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Calibration and evaluation of an unsupervised machine learning algorithm for β+ imaging using an intracerebral micro probe

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Purpose: The correlation of molecular neuroimaging and behavior studies in the preclinical field is of major interest to unlock progress in the understanding of brain processes and assess the validity of preclinical studies in drug development. However, fully achieving such ambition requires being able to perform molecular images of awake and freely moving animals whereas currently, most of the preclinical imaging procedures are performed on anesthetized animals. To achieve such a combination, MAPSSIC, a pixelated intracerebral probe based on the CMOS technology, has been developed in order to be implanted on awake freely moving rats. This probe is set to image β+ radioisotopes. Thanks to its in situ position, the probe is able to directly detect positrons unlike PET scans that use the coincidence gammas from annihilation as a relevant signal. The aim of this study is to asses the ability of an unsupervised Machine Learning algorithm to provide tangible information on the actual interaction processes in a sensor in terms of identification and localization of interaction events in the probe images.

Materials and methods: The probe relies on MAPS (Monolithic Active Pixel Sensors) 6400 µm x 610 µm MAPS containing 2048 (16 x 128) pixels including a one bit digitizer. The thickness of the sensible area is set to a compromise to ensure a high sensitivity to positrons and a good transparency to γ-rays, ensuring a very local information. When a positron interacts within the sensitive area of the sensor, this usually results in a cluster of activated pixels due to the ionizing track of β-particles in silicon and charge sharing between pixels. As the readout is based on a rolling shutter, pile-up occurs by the accumulation of counts in one or several pixels that have already been activated after the last read-out. At low activities, a simple cluster segmentation can quite easily allow to determine the number and position of each cluster and therefore the detected activity in a frame. Higher activities require, however, alternative pixel clustering in order to avoid wrong segmentation that leads to a loss of sensitivity and bias in event localization. In order to overcome segmentation issues due to pileup in sensors images (frames), the Affinity propagation (AP) clustering algorithm based on an iterative measure of similarity between points in a given data set has been utilized. Each cluster determined by the AP algorithm is composed by one "exemplar"(point that represents the best a cluster distribution) and zero to several other data points. The key parameter in the AP algorithm is the preference, which controls how many exemplars are used at the initialization and thus, influences the resulting cluster number in the output. Frames from experimental measurements obtained with a sensor and a 18F source and containing only one cluster have been used to randomly generate 1,000,000 frames containing 1 to 100 clusters each. This process has been done twice in order to get 2 sets of data: a calibration data set and a validation one. The calibration data set was used to determine the optimal preference value used to correctly identify the clusters in each frame. The preference value has been determined for frames containing from 1 to 100 clusters. The affinity propagation algorithm has then been applied to the validation data set using the previously determined preferences values and after a first rough estimation of the cluster number in each frame.

Results: The output were analyzed both in quantitative and spatial terms. The results show that the affinity propagation is well suited for the clustering of the MAPSSIC microprobe, up to about 100 clusters per frames. It also has comparable or better quantitative results to cluster estimations using the mean number of activated pixels by clusters. On top of that, the latter does not allow for spatial localization of each event unlike the AP algorithm. The calculation time varies from few milliseconds to 0.5 seconds and appears to be dependent to the number of activated pixel in the frame. The spatial analysis shows a great localization accuracy using the affinity propagation algorithm. For more than 95% of the clusters, the spatial error on the cluster's barycenter is basically equal or smaller than the pixel dimensions. The affinity propagation algorithm proves to be a very strong tool in image processing of a β-sensitive intracerebral microprobe such as MAPSSIC.

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