Are model-based tools still relevant for bioimage analysis?

New methods for background estimation and denoising fight back

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Artificial Intelligence (AI) methods have taken the field of bioimage analysis by storm, eclipsing **model-based methods** with their promises of ***learning* the *model* from the data**.

But model-based methods offer several **advantages**:

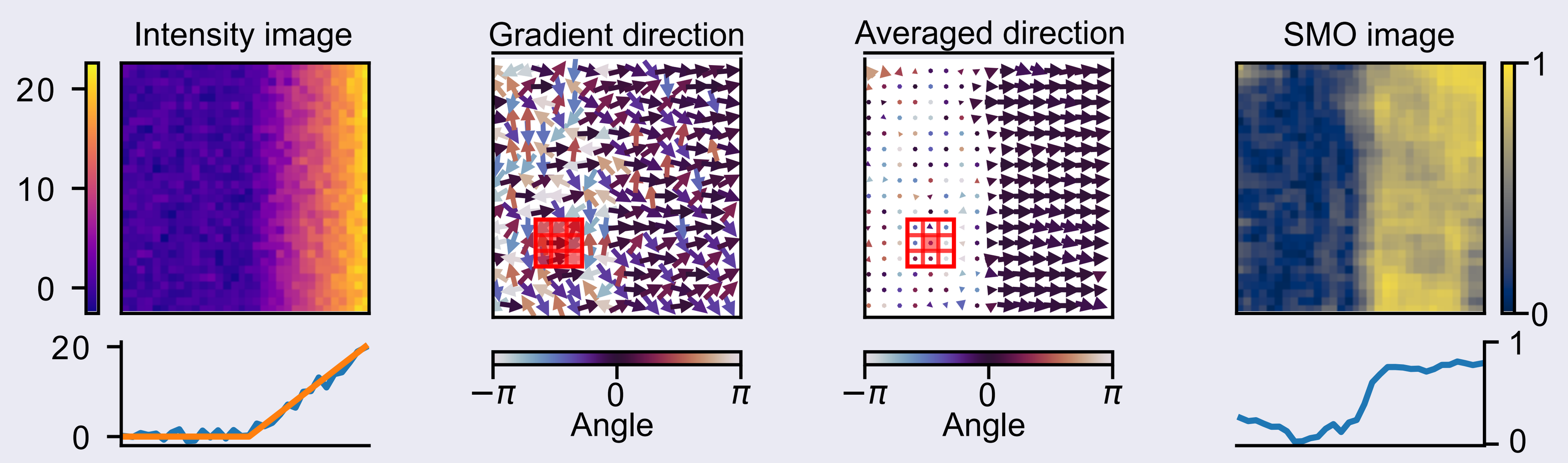
1. avoid the ***training*** process, which requires big datasets
2. provide better **generalization** for out-of-distribution samples
3. are **explainable**, based on hypotheses to understand *a priori* their applicability

SMO: robust estimation of the background distribution

What it does: selects a subset of pixels that provide an unbiased estimation of the background distribution. **Hypothesis:** background regions are *locally flat* when compared with the noise, while foreground regions are not.

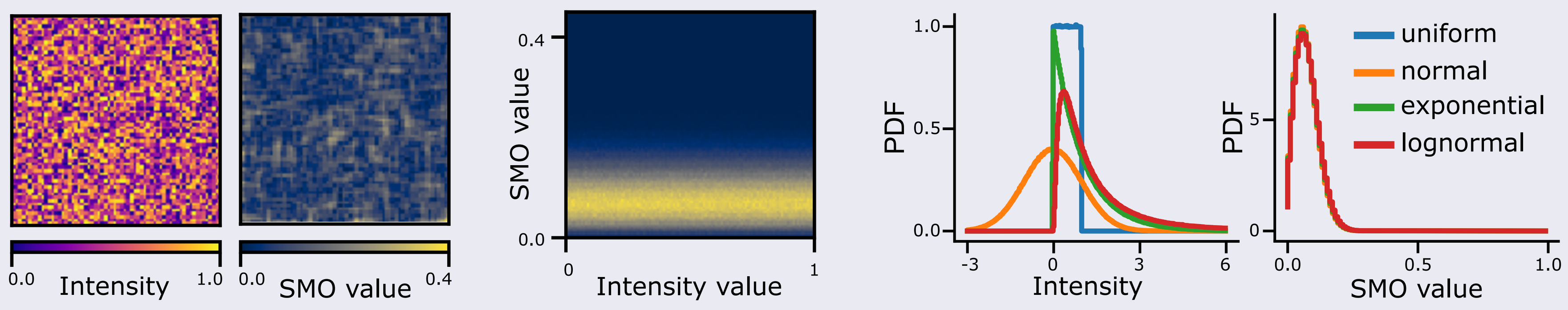
SMO definition: length of the average gradient direction

Take the gradient of an intensity image, and normalize by its length to obtain a direction vector. In flat regions, it is **uniformly distributed in every direction** due to noise. Then, we compute the local average direction and finally its length.



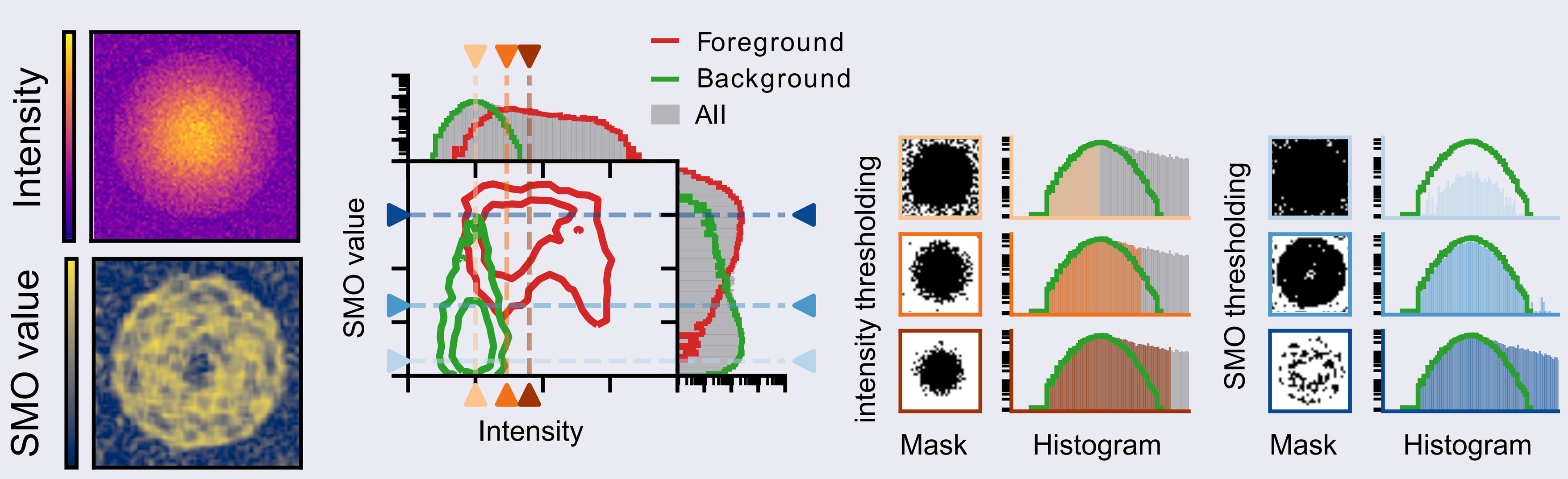
SMO is non-parametric or distribution-independent

For intensity values sampled from the same distribution, the SMO values are **independent** and **only depend on** the size of the local averaging of direction vectors. The null-distribution can be precomputed using a random image.



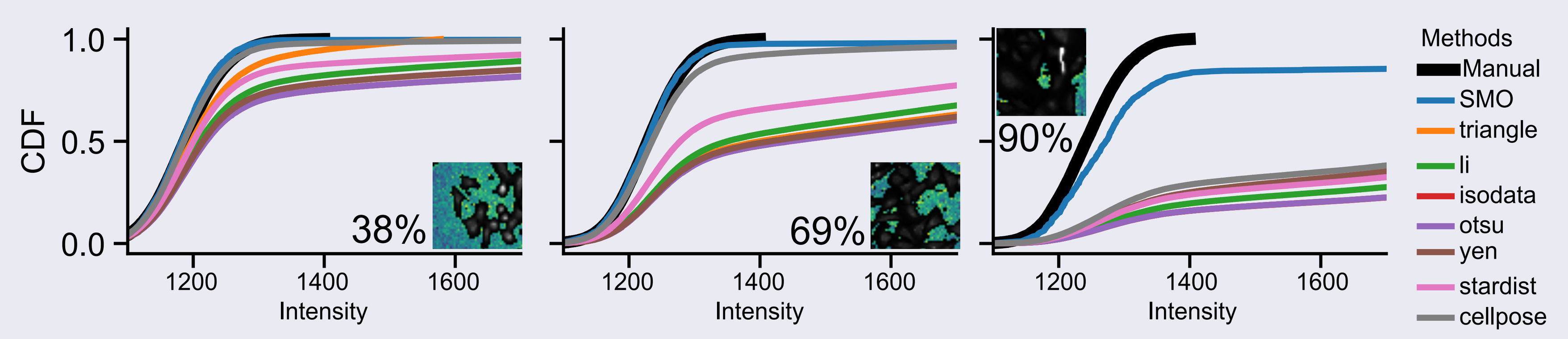
Thresholding the intensity histogram introduces bias

It is not possible to fully split it into foreground and background, as they tend to overlap. Selecting pixels with **small SMO values**, we can **exclude most of the foreground**, while **sampling the background fairly**.



Comparison against intensity thresholding and DL segmentation methods

Comparing with a manually-selected background region, SMO is robust against changes in **foreground to background ratios**, while the performance of other methods degrade including ML-based methods like stardist and cellpose.



Binlets: denoising for multichannel datasets

What it does: adaptive binning based on the Haar wavelet transform. Applicable to multidimensional and multichannel datasets.
Hypothesis: smoothness, i.e. neighbouring pixels could be averaged.
Requires: test to compare if neighboring pixels are similar.

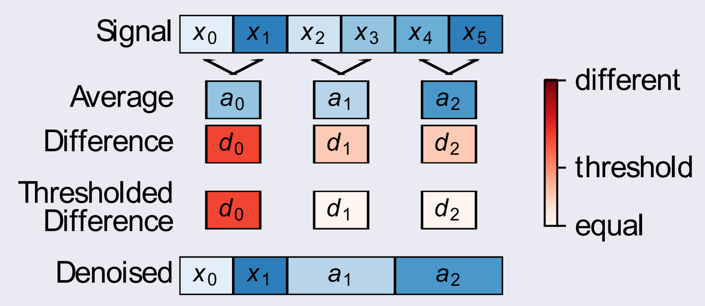
Haar wavelet transform and coefficient thresholding for denoising

Forward transform

$$a_i = x_{i+1} + x_i$$
$$d_i = x_{i+1} - x_i$$

Reverse transform

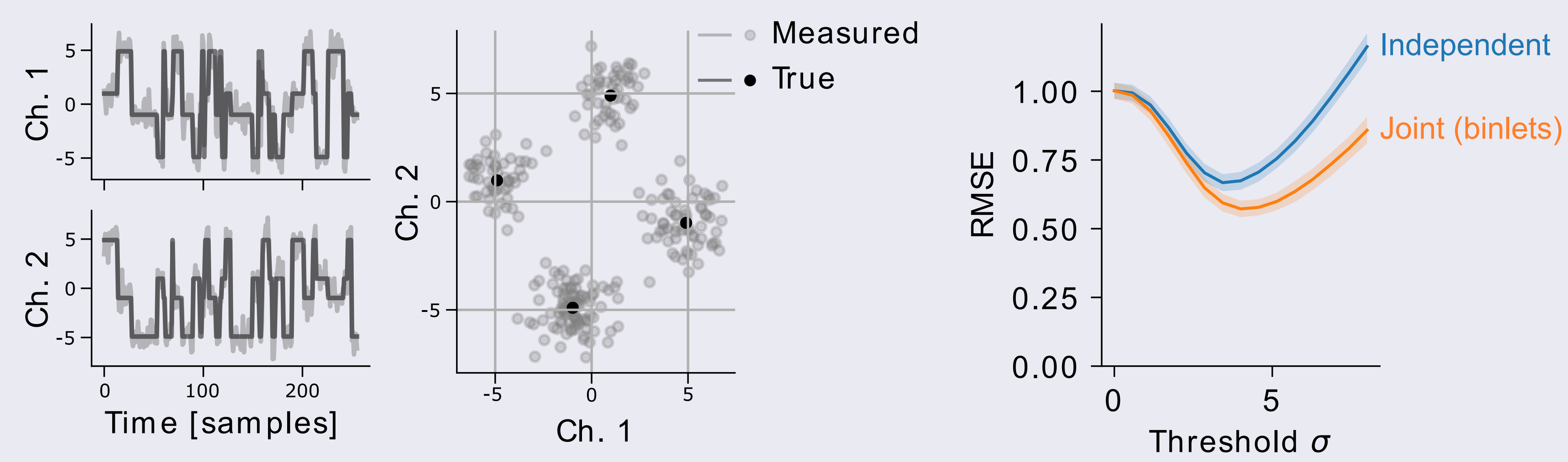
$$x_{i+1} = (a_i + d_i)/2$$
$$x_i = (a_i - d_i)/2$$



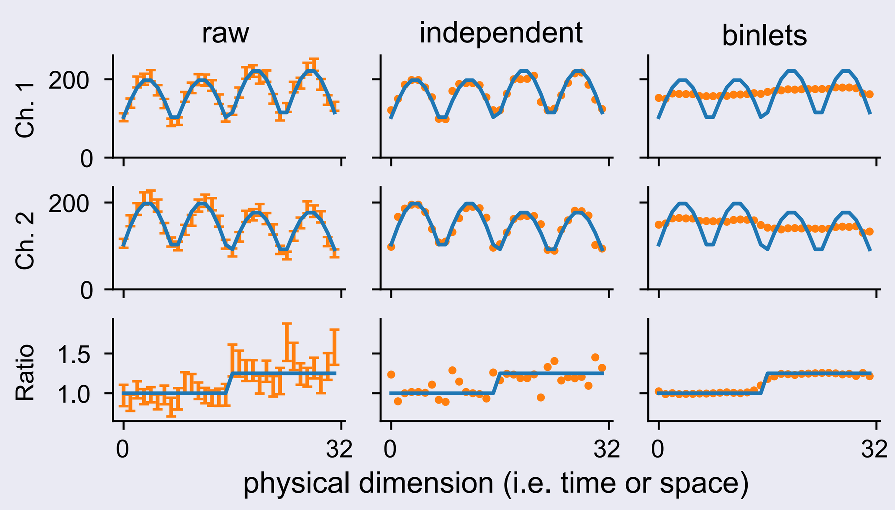
It can be thought as a recursive series of sums a and differences d between neighboring pixels. **Zeroing** the difference d, **results in averaging them**.

Multichannel thresholding: component-wise vs vector

Thresholding simultaneously prevents averaging components that have a small difference, but correspond to different values as a whole.



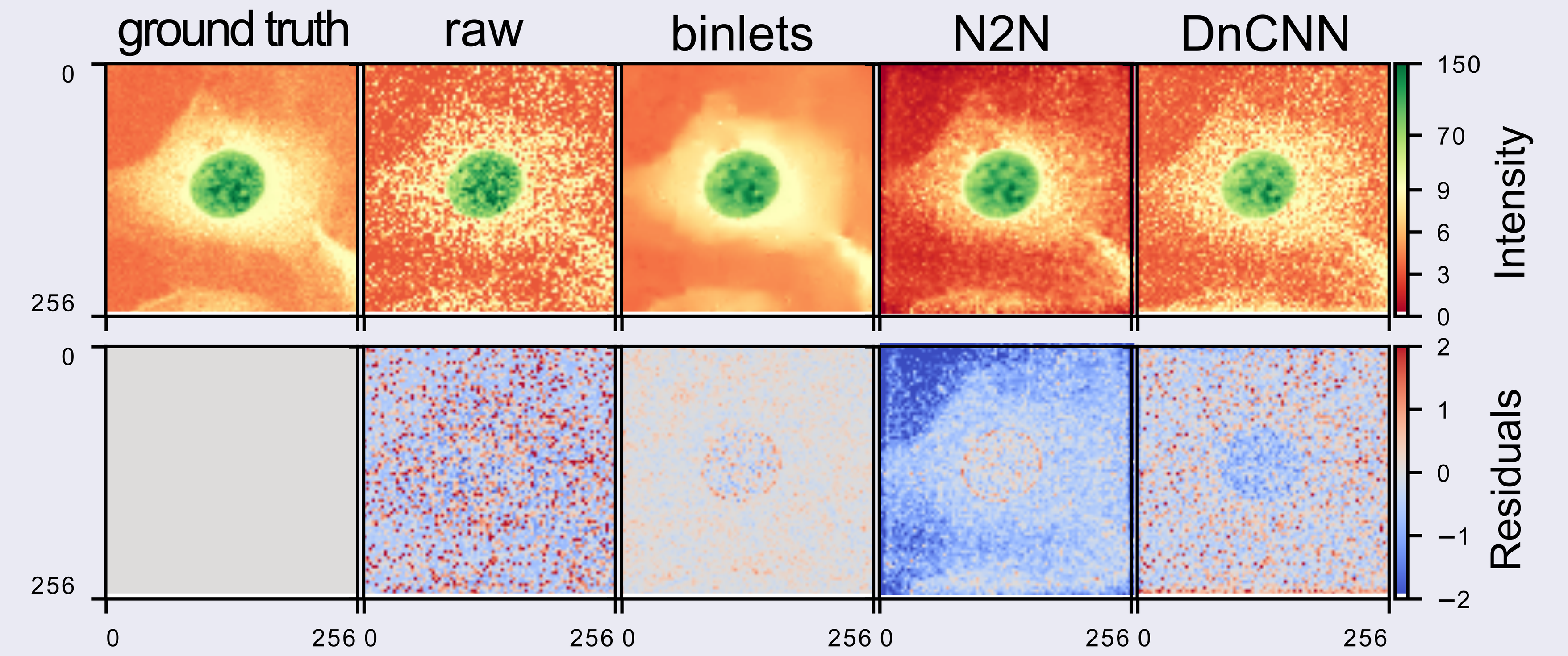
Thresholding based on a target transformation



For **transformations** of multichannel signals, such as a ratio between channels, the **decomposition** is performed in **the original signal**, but the **transformation** is used to **to decide the averaging**.

A comparison against Deep Learning denoising methods (for single channel data)

Fluorescence imaging microscopy of cells. **Dataset:** 20 different cells, 50 frames per cell. **Ground truth:** average of 50 frames. **Result:** binlets shows less bias than the Deep Learning methods Noise2Noise (N2N) and DnCNN.



Model-based methods can leverage ***prior* knowledge** of the **measurement process** and obtain better results than data-driven-only methods. After all, super-resolution (structured illumination, stimulated depletion, stochastic activation) was achieved by **modelling the illumination**. The diffraction limit applies when we ignore it.

Use them before turning to AI to reduce the parameter space, for instance, by removing the background. If each image y_i has a different background b_i:

$$y_i = f(x_i, p) + b_i \qquad \text{vs} \qquad \hat{y}_i = f(x_i, p)$$

an AI model has to *learn them*, and will **not be transferable** to other microscope settings.