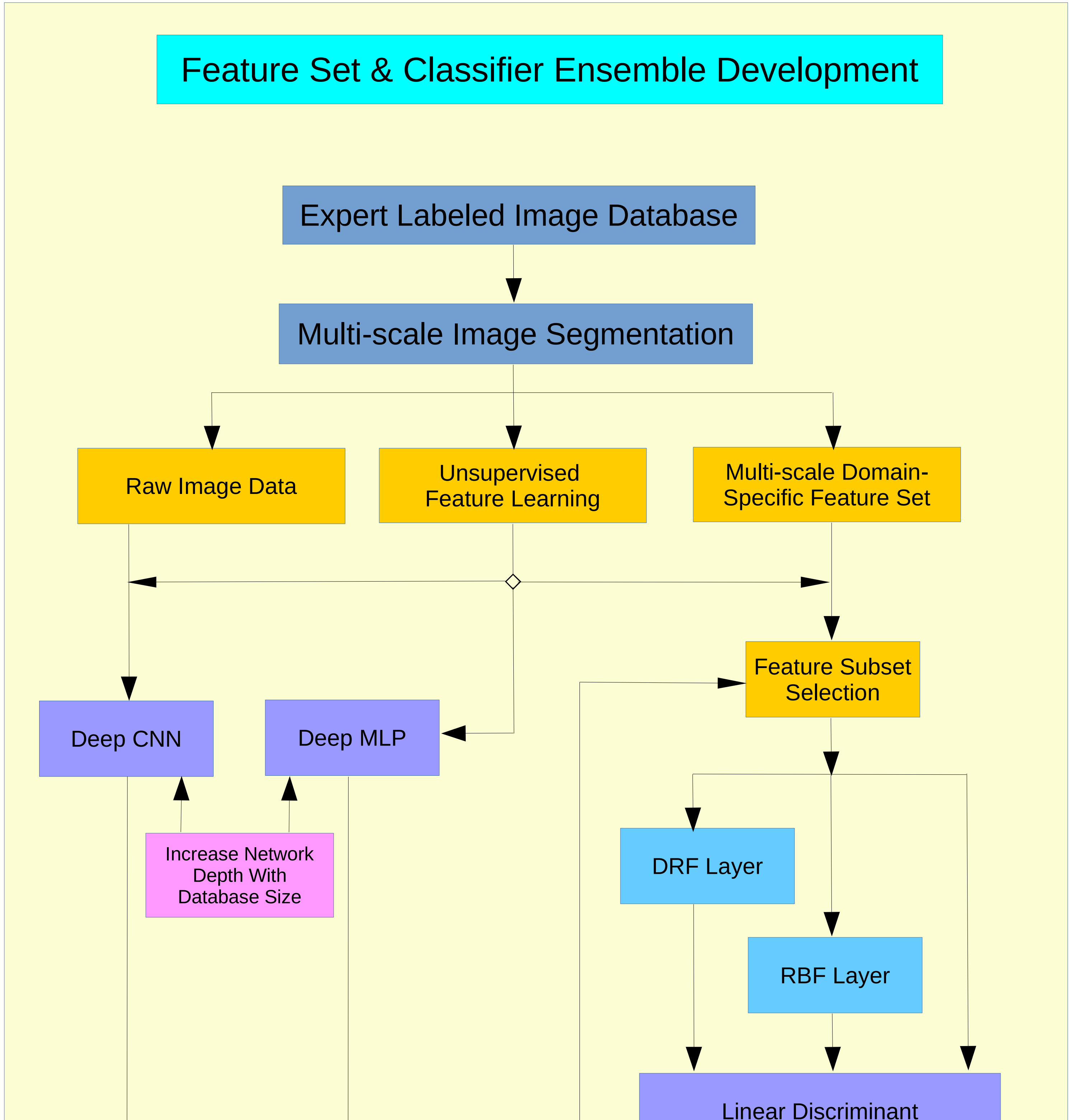
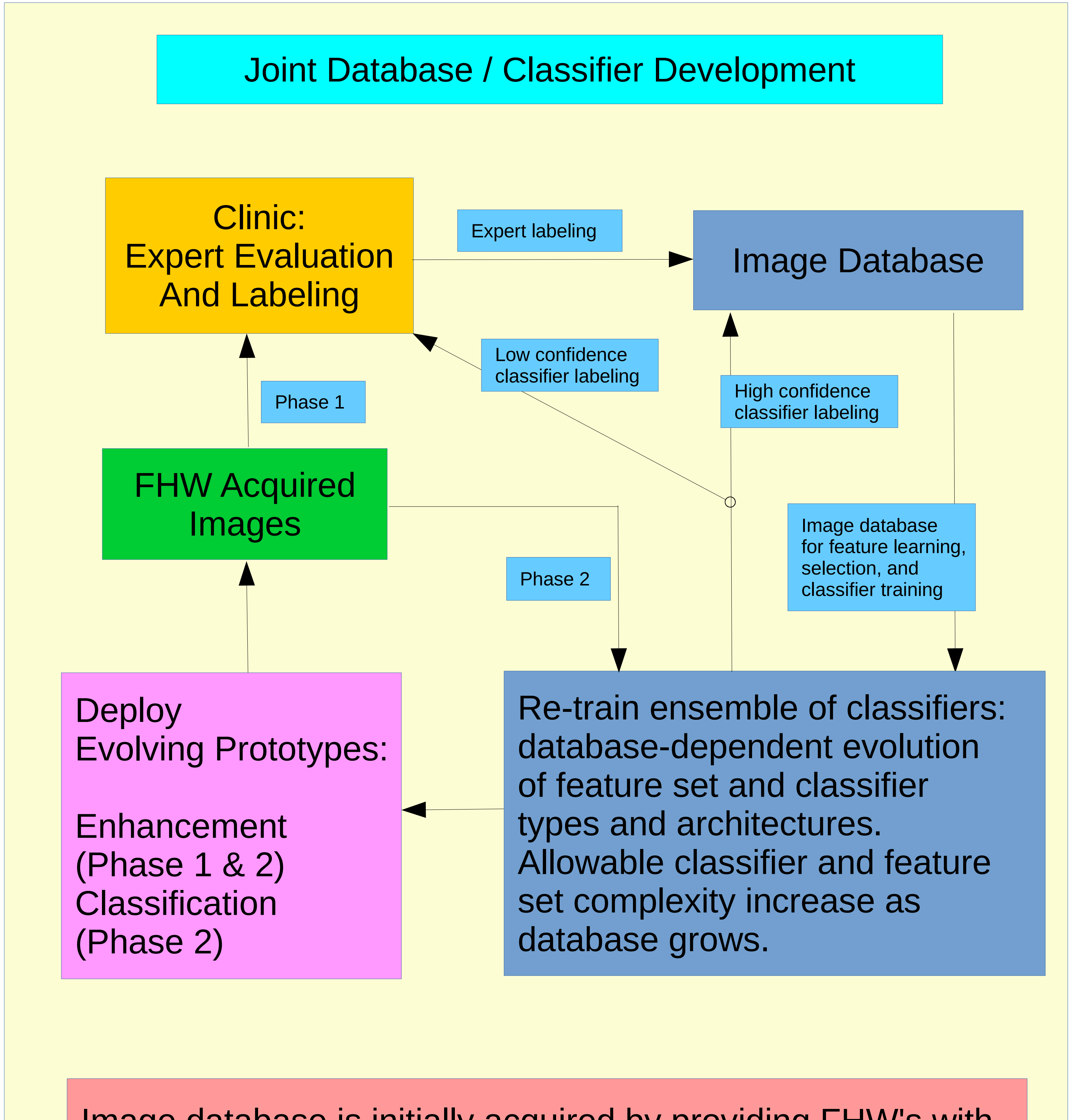
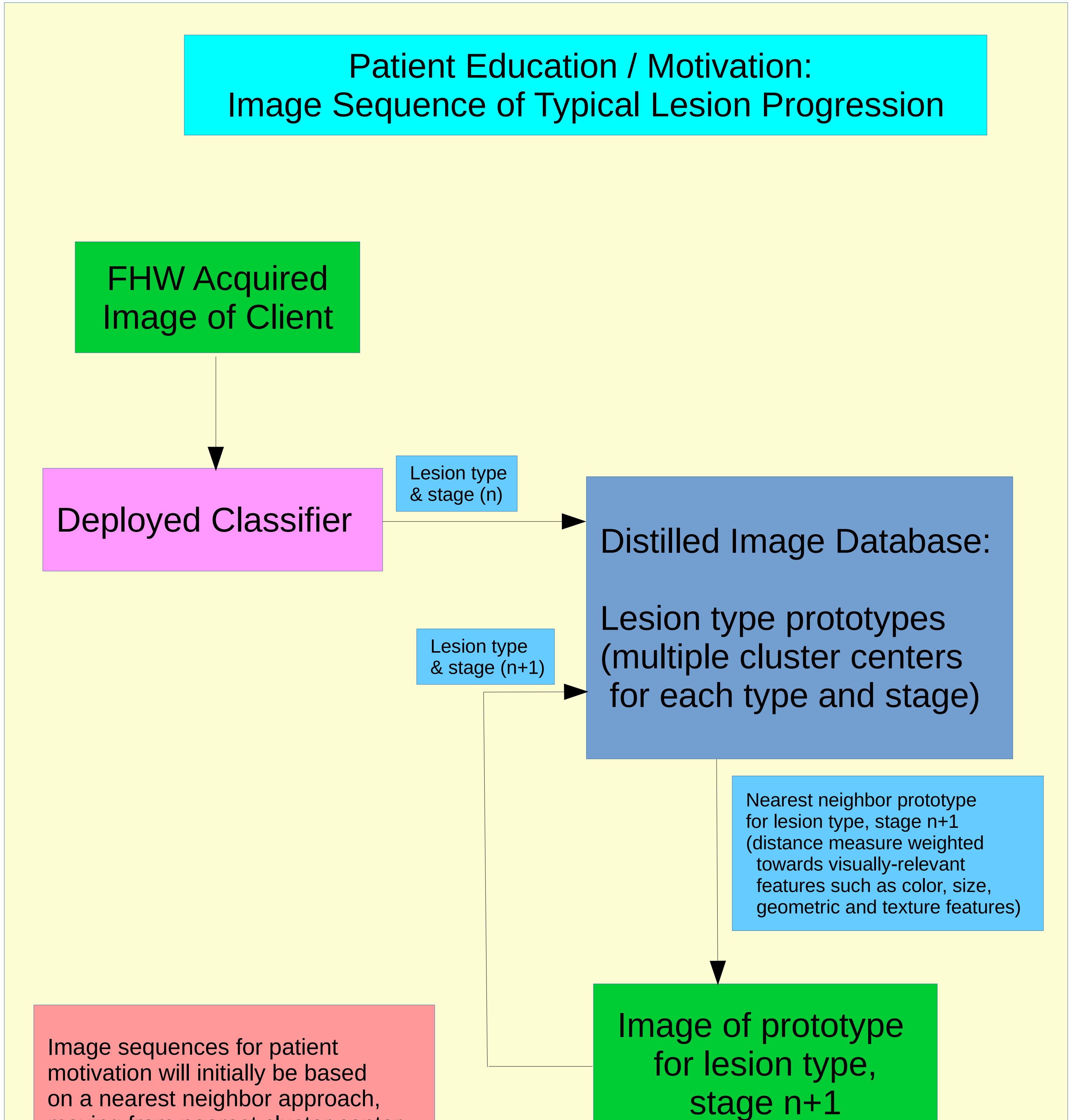


Image Enhancement
"Map" of captured image set for FHW navigation of image set
FHW map navigation control
Ease of FHW navigation to individual oral cavity regions using the composite image "map"
Extract image from specified region
Selected Image For Enhancement
FHW enhancement mode select
FHW can use either "automatic" or "expert" image enhancement modes
Enhancement For FHW
Raw selected for classification
Standard Image Enhancement Options
Expert mode:
- Brightness
- Contrast
- Histogram equalization
- Gamma
- Sharpness
Adaptive Multi-scale Image Enhancement
Automatic mode:
- Degree of enhancement
- Scale focus


Feature Set & Classifier Ensemble Development
Expert Labeled Image Database
Multi-scale Image Segmentation
Raw Image Data
Unsupervised Feature Learning
Multi-scale Domain-Specific Feature Set
Feature Subset Selection
Deep CNN
Deep MLP
Increase Network Depth With Database Size
DRF Layer
RBF Layer
Linear Discriminant


Joint Database / Classifier Development
Clinic:
Expert Evaluation
And Labeling
Expert labeling
Image Database
Low confidence
classifier labeling
High confidence
classifier labeling
Phase 1
FHW Acquired
Images
Phase 2
Image database
for feature learning,
selection, and
classifier training
Deploy
Evolving Prototypes:
Enhancement
(Phase 1 & 2)
Classification
(Phase 2)
Re-train ensemble of classifiers:
database-dependent evolution
of feature set and classifier
types and architectures.
Allowable classifier and feature
set complexity increase as
database grows.
Image database is initially acquired by providing FHW's with


Patient Education / Motivation:
Image Sequence of Typical Lesion Progression
FHW Acquired Image of Client
Deployed Classifier
Lesion type & stage (n)
Distilled Image Database:
Lesion type prototypes (multiple cluster centers for each type and stage)
Lesion type & stage (n+1)
Nearest neighbor prototype for lesion type, stage n+1 (distance measure weighted towards visually-relevant features such as color, size, geometric and texture features)
Image of prototype for lesion type, stage n+1
Image sequences for patient motivation will initially be based on a nearest neighbor approach,