

Softwell[®] 

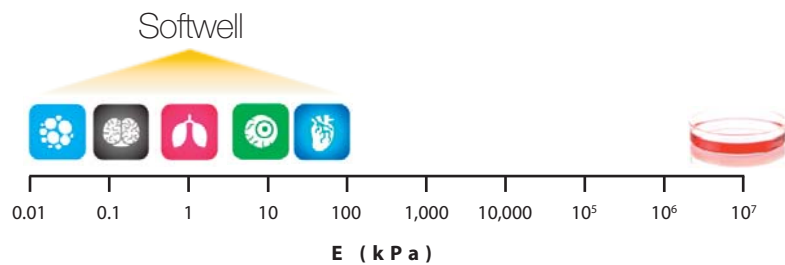
Hydrogel-coated wells for cell culture

Non-activated 0.2 kPa Easy Coat
25 kPa 8 kPa Petrisoft 1 kPa
Collagen Ultrasoft Softview



Introducing Softwell

It's like a Petri dish. Only to a cell, it's much softer. And not just perceptibly so, but specifically tuned to the softness of the body's tissues. That means you can culture neurons in an environment as soft as the brain, cardiomyocytes on the stiffness of muscle, or whatever your cells' tissue of origin may be.



The stiffness of a material is commonly quantified by its elastic modulus (E). Conventional tissue culture plastic is nearly one billion times stiffer than the body's softest tissues.

Softwell is a transparent hydrogel bound to the surface of any cell culture well. It's less than a millimeter thick, so you might not notice it's there, but a cell can feel the difference. Importantly, it won't interfere with most cell-based assays and detection methods, so you can make cell culture more biologically relevant without complicating your life at the benchtop.

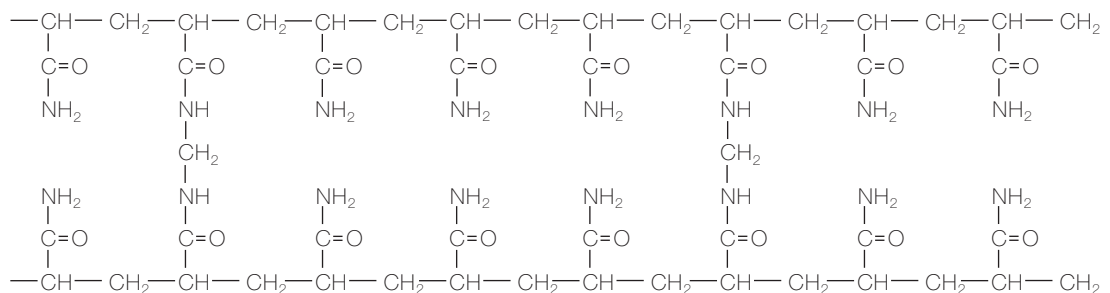
If you've ever run a Western blot, you're already familiar with what Softwell hydrogels are made of: **polyacrylamide** crosslinked with bisacrylamide. Although unmodified polyacrylamide does not bind to proteins (a property that makes it suitable for gel electrophoresis), it can be functionalized with biological ligands to enable cell attachment and growth. This was first demonstrated in 1976, when researchers adhered chicken hepatocytes to polyacrylamide hydrogels covalently coupled with N-acetylglucosamine.¹ Polyacrylamide continues to serve as a versatile scaffold upon which to immobilize biomolecules and specify cell-matrix interactions.

A familiar matrix



1. Schnaar, R. L. (1976) Ph.D. dissertation, The Johns Hopkins University, Baltimore, MD.

So, while Softwell is the first platform of its kind, there is nothing newfangled about its principle hydrogel component. Rather than reinvent the wheel, we simply decided to teach an old dog some new tricks.



Polyacrylamide-co-methylene-bisacrylamide

Stiffness matters



In 1997, researchers grew cells on polyacrylamide hydrogels that varied in flexibility.² They observed striking differences in morphology, motility, and focal adhesion dynamics, demonstrating that cells can sense and respond to the stiffness of their underlying substrate.

In the years since, the influence of extracellular matrix stiffness has been documented across a number of cell types. A few examples:

2. Wang, H.B., Dembo, M. & Wang, Y.L. Substrate flexibility regulates growth and apoptosis of normal but not transformed cells. *Am. J. Physiol., Cell Physiol* 279, C1345-1350 (2000).

3. Chowdhury, F. et al. Soft substrates promote homogeneous self-renewal of embryonic stem cells via downregulating cell-matrix tractions. *PLoS ONE* 5, e15655 (2010).

4. Saha, K. et al. Substrate modulus directs neural stem cell behavior. *Biophys. J* 95, 4426-4438 (2008).

5. Lam, W.A. et al. Mechanics and contraction dynamics of single platelets and implications for clot stiffening. *Nat Mater* 10, 61-66 (2011).

6. Liu, F. et al. Feedback amplification of fibrosis through matrix stiffening and COX-2 suppression. *J. Cell Biol* 190, 693-706 (2010).

7. Gilbert, P.M. et al. Substrate elasticity regulates skeletal muscle stem cell self-renewal in culture. *Science* 329, 1078-1081 (2010).

8. Engler, A.J. et al. Embryonic cardiomyocytes beat best on a matrix with heart-like elasticity: scar-like rigidity inhibits beating. *J. Cell. Sci* 121, 3794-3802 (2008).

Mouse embryonic stem cells generate homogenous undifferentiated colonies in the absence of exogenous LIF on $E=0.6$ kPa substrates.³

Adult neural stem cells differentiate into neurons on $E=0.5$ kPa substrates close to the stiffness of brain tissue.⁴

Platelets contract more forcefully as they sense increasing substrate stiffness.⁵

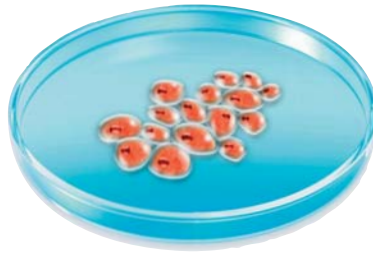
Lung fibroblasts are relatively quiescent on substrates that approximate the stiffness of lung parenchyma ($E=1$ kPa), but increase expression of fibrogenic markers on stiffer substrates.⁶

Muscle stem cells sustain their ability to regenerate damaged muscle tissue in mice when cultured on $E=12$ kPa substrates replicating muscle stiffness.⁷

Embryonic cardiomyocytes beat at 1 Hz and develop actomyosin striations on $E=11$ kPa substrates.⁸

Scientists have long been using soft hydrogels, such as collagen, fibrin, and Matrigel™, to elicit cell phenotypes that are not expressed on conventionally rigid substrates. In fact, when mammalian cell culture was invented more than 100 years ago, it happened not in a Petri dish, but within a matrix of clotted lymph.⁹ In recent years a number of synthetic matrices have emerged, but like their biological counterparts, they are typically challenging to use for routine or large-scale applications.

Softwell grew from a desire to simplify the practice of culturing cells on soft hydrogels. More than being vaguely 'soft', we sought to quantitatively replicate the stiffness of a broad range of physiological tissues in conventional cell culture formats. Because cell behavior is also influenced by the presentation of ECM ligands, we developed an efficient method to couple them to the hydrogel. The result is a platform that provides control over matrix stiffness *and* ligand specificity.



To find the optimal condition for your cell type, we suggest screening across a range of hydrogel stiffness and ligand concentrations for a desired phenotype or response. Or, if the elastic modulus of your cells' native tissue is known, start there.

A practical solution

Hydrogel
stiffness
+
ECM
ligand

9. Harrison, R.G. The outgrowth of the nerve fiber as a mode of protoplasmic movement. J. Exp. Zool. 9, 787-846 (1910).

Soft yet confident



Softwell is softer than an ordinary cell culture well. But you can treat it like one, because the hydrogels are:

Thin. Wash away unbound detection molecules and perform cell-based assays with minimal interference from the hydrogel.

Transparent. The hydrogels are optically clear and compatible with all types of microscopic imaging.

Bound to the well. Don't be afraid to aspirate media, flick out solution, or shake vigorously. Trypsinize, passage, and keep cells in culture as long as you'd like. You can even (gently) scrape cells off the surface.

A 2D system. Cells are restricted to the hydrogel surface, making them readily accessible for isolation and analysis.





Activated to bind ECM proteins. Specify the cell-matrix interaction simply by adding your desired protein prior to seeding cells. Or, go straight to culture using hydrogels pre-coated with collagen or gelatin.

Robust. Softwell is stable at room temperature from three months of the manufacture date.

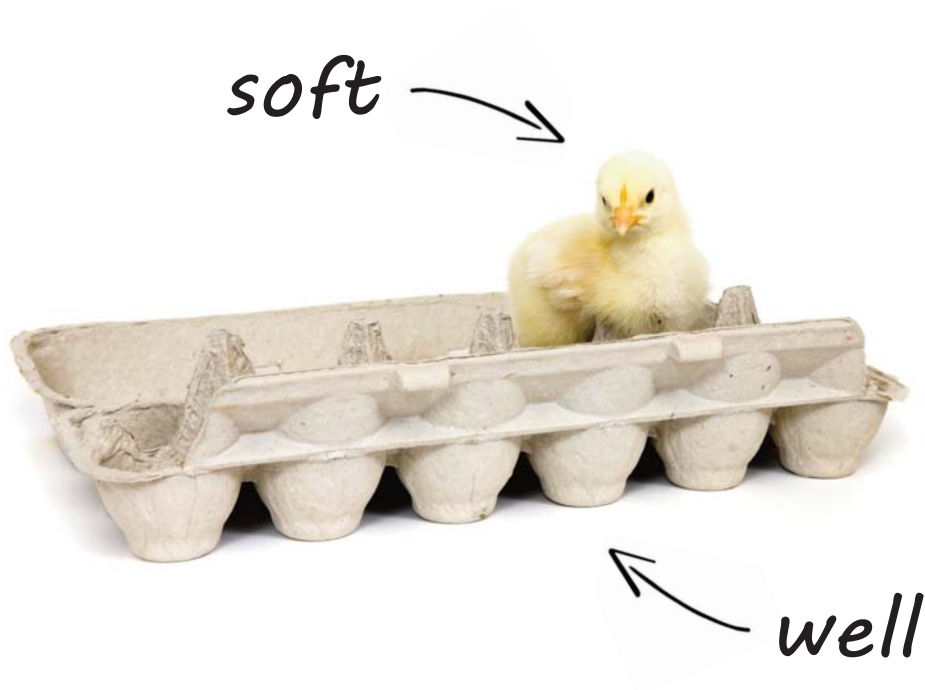
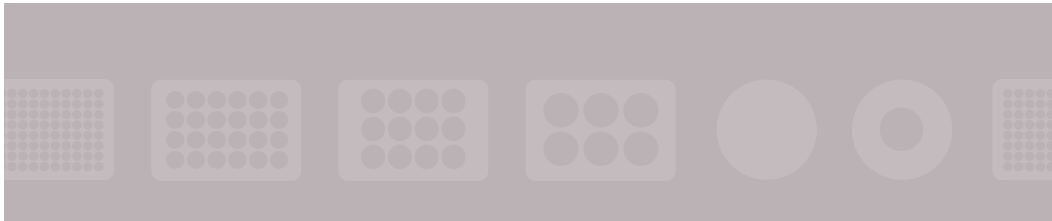
Safe. Softwell is certified non-cytotoxic and pyrogen free.

The Softwell product line is currently available in standard dishes, multiwell plates and glass coverslips, specifiable in 9 stiffness values and 3 matrix coating options.

Choosing your well

Cell culture format			
			
Softwell® Hydrogels bound to 6, 12, 24 and 96 well plates.	Petrisoft™ Hydrogels bound to 35, 100 and 150 mm diameter dishes.	Softview™ Hydrogels bound to glass-bottom dishes.	Softslip™ Hydrogels bound to glass coverslips in 6, 12 and 24 well plates.
Hydrogel elastic modulus (kPa)			
0.2, 0.5, 1 Soft Range	2, 4, 8 Mid Range	12, 25, 50 Stiff Range	
Matrix coating			
Easy Coat™ Hydrogels activated to bind ECM proteins such as collagen, fibronectin and laminin.	Collagen Hydrogels bound with type I collagen from bovine skin or rat tail.	Non-Activated Use as an ultra-low protein and cell attachment surface or couple ligands using your own methods.	

Coming soon. Softwell 384, SoftFlask™, Softcert™ inserts, Softslide™ chambers, SoftFlex™ membranes, SoftTrac™ for traction force microscopy, SoftGroove™ and SoftIslet™ micropatterned surfaces, SoftTerrain™ hydrogels with 3D surface features, an Ultrasoft™ range, and more ECM coatings.



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