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Motion Solutions for Digital Pathology

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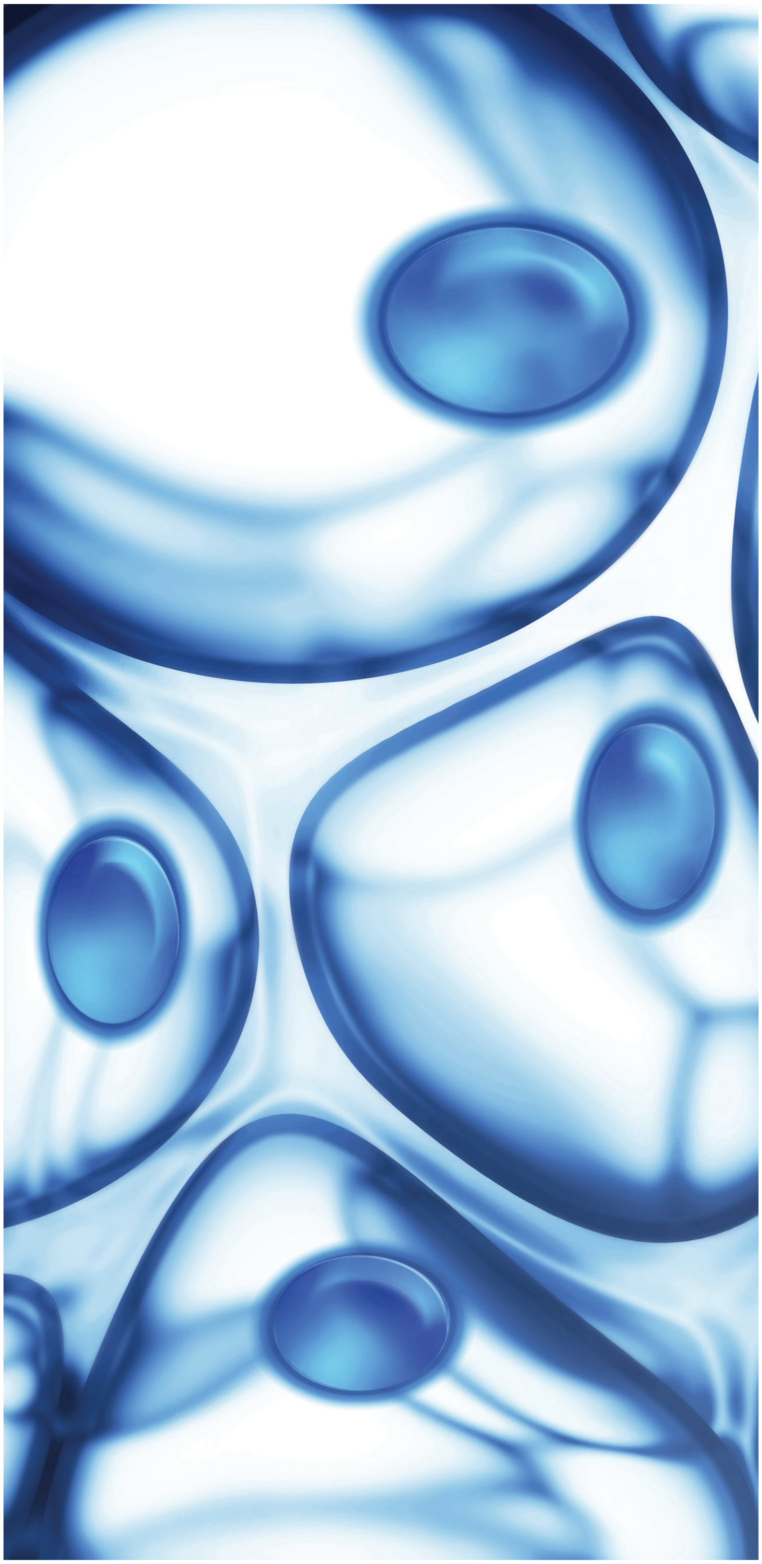
Design Considerations for Digital Pathology Instruments

With an ever increasing demand on throughput, pathology scanning applications are some of the toughest to solve.



Digital pathology is a rapidly growing segment of invitro-diagnostics with the potential to streamline the overall pathology process for the benefit of both doctors and patients. This relatively new market segment requires motion systems that support both high quality and high speed imaging. In addition, the scanners are dispersed globally, which drives the demand for extremely high reliability. Lastly, as with all diagnostic instruments, laboratory space is at a premium, so minimizing the overall footprint is critical.

Automated pathology scanners require unique positioning specifications that are not found in off the shelf components and will not fit into the instrument required footprint. Because of the packaging challenges, the motion system is often integrated into structural elements of the instrument. Product consistency is required for high-volume manufacturing at a globally competitive cost. Whether you are designing your own pathology scanning stage or working with a motion control partner, this paper covers key considerations for creating a successful design.

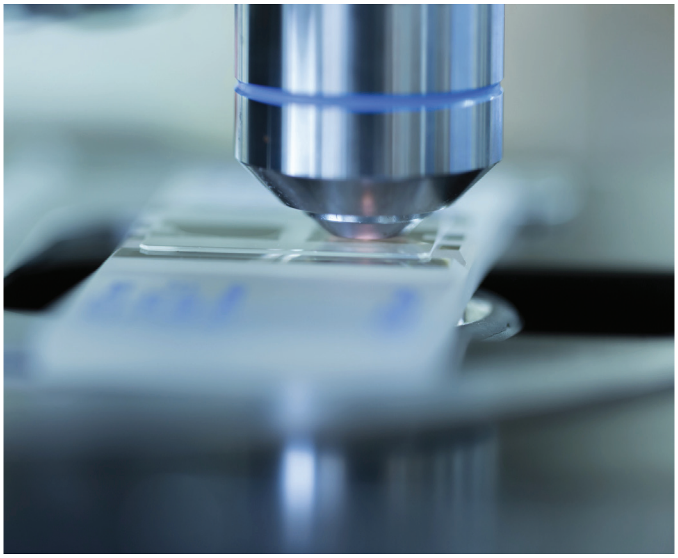


Figure 1: In addition to requiring high throughput, digitial pathology electromechanical systems must have excellent straightness, flatness and produce exetremely smooth motion.

Digital Pathology Motion Overview

Pathology scanners present OEMs with some of the most demanding motion control requirements in life science equipment. These scanners rely on the quality and performance of positioning systems to allow for the capture of the high definition images possible with their imaging components. The advent of digital Whole-Slide Imaging has made these devices one of the most promising tools in diagnostic medicine today, producing better quality, faster and less costly prediction, diagnosis and prognosis of diseases such as cancer.

In a pathology scanner, several slides are loaded into a cassette. The cassette is placed on an XY stage, which is mounted to the scanner frame. A vertical Z stage is mounted to the scanner frame above the XY stage, carrying the focusing optics. During the scanning process, the XY stages move the slides under the camera at a typical rate of 5 mm/s. The camera takes digital images within its field of view, which is on the order of 1 mm^2. While the XY stages are moving, to cover the entire slide area, which is typically on the order of 50 mm x 25 mm, the Z axis focuses the camera and holds a stable position for a fraction of a second, while snap shots are being taken by the camera.

Figure 2: An example of a high precision, monolithic pathology scanner

All of this must be accomplished, of course, within a defined space. The market demands a minimized footprint, which factors in the given camera's shape and size, illumination requirements, and special slide holder requirements. The space constraints required limit the choice of XYZ stage configurations, often requiring low profile, built-in apertures and highly customized axes with miniaturized motion control components.

Scanning Stages

The scanning XY stages typically move the slides beneath a fixed microscope or camera system so that images can be captured at a high rate of speed. To improve throughput, images are often captured on-the-fly. The key motion characteristics are:

- Flatness – Scanner flatness must be tightly controlled to reduce the dynamic of the Z axis to auto focus
- Straightness – Scanner straightness is required to minimize overlap between scanning passes and increase process throughput
- Smoothness of motion – Smoothness of motion is required to assure the highest possible image resolution.

Flatness

Flatness of motion is determined by several factors, including flatness of the slide and base surfaces of the stage and flatness of the linear guidance system. Typical flatness requirements for pathological scanners are on the order of sub-micron per mm. For example, consider an X stage which scans at 5 mm /sec and has a flatness of +/- 1 μm / mm. This flatness and scanning rate represents a position disturbance to the autofocusing stage with amplitude of 1 μm and a frequency of 5 Hz. This in turn implies that the required bandwidth of the Z stage should be at least three times higher than the disturbance frequency. It also implies that the natural frequency will be three times higher than the bandwidth. The flatness of Parker scanners as an example is on the order of submicron levels. This flatness performance is achieved by using linear bearing technologies that are specifically selected for this type of application.

Straightness

Straightness is determined primarily by the rails and their assembly procedures. These systems require a straightness spec, using high-precision rails and special assembly fixtures that are smaller than +/- 0.25 μm / mm.

Smoothness of Motion

As shown in Figure 3, this system is using miniature linear motors to drive the XY stages with linear encoders as feedback. Miniature linear motors have the advantage of being compact with low profile size and are completely non-contact. They therefore have an advantage in applications with limited space, such as pathology scanners. Linear motors are virtually jitter- and friction-free positioning technology, resulting in high smoothness of motion and long life. The linear encoders used in Parker scanners have resolution on the order of 10 nanometers. The mounting design of feedback and other elements, critical to the operation, are designed to achieve very high system response and reduce vibrations, which may otherwise limit the optical resolution.

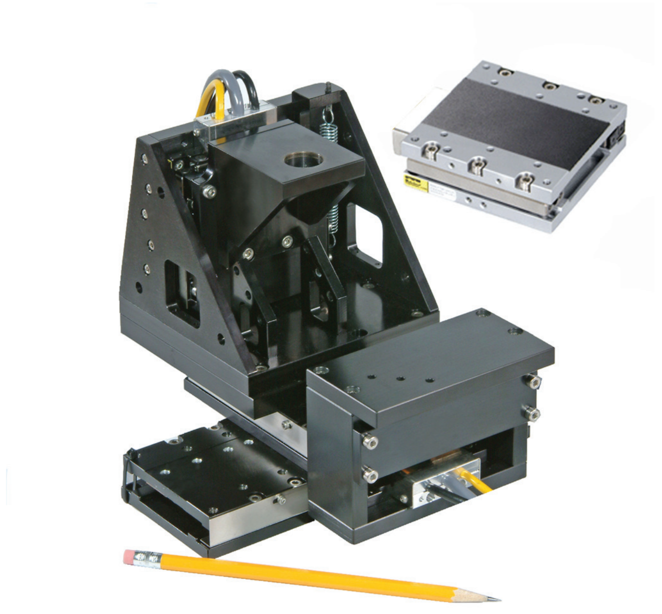


Figure 3: An example of Parker single linear motor stage (upper right) and XYZ Stages (lower left).

Auto Focus Z Stage Options

The Z axis stage, as shown in Figure 4, supports the optical head, including lenses and mounting bracket of the for focal adjustment. The operation of the auto focus stage is critical to the performance of the scanner and to the image clarity of the scanned objects. It must have extremely high resolution (in the nanometer range), fast response, short settling time, stable holding position and repeatable operation. It also requires a precision controller with very consistent performance from one stage to the next.

The following are alternative options for this stage configuration:

Stacked Piezo Stage

Stacked piezo stages have very fast response and excellent position holding stability. Their limitations are in positioning hysteresis, which makes the servo control non-linear and more difficult to tune. They also have extremely short travel, on the order of a few hundred μm, which limits other tasks needed by the Z stage, such as mapping the entire XY range for Z height, or adapting to several chuck sizes or optics with different heights.

Hybrid Piezo Stage

Hybrid piezo stages consist of a combination of a ball screw stage and a stacked piezo stage mounted on top. The ball screw stage provides long travel at low accuracy. The precision stacked piezo stage provides holding stability and precise positioning. The advantage of this hybrid configuration is in increased travel as a result of the two positioning technologies used. Its disadvantage is its larger size, additional servo axis to control and difficult tuning of both stages.

'Walking' Piezo Stage

These stages have the advantage of miniature size, holding stability and long travel. Their disadvantage is in their change of performance over time. Most OEMs require that the system will be tuned with a consistent set of parameters for all similar stages. They expect all stages of the same type to act the same way over the lifetime of their systems.

Voice Coil or Linear Motor Stages

These stages have the advantage of offering long travel, miniature size, frictionless operation, low maintenance and consistent performance over the lifetime of the stage. Their disadvantage is in the need for a counterbalance in vertical applications. Parker has developed unique solutions to solve this limitation, including, among others, a non-contact magnetic counterbalance with a uniform force constant throughout the travel range of the state, with a repeatability of 0.1 μm.

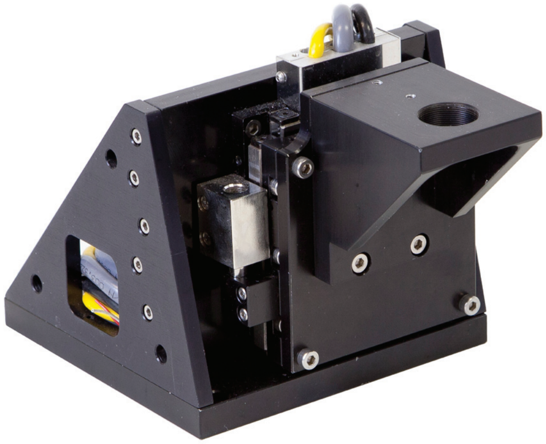


Figure 4: An example of a magnetically counter balenced Parker linear motor stage used for auto focussing.

Recommendations for Additional Design Considerations

For high smoothness of motion and short settling time, there are several additional design considerations OEMs should consider for any positioning systems being developed:

- Cables that are part of the design must be managed properly to minimize rattling effects.
- Wires need to be shielded and grounded to a common ground to reduce EMI and RFI noise.
- The equipment frame should be isolated from ground disturbances.
- Structural damping should be optimized to attenuate high-frequency noise amplification.
- Stage structure and machine frame natural frequency should be designed to meet the required move and settle frequency response.
- A controller's capability should be matched to the required frequency response.
- Proper servo filtering will attenuate high frequency noise.

Manufacturing the Solution

When looking for positioning solutions for automated pathology scanners, the key is understanding the importance and role of every component in the required design. These products have very specific and unique positioning motion specification requirements that off-the-shelf products often are not designed to meet. Positioning solutions can meet these requirements, but producing the best possible custom-designed solutions requires a technology partner with specialized knowledge and experience in the design and manufacturing of custom positioning systems as well as their components, with access to testing environments specific to the life science industry. Following a careful design process with experienced partners will lead to the best design solution that can also be affordably produced and still offer the reliability and demanding performance required for life science equipment.

About the Authors:

Jim Monnich is the Engineering Manager in Parker's Life Science Automation group. Jim has over 30 years of experience in the electrical motion and control industry, specializing in mechanical and electrical design. His primary expertise is in servo and stepper systems, position feedback technologies, as well as design and development of motion mechanics - focussing in on the areas of sub-micron positioning, and ultra precision velocity control for scanning.

Brian Handerhan is a Business Development Manager focusing on Parker's Life Science Automation group. Brian has over 20 years of experience in the implementation of automation across a broad range of industries. His primary expertise has been as a process improvement leader, change agent, and P&L owner. He now focuses that broad experience working with industry OEM's to develop lasting business relationships built on both operational and technical value.

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