Image Processing Technologies for Motion Compensation

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Introduction

The impact of image processing in medical image analysis has increased in recent years concurrently with the development of novel imaging modalities and new user interfaces, facilitating both image analysis and maximizing the use of information present within the images.

One of the most important imaging processing technologies involves motion compensation. While images are assumed to contain information of a subject at one moment in time, measurements are, in general, severely hampered by the movement of the imaged organ. Specifically, physiological tissue motions give rise to strong artifacts, which vary in severity depending on the organ under investigation, the acquisition parameters (e.g., integration time and resolution), the imaging modality, and the ultimate imaging resolution, contributing in creating image distortion, blurring, and making image sequences highly unstable. Historically, the imaging techniques that have more extensively dealt with motion reduction methods are magnetic resonance imaging (MRI), particularly for high-resolution cardiac MRI, and X-ray computed tomography (X-CT). However, more recently, image processing approaches have been translated to other existing or newly developed imaging modalities.

In this chapter, we present several solutions that we and other groups have recently proposed for intravital laser scanning optical imaging, which could also be easily extended to widefield fluorescence imaging. Intravital microscopy is a relatively new imaging modality, which allows for investigating biological processes at the single cell level and in vivo due to its extended imaging depth, high resolution, and ease of implementation. Apart from its success in the biomedical field, intravital microscopy has also shown promise in the clinical settings, specifically for intraoperative imaging. Advancements in novel imaging systems in combination with the development of new targeted probes have provided a new platform and new capabilities to explore cell biology, and immunological response [1–3]. Unfortunately, motion artifacts have so far limited the full potential of optical microscopy for small animal and clinical imaging.

Respiration and cardiac activity are the major contributors to image artifacts; respiration is the most significant, affecting, in particular, the lungs and extending to all abdominal organs such as the liver, kidneys, pancreas, and spleen. Cardiac

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activity also has a broad effect on many organs, and so far has prevented collecting information of the heart itself at the single cell level. Several other sources may contribute to tissue movement, such as peristalsis, muscle contraction, and organ drifting. Generally, these sources can be prevented, but apart from simple image drifting no compensation schemes can be adopted.

All physiological activities give rise to motion induced distortions within acquired images or sequences of images. These motion artifacts can be classified into two groups: in-frame and inter-frame motion distortions (Fig. 14.1). In-frame motion artifacts arise when the object of interest moves within a time scale of the order of the acquisition time. Inter-frame motion artifacts, instead, are due to motion events which occur between the acquisition of consecutive frames or scans and are not present, or at least are not noticeable, within a single acquired image (Fig. 14.2).

Various solutions for inter-frame and in-frame motion artifacts have been proposed, and the

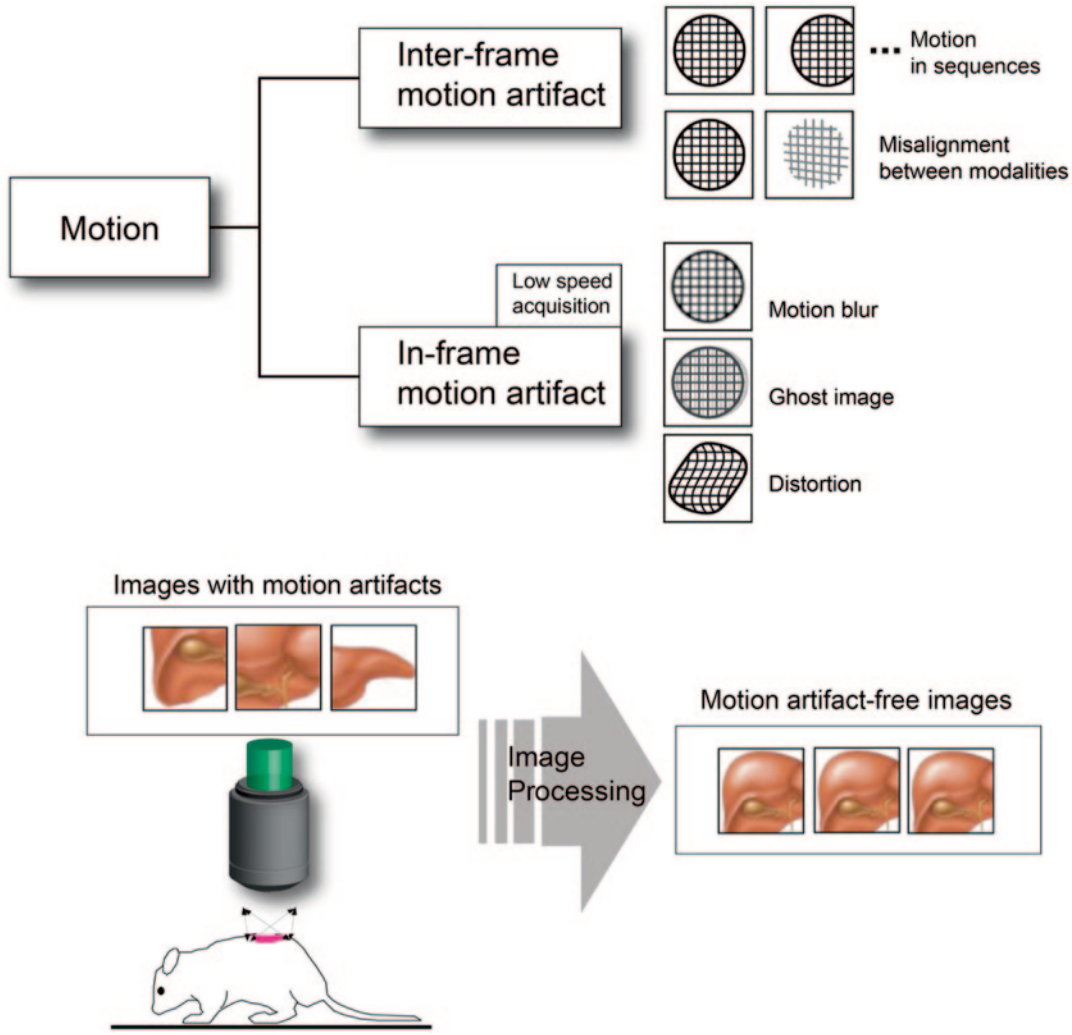

Fig. 14.1 Schematic showing different types of artifacts present during a typical image acquisition of an object in motion. Inter-frame and in-frame motion artifacts present different characteristics with the former affecting images over a long period of time (e.g., acquired sequences) and the latter giving rise to visible effects within single acquired images

literature is abundant with innumerable image processing algorithms [4–13]. We briefly discuss these solutions.

Inter-frame Motion Compensation

Inter-frame motion refers to motion caused by the imaging subject, with respect to the imaging device, and/or due to misalignments between different imaging modalities. The effect is typically evident over multiple image acquisition, such as time-lapse imaging sequences. In image sequences like video frame rate movies, inter-frame motion is, for the majority of cases, compensated by techniques known as "video stabilization," with the intent to remove unwanted artifacts due to relative movements, changes in the relative orientation of the imaging device and subject, or to the shaky motion of the acquisition apparatus (e.g., handheld charge-coupled device (CCD) for panoramic organ exploration). Historically, video stabilization has been developed to fix shaky videos by removing unwanted motion through image processing [6]. Recently, a similar idea has been successfully applied to in vivo microscopy where continual physiological movements severely impede microscopic observation of dynamic events in live tissues [7].

"Image registration" algorithms have been widely utilized as key technologies for aligning multiple images, acquired mainly from different modalities (e.g., MRI and CT or positron emission tomography, PET) into one coordinate system [8, 9], but they can also be applied to image sequences for inter-frame motion compensation. A typical application, as an example, arises when acquiring fluorescence contrast images in arteries by way of an imaging catheter and co-registering the signal with a simultaneously acquired angiogram [14]. Here the registration algorithm aligns multiple images from the different imaging techniques into one single coordinate system.

Both video stabilization and image registration are fundamentally based on the transformation motion models, which are historically classified as linear (global) or nonrigid (local) transformations. Linear transformations span from simple translation models to projective transformation models. Nonrigid transformations, instead, range from small regional variations describable with a small number of increased parameters to very dense displacement vector fields such as optical flow (Fig. 14.3). These algorithms can be utilized not only to align images but also to extend the imaged area by stitching separately acquired images. This is a typical case where motion (e.g., handheld reposition of the imaging device) is positively utilized to increase the field of view (Fig. 14.4) [10].

In-frame Motion Compensation

In-frame motion artifacts are present within single images and their origin can be ascribed to the relatively low-speed acquisition with respect to the imaged subject's motion. Common examples include image blurring in CCD acquired images, caused by the high-speed motion of the subject and the

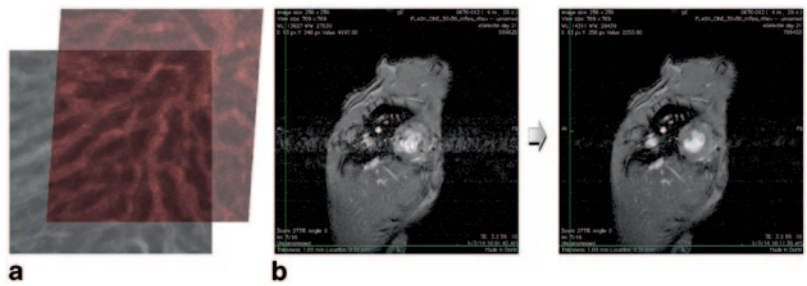

Fig. 14.2 Examples of motion compensation. **a** Inter-frame motion compensation: two microscopic images of mouse liver vessels are registered using an affine transformation model. **b** In-frame motion compensation: motion artifacts within an MRI image (*left*) are removed by motion-gated acquisition, leading to an artifact-free image (*right*)

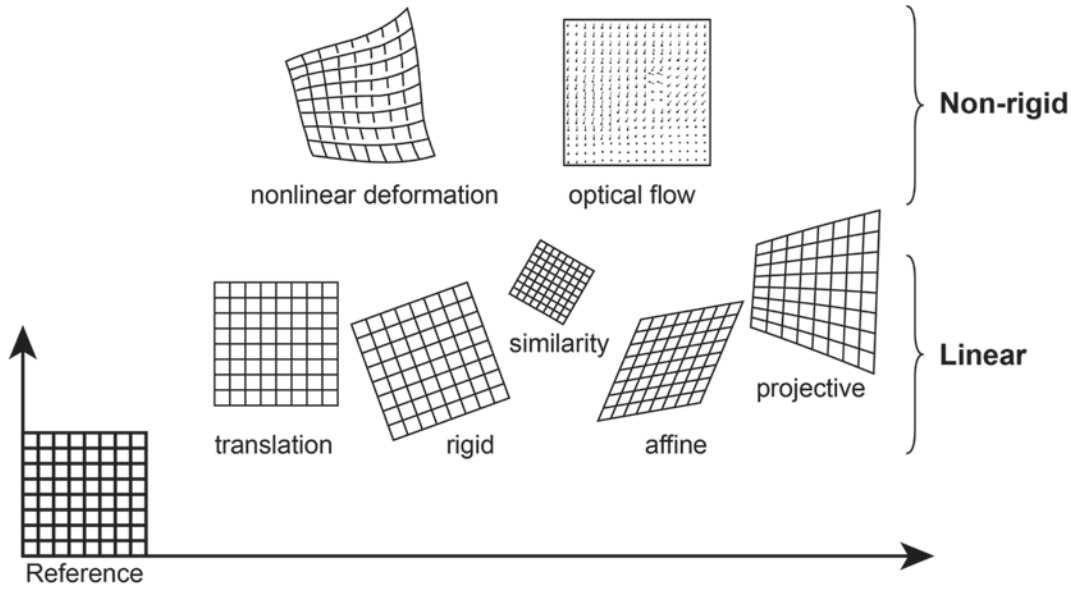

Fig. 14.3 Various transformation models, including both linear and nonrigid ones, which are commonly used for postprocessing acquired data. The final goal is to reduce image distortions induced by the imaged organ or the operator

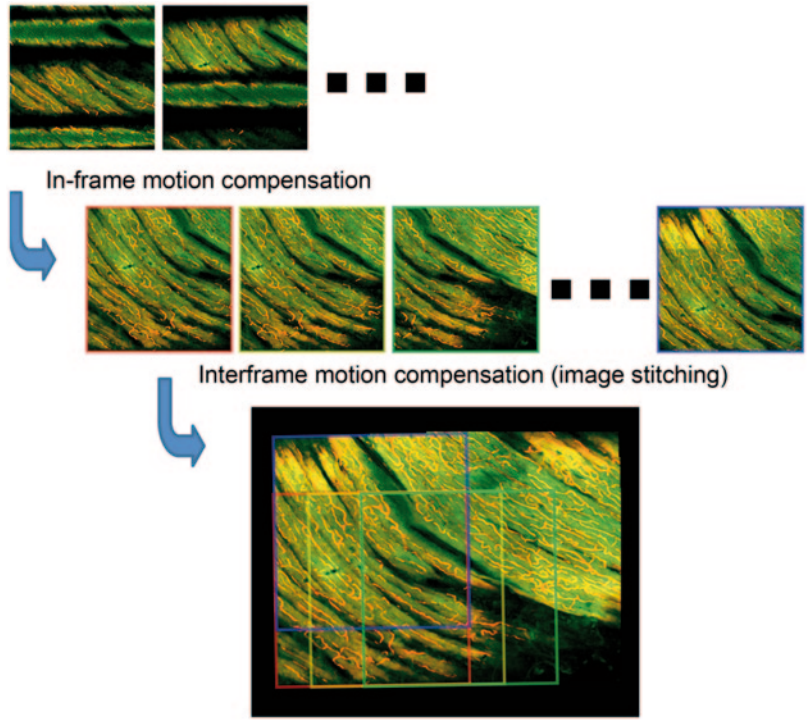

Fig. 14.4 Image mosaicking through in-frame and interframe motion compensation of a sequence of images obtained by laser scanning microscopy (LSM). During a first initial image processing phase, an automatic motion artifact removal algorithm [13] eliminates in-frame motion artifacts due to the heart beating. During a second phase, when the operator collects images over several adjacent areas of the heart, in-frame motion compensated images are combined together using a stitching algorithm, to give rise to a final panoramic image

relatively long exposure times (slow shutter speed) of the imaging devices. Ghost images in MRI are also well known to induce in-frame motion artifacts due to movement of subject and slow MRI scanning time. The effects can be mitigated by choosing a high-speed acquisition modality minimizing the motion during acquisition, leading to the elimination of the artifacts. For example, high shutter speed of a CCD can freeze a fast-moving object without motion blur in the resulting image. Although this simple high-speed approach can in principle reduce the motion artifacts, a reduced signal-to-noise ratio occurs as the absolute exposure time decreases depending on the speed increase.

Alternatively, slight motion blur artifacts can be removed from images through an image processing technology known as "motion deblurring," which needs no other images and information regarding the nature of the motion [11, 12]. Although these techniques are quite impressive in terms of visual appearance, in-frame motion compensation, in general, needs additional information such as motion parameters and multiple images in order to achieve a successful degree of motion compensation. To date, various motion reduction methods have been developed, particularly for high- resolution cardiac MRI, that speed up scanning acquisition times and/or involve the use of temporal or spatiotemporal redundancy [15–18]. Here the key principle underlying scan acceleration is based on the presence of quasi-periodic motion components, i.e., the predictable reproducibility of tissue position at certain time points during physiological (cardiac and respiratory) cycles, which allows for assisted motion-synchronized scanning [15]. A priori knowledge of the position, in combination with prospective triggering or retrospective gating acquisition schemes, can therefore enable fast-moving object imaging.

Acquisition Schemes for Motion Compensation in Laser Scanning microscopy

During LSM acquisition, an excitation laser scanning point moves along a predefined trajectory across a horizontal imaging plane. Due to the presence of physiological or operator induced motion components, the point along the described raster trajectory will not lie at the same depth within the imaged organ. Therefore, the acquired image is not representative of a single horizontal imaging plane across the sample but instead coincides with a curved surface with its profile modulated by both the speed of the motion and the microscope acquisition parameters (Fig. 14.5). The final image will then present in-frame artifacts such as distortion and blurring, the severity of which varies along a physiological cycle in relation to the instant speed (e.g., cardiac-induced motion will be minimal during the diastole, a cardiac phase with the heart at resting state).

Through the years, several acquisition schemes have been developed for cardiac and respiratory MRI with the intent to mitigate motion-induced artifacts. While the basic imaging principles of MRI and optical microscopy are different, the principles of image stabilization are adaptable to both techniques (Fig. 14.6) and we have recently successfully translated some of them to optical microscopy [19].

In cardiac MRI, "segmented cardiac-gated acquisition" has been widely and extensively used to correct for cardiac motion artifacts. Here, to acquire an MRI image at a specific time point during the cardiac cycle, only the data corresponding to a well-defined time window in the k-space are selected and gathered until the entire k-space is filled ("view per view" acquisition). Thanks to the quasi-periodicity and reproducibility of the cardiac motion, at least on the scale of the MRI resolution, a full k-space image can be reconstructed by collecting all segments acquired at different time points within a well-defined cardiac phase. This procedure can be done both in an active (prospective triggering) or passive mode (retrospective gating). In retrospective gating the electrocardiogram (ECG) signal is continuously measured during MRI acquisition. ECG-gating is then applied on all acquired images selecting the k-space lines corresponding to specific time intervals of the cardiac cycle. All segments are then postprocessed and combined to give rise to a final image representative of the organ at

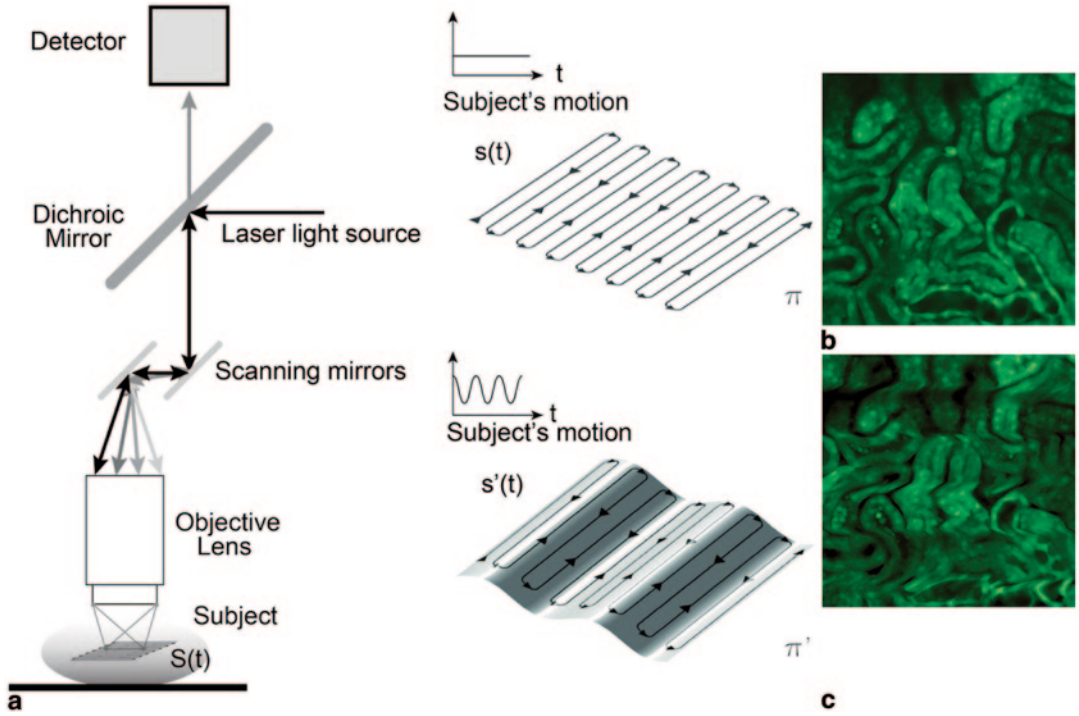

Fig. 14.5 **a** Scheme of principle for laser scanning confocal microscopy. Two galvanometer mirrors oscillating along orthogonal axes scan the excitation laser beam along a raster path. Light is focused onto the sample and the emission light is detected through a dichroic mirror. **b** When the subject is stationary, the raster scanning path lies on a horizontal imaging plane perpendicular to the imaging objective. **c** When the subject moves, the imaging plane in the organ's reference frame will appear as a curved surface modulated in time according to the motion periodicity [19]

a specific time of the physiological cycle. Prospective triggering, instead, requires acquisition directly initiated by the ECG signal. By varying the delay between a specific time point of the ECG and the acquisition, all k-space segments representative of a time point within the cardiac cycle are collected and a final artifact-free image is then reconstructed (Fig. 14.6).

Recently we have extended these imaging schemes specifically to LSM to image beating heart in mice (Fig. 14.7). Here, analogous to MRI, multiple images are acquired sequentially; by gating to specific time points in the ECG, views are grouped into segments to give rise to a final reconstructed image representative of a horizontal imaging plane free of any motion-induced artifact. While acquiring physiological parameters could facilitate image processing and artifact removal, other possibilities are available which do not require direct or indirect monitoring of the tissue under investigation. Recently, we have proposed several automatic artifact removal image processing algorithms which utilize correlation between individual image segments instead of using motion information in order to identify the data corresponding to the same specific cycle phase [13], combining them into a final "stabilized" image (Fig. 14.8).

Passive and Active Mechanical Stabilizers

Because LSM usually operates at higher resolutions than MRI, it is very important to reduce, as much as possible, the total displacement due to physiological motion, and to introduce high reproducibility in the motion in order to implement

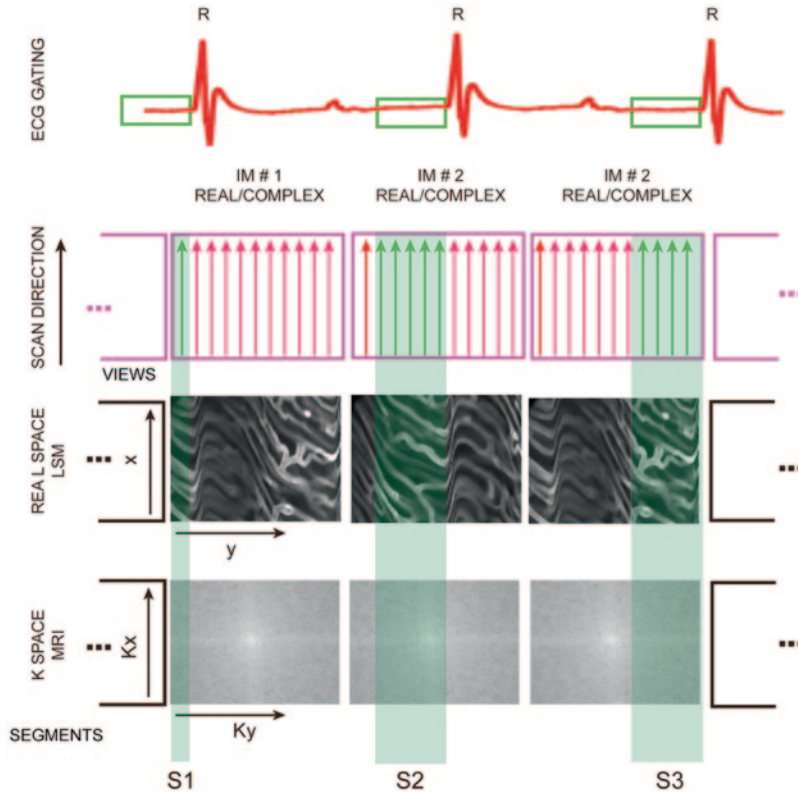

Fig. 14.6 Principle for sequential retrospective electrocardiogram (ECG)-gated imaging [19]. In MRI, a sequence of views is collected in the k-space by varying the phase-encoding gradient. Laser scanning microscopy (LSM) images are acquired pixel by pixel in the real space, with the excitation scanning laser beam moving along a predefined path. Groups of views are sequentially collected within a time-gated window corresponding to the end-diastole. The process is then repeated until the entire real space (LSM) or k-space (MRI) is filled. (Figure adapted from [19])

the reconstruction algorithms indicated above. Only under this assumption, segments belonging to the same specific phase of the cardiac cycle but collected at different point in times are equal and therefore can be patched together. In the absence of reproducibility the segments will be uncorrelated to each other, even if gating or triggering schemes are implemented.

One of the most obvious and easily implemented methods to attenuate motion-induced image artifacts consists of establishing physical immobilization, for example when imaging the skin of a patient during a routine dermatological check. When imaging inner organs, however, immobilization cannot always be achieved and mechanical restriction is commonly used to limit and confine tissue motion, for example by applying a gentle pressure. The limitation of this strategy is that it can negatively impact the physiological functions. Moreover, it will not completely suppress motion-induced artifacts and may fail to provide enough high-resolution images due to the random nature of the motion. For this reason, various mechanical stabilizers have been proposed and extensively used in small animal imaging (Figs. 14.9a, b) [20, 21], which could be translated with some degree of success into patients [22]. Although passive stabilizers are more commonly used, to further compensate residual motion components (Fig. 14.9b) gating algorithms or active tracking devices are highly recommended. Here, relative motion between the imaged organ and the imaging lens is completely removed by keeping their relative po-

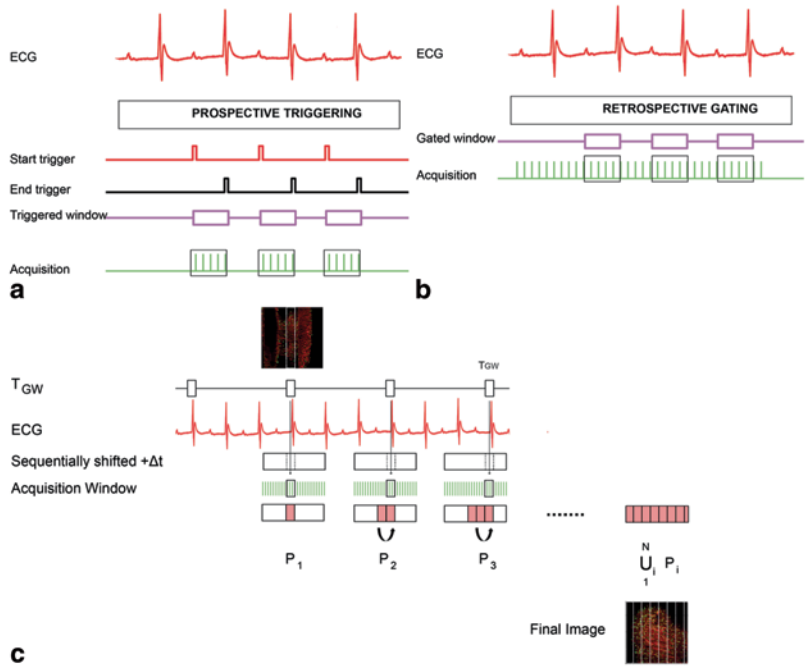

Fig. 14.7 **a** Prospective triggered acquisition scheme: images are acquired only during a specific triggered window, which is determined by the ECG. All acquired data are therefore used for image reconstruction. **b** Retrospective gated acquisition scheme: data for images are continuously acquired together with the ECG signal. Following this nonselective acquisition, only the data that were acquired during the time of a specific gated window, which is determined by ECG, are chosen for image reconstruction. **c** Simplified timing diagram and image reconstruction scheme for sequential retrospective cardiac-gated segmented microscopy. Segments from a continuous sequence of images are grouped together and a final image is reconstructed, which provides a true representation of the heart's morphology at the cardiac phase corresponding to a specific time-gated window [19]. (Figure adapted from [19])

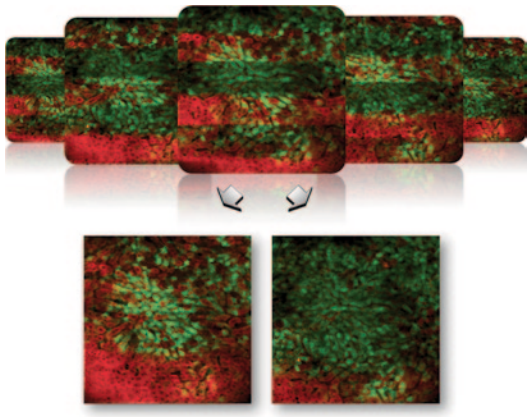

Fig. 14.8 Results of automatic artifact removal image processing [13]. The basic idea is to automatically identify within a sequence of images all artifact-free segments, combining them into a final "stabilized" image. Raw images (*upper part*) are in vivo microscopic images of a mouse liver. (Figure adapted from [13])

sition to each other constant over time. While in small animals this could be achieved sometimes by moving the subject, in human patients this strategy is not feasible and the imaging objective is typically tracking the moving organ. The objective lens is attached to a fast moving mechanism controlled with a feedback loop to track the tissue motion, while the organ's position is tracked with a high-speed imaging system. The relative position of both objective and tissue is therefore kept constant over time providing virtual, free of motion artifacts images. Recently, robotic systems have been developed based on this principle [23] that make use of visual information or contact-type displacement sensing. In the first solution, a vision based compensation system (Fig. 14.10a), a high-speed camera (955 fps) collects 2D images of the moving organ, which is preventively stabilized along the third dimension (vertical axis) by way of a compressive cover

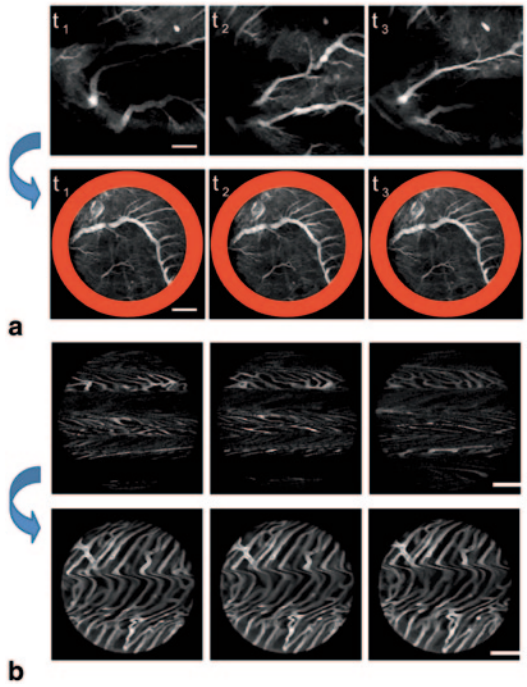

Fig. 14.9 Cardiac vasculature image sequence of a beating mouse heart at **a** low and **b** high resolution. Passive mechanical stabilization as proposed by [20, 21] were used to reduce image artifacts. At low resolution (**a**), motion artifacts look almost absent following mechanical stabilization. However, at high resolution (**b**), artifacts are still present, requiring further postprocessing. Scale bars: **a** 500 μm and **b** 50 μm. (Figure adapted from [13])

slip. A piezo-driven robotic closed arm with 2 degrees of freedom and consisting of a five-bar linkage with living hinges is then used to control the position of the imaging objective lens. Demonstrating optimal motion compensation for kidney imaging, the residual motion of this setup was less than 10 μm, while the maximum amplitude of the compensated motion was in excess of 150 μm. The second solution, instead, relies on motion compensation by contact-type displacement sensing (Fig. 14.10b). This solution is sometimes preferable over the first because of the reduced costs and the possibility to track motion in 3D. The signal from three strain gauges of a contact-type sensor consisting of three cantilever beam in direct contact with the imaged tissue is used to estimate the displacement and track tissue positions over time. Here a piezo-driven robotic closed arm with 3 degrees of freedom, one more than in the former configuration, is used.

Conclusion

Imaging technologies such as MRI, CT, and ultrasound have considerably improved over the course of the last two decades and novel image processing technologies for motion compensation have been proposed in part because of the implementation of implemented. Due to their portability and low cost integration, intraoperative optical imaging systems with different resolution scales are also increasingly used. While optical imaging techniques potentially offer the ability to acquire data at the single cellular level, physiological motion components have quite limited their application at the microscopic scale. Here we have presented different solutions that are currently available to suppress motion-induced image artifacts, which can be implemented for both wide field and laser scanning fluorescence optical microscopy. Translation into the clinical environment should be pretty straightforward and further facilitate the implementation of CCD and laser scanning based imaging technologies. Among the different applications, cardiovascular and tumor surgery would benefit the most by adoption of these methods. For example, intraoperative motion compensation in the beating heart could help detect differences between noncontracting necrotic myocardium and noncontracting viable but stunned or hibernated myocardium. These limitations are particularly problematic in the case of surgical revascularization of patients with severe myocardial dysfunction, where it may be impossible to ascertain which areas can or cannot be recovered to contraction by means of revascularization. Also, during typical cancer resections, tissue margins could be evaluated more accurately during the procedure itself without additional postoperative intervention.

Image processing technologies for motion compensation will also be enormously facilitated by the implementation of graphics processing units (GPU) for real-time processing acceleration, further allowing the adoption of these technologies to be seamless and immediate.

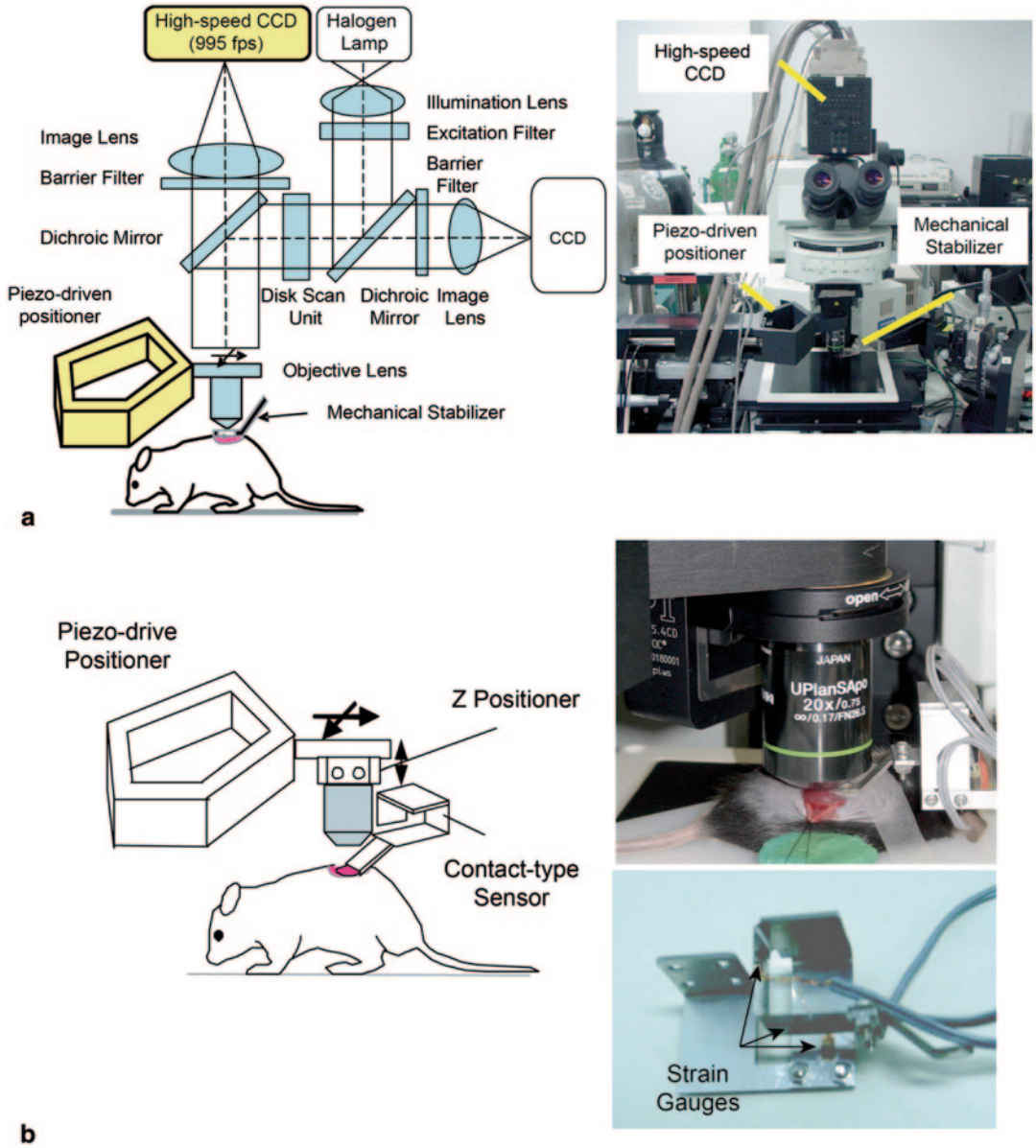

Fig. 14.10 Active motion compensations schemes [23]. **a** "Visual information"-based active motion compensation: a high-speed camera (955 fps) collects 2D images of the moving organ which is preventively stabilized along the third dimension (*vertical axis*) by way of a compressive cover slip. A piezo-driven robotic closed arm with 2° of freedom and consisting of a five-bar linkage with living hinges is then used to control the position of the imaging objective lens. **b** Contact-type sensing-based active motion compensation: The signal from three strain gauges of a contact-type sensor consisting of three cantilever beams in direct contact with the imaged tissue is used to estimate the displacement while a piezo-driven robotic closed arm with 3° of freedom moves the objective lens following the tissue position over time. (Figure adapted from [23])

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