A registration error estimation framework for correlative imaging

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Image registration

Point-based image registration is the process of searching the best geometric transformation linking two images using a set of fiducial pair of points and a theoretical model.

A theoretical model describes how we think the actual transformation between the images looks like.

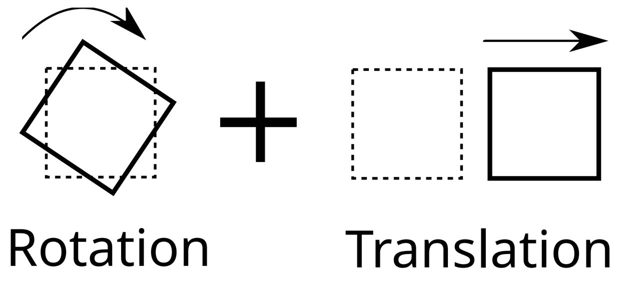


Figure 1. Description of a rigid transformation

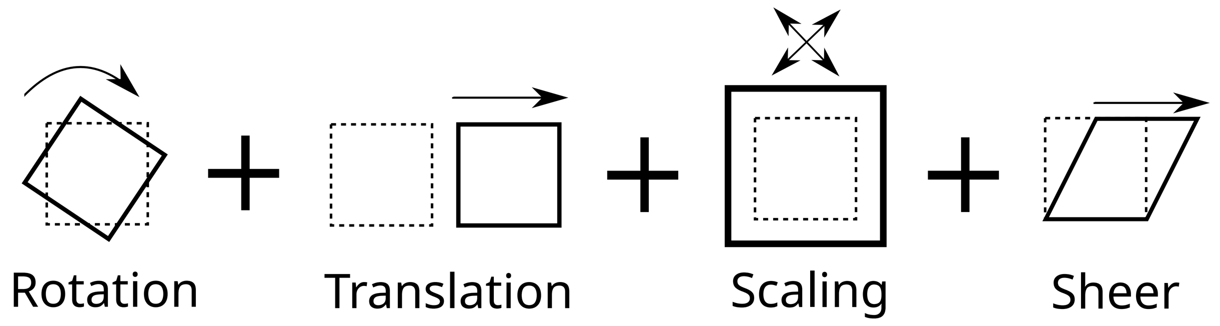


Figure 2. Description of an affine transformation. The affine model is the most general of all linear models.

Correlative light-electron microscopy

Correlative imaging workflows are now widely used in bio-imaging and aims to image the same sample using at least two different and complementary imaging modalities. Part of the workflow relies on finding the transformation linking a source image to a target image. We are specifically interested in the estimation of registration error in point-based registration.

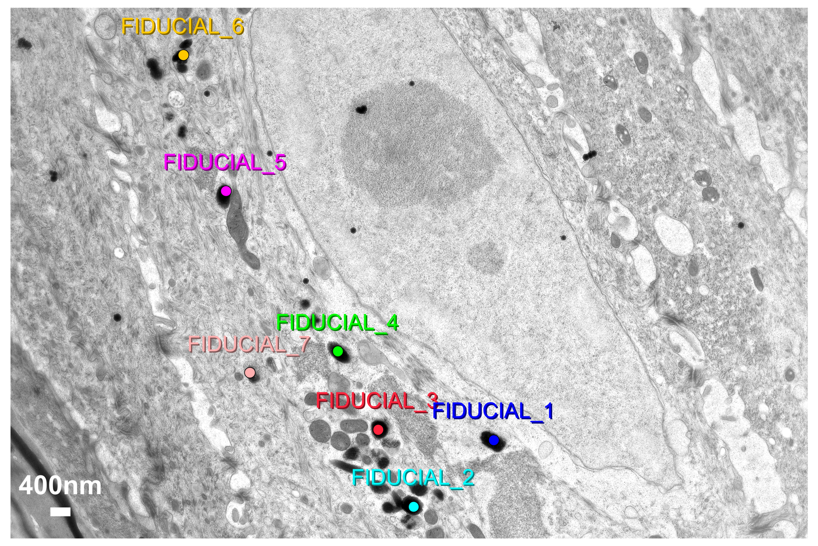


Figure 3. Electron microscopy with fiducial points set on cellular components

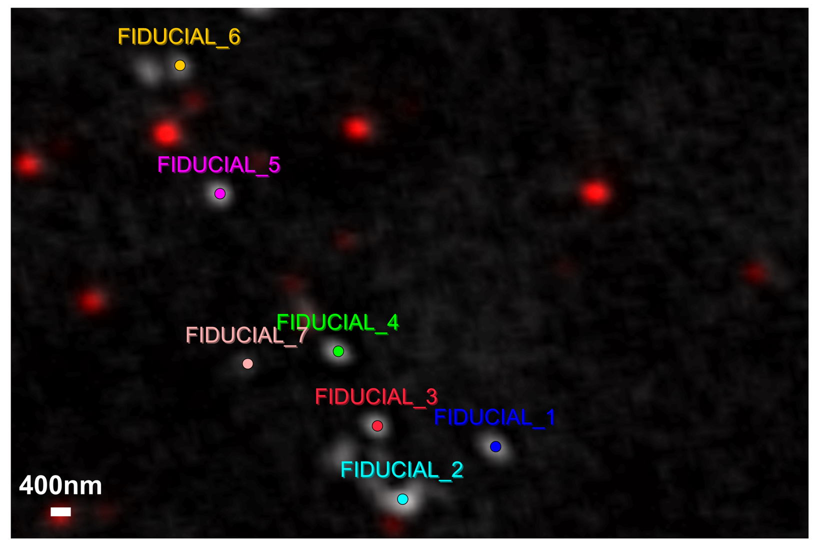
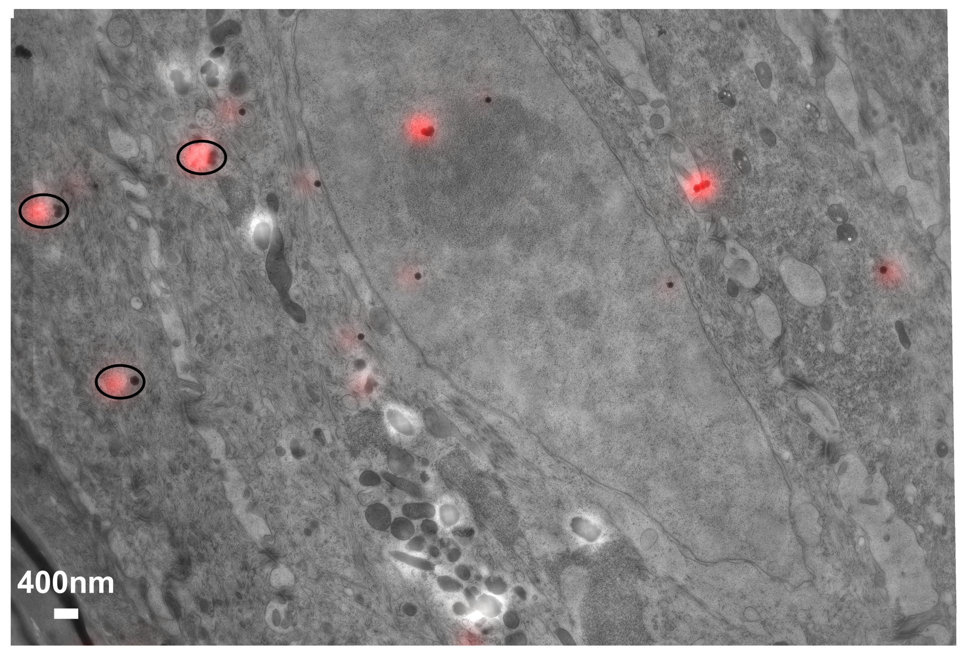


Figure 4. Fluorescence microscopy, white: cellular components , red: qdots

Registration error



The localization of fiducial points is prone to error, due to imaging resolution, method of localization or of sampling. This will create a registration error for all points of the image having consequences on the overlaying of points of interest.

Figure 5. Overlay of registered images from figures 3 and 4 using previously set fiducial points, showing discrepancy of points of interest (black and red)

Error estimation using leave-one-out cross validation

For each pair of fiducial points, perform registration using all fiducial pairs of points but one left out. Measure the error between the pair of points not used for registration. Compute the mean or median or 95th percentile of measured errors and use it as the registration error estimation at any point of interest. However this method has several drawbacks :

- Only computes a rough average
- Does not take the location of the point of interest into account
- Does not take the registration model into account
- Leads to a poor and sometimes wrong error estimate

Error estimation using an analytic registration error estimation framework

Our framework is divided in three parts: Start from the selected registration model. Derive an analytic expression for the covariance matrix of the prediction error. Construct a confidence area enclosing the registration error at a given point of interest.

For the rigid model we have to find the rigid transformation in the general case using a numerical solver. There exists a closed form solution for the special case of isotropic noise. Then use the Cramer-Rao asymptotic lower bound to get an estimate of the covariance matrix of the prediction error. Finally construct an asymptotic confidence area enclosing the registration error at a given point of interest.

For the affine model we can find the affine transformation in the general case by **casting the problem as a multivariate linear regression**. Then we can derive the prediction error covariance matrix using the linear regression theory. Finally construct an asymptotic confidence area enclosing the registration error at a given point of interest.

Results

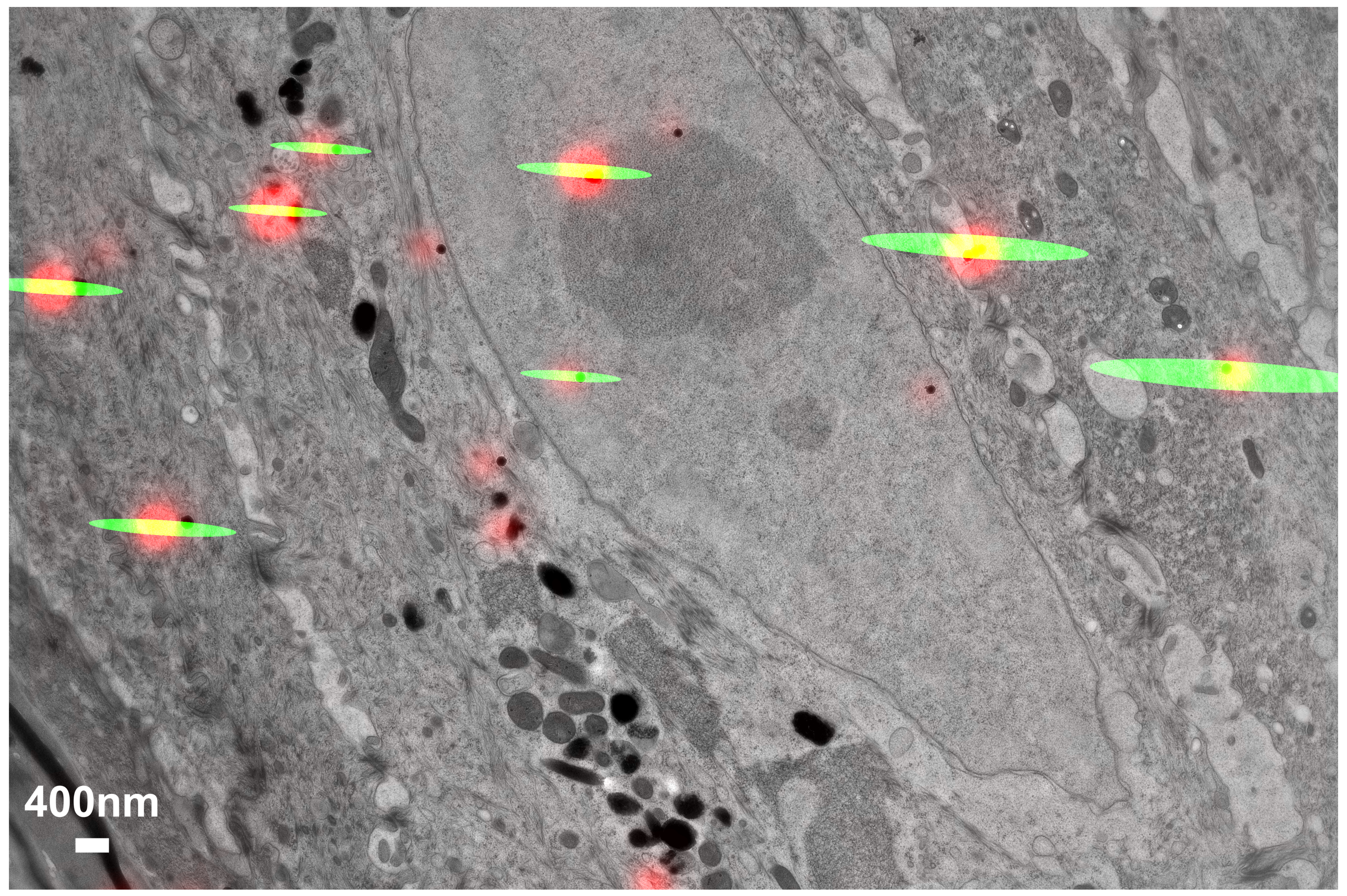


Figure 6. Computed confidence ellipses at 95% for points of interest

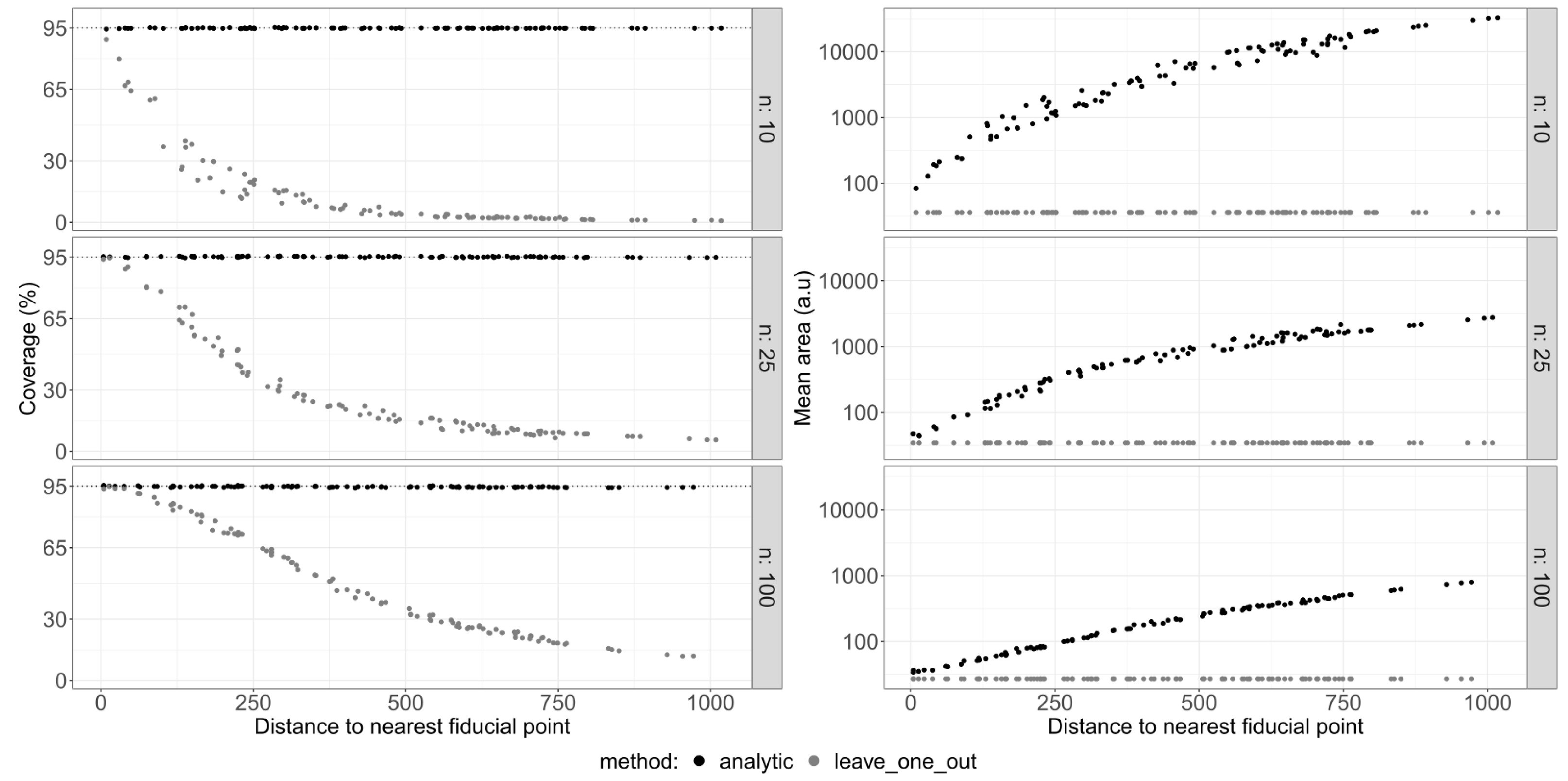


Figure 7. Coverage and mean area of 95% prediction ellipses at different test points for an affine model computed with analytic and LOOCV methods using 10, 25, or 100 fiducial points under an affine transformation. Coverage is the proportion of times the registered target point fall inside the confidence area during a stochastic simulation. For a 95% confidence area, the theoretical value of the coverage is 95%.

Transformation	Model	Coverage% n=10 mean/STD	Coverage% n=100 mean/STD
rigid	rigid	99.35 / 0.08	95.68 / 0.21
rigid	affine	94.98 / 0.14	94.57 / 0.22
affine	rigid	3.53 / 17.51	2.00 / 14.07
affine	affine	95.05 / 0.21	94.62 / 0.34

Table 1. Distribution of the coverage rate of 95% prediction ellipses (Coverage%, target value is 95%) for rigid and affine models (model) computed with analytic method under rigid and affine transformations (Transformation) using 10 and 100 fiducial points

Conclusion

- Leave-one-out methods fail to estimate registration error reliably
- Analytic expressions can be derived for rigid and affine registration models
- Fast and robust registration error estimation is provided for the affine registration model through multivariate linear regression
- Affine registration model being more general supersedes rigid registration model unless specific hypothesis are required