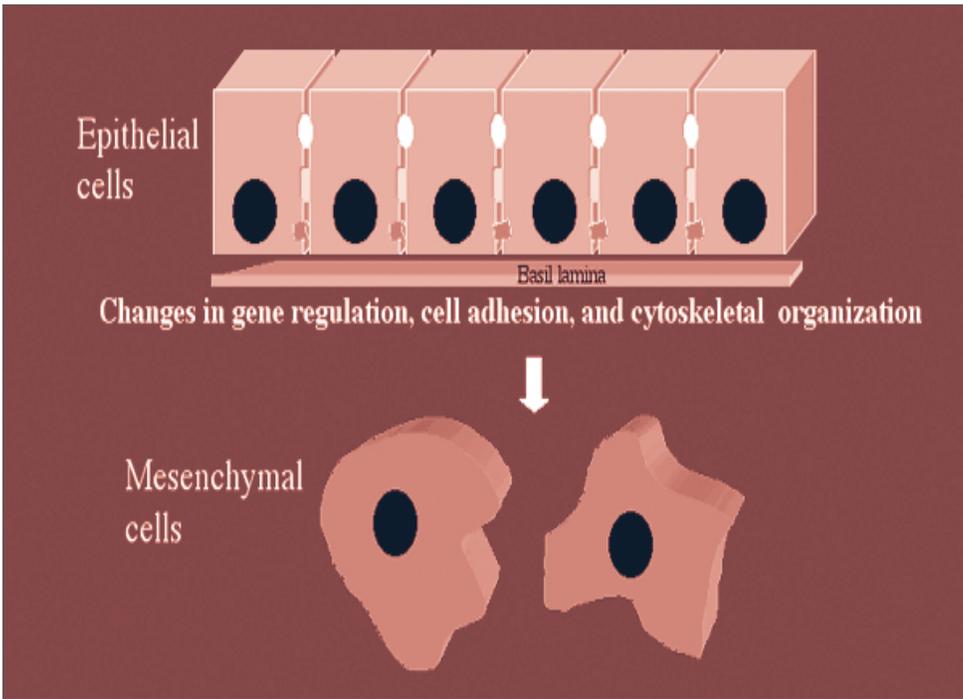


MIT Student | **EMT variations in cancer**

Epithelial mesenchymal transition is a transformative process that normal cells, as well as cancer cells, undertake. Throughout the life cycle of a tumor, the environmental conditions change. These environmental changes, like Hypoxia, make the environment unfavorable for the cells to remain there, therefore inducing the process of emt.

This process will allow cells that have previously been unable to migrate to loosen their cell junctions between other cells and enter the blood stream. This is very important for the tumor because under hypoxic conditions the tumor would not be able to survive for long. Therefore, its ability to transform makes it highly resilient

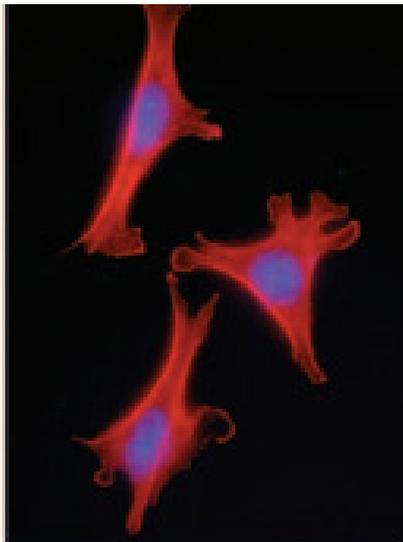
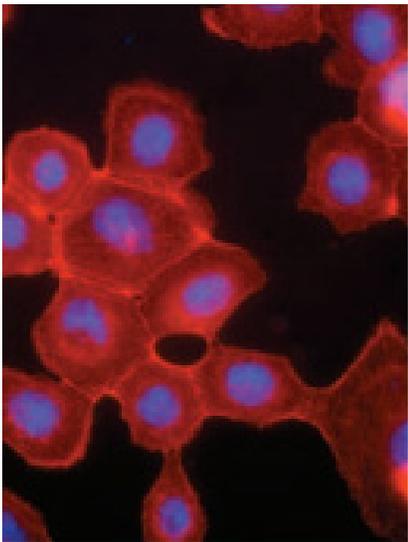
Image of prostate cancer mesenchymal cells removed due to copyright restrictions.



Courtesy of Denise Montell. Used with permission.

Montell, 2003

Epithelial cells as seen in the diagram to the left are spindle shaped and form cell to cell junctions. A number of inducing factors and environmental factors will cause the process of EMT. Mesenchymal cells are more heterogeneous and do not have the ability to form cell junctions. The varied nature of Mesenchymal cells is an added advantage for tumor cells because they will be harder to detect in the blood stream.



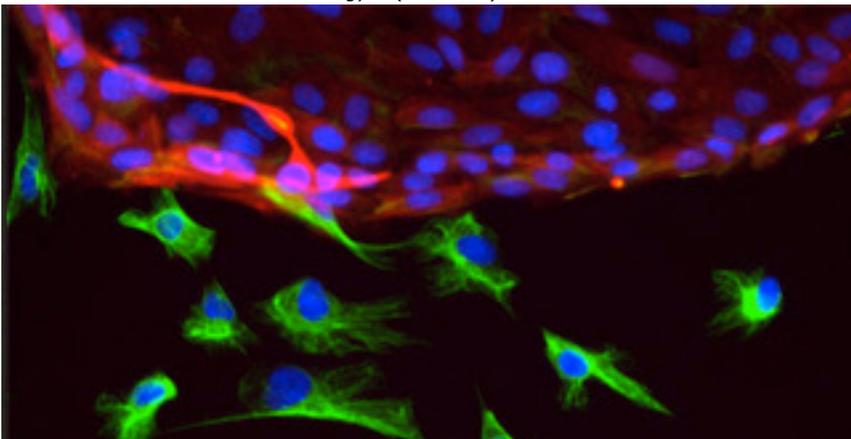
The image on the left shows a cluster of epithelial cells. As is evident in the image, these cells clearly form junctions with other and are uniform in shape. The image on the right, is an image of mesenchymal cells. Here, there are no more cell to cell junctions and they are more diverse in shape. The bottom image shows newly transformed mesenchymal cells migrating whereas the red, epithelial cells, are still joined together as a mass.

Reprinted by permission from Macmillan Publishers Ltd: *Nature Reviews Molecular Cell Biology*.

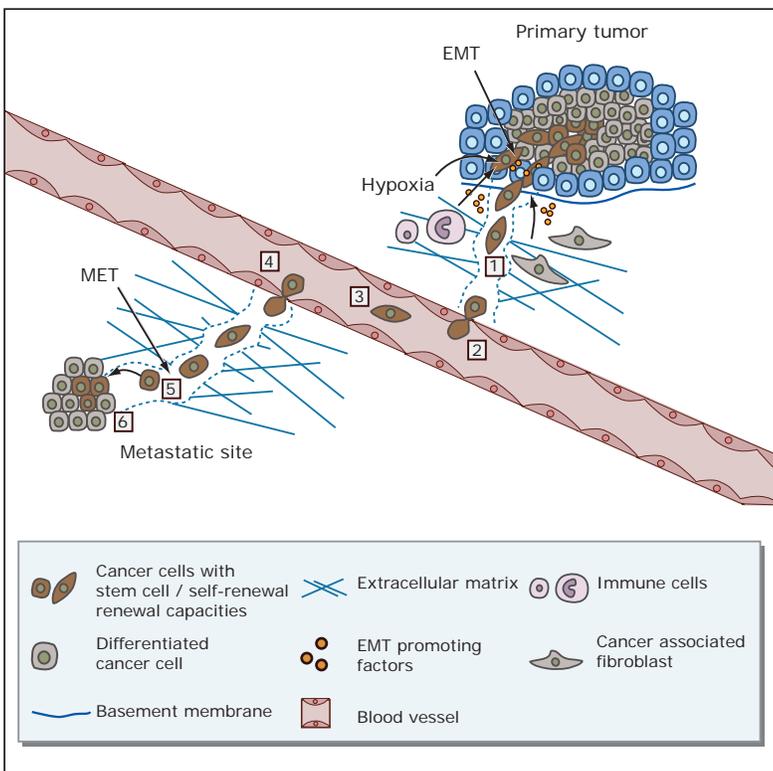
Source: Figure 1a and 1b in Thiery, Jean Paul, and Jonathan P. Sleeman.

"Complex networks orchestrate epithelial-mesenchymal transitions."

Nature Reviews Molecular Cell Biology 7 (Feb 2006): 131-42. © 2006.



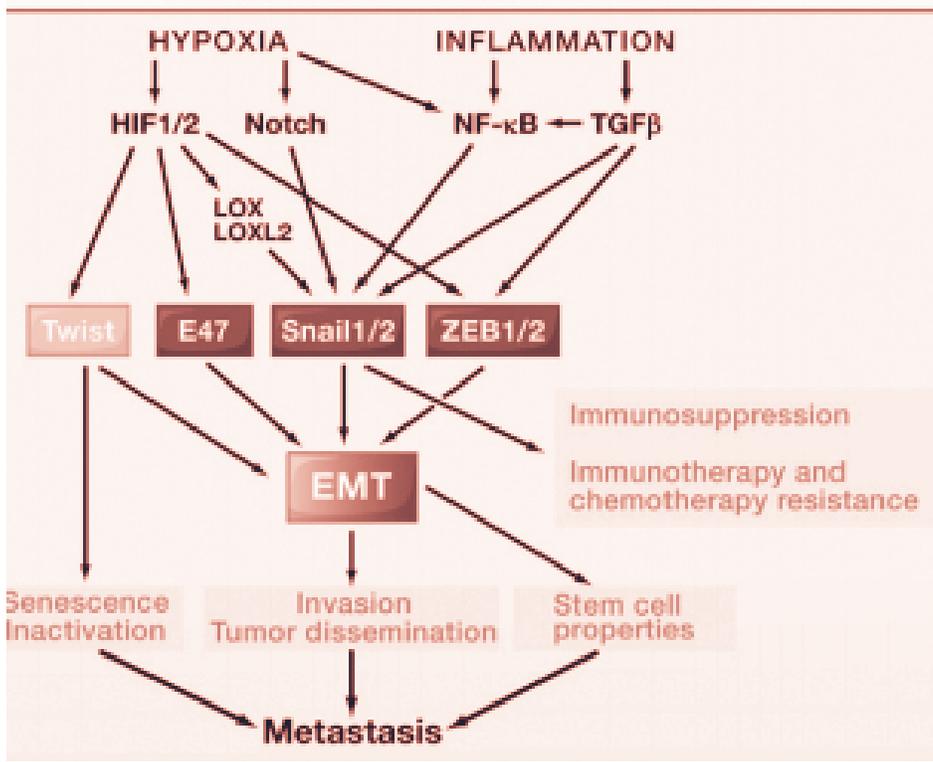
Courtesy of Christina Scheel/Whitehead Institute. Used with permission. Thiery et al., 2006



If the tumor is in an environmentally unfavorable condition like Hypoxia (too little oxygen) the process of EMT is likely to be induced because otherwise the tumor will die. As is seen in the diagram, the tumor cells transform into mesenchymal cells, enter the blood stream, and then metastasize at a distant site. This is a very important step in tumor aggression

Bastid, 2011

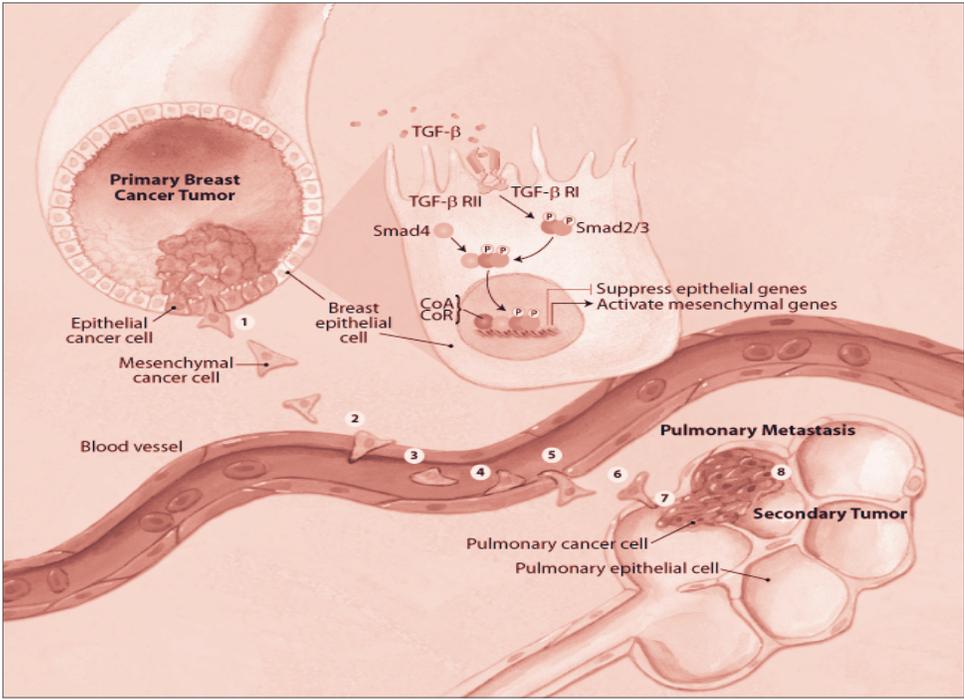
Image by MIT OpenCourseWare.



Here, in more detail, the process of how EMT is induced is depicted. Hypoxia (in the case of tumor cells) will cause the activation of EMT inducers like Notch. These inducers will down regulate or up regulate the expression of certain proteins crucial in the EMT process. This is done through the regulation of gene expression.

Thierry et al., 2009

Courtesy of Elsevier, Inc., <http://www.sciencedirect.com>. Used with permission.



Courtesy of R&D Systems, Inc. Used with permission.

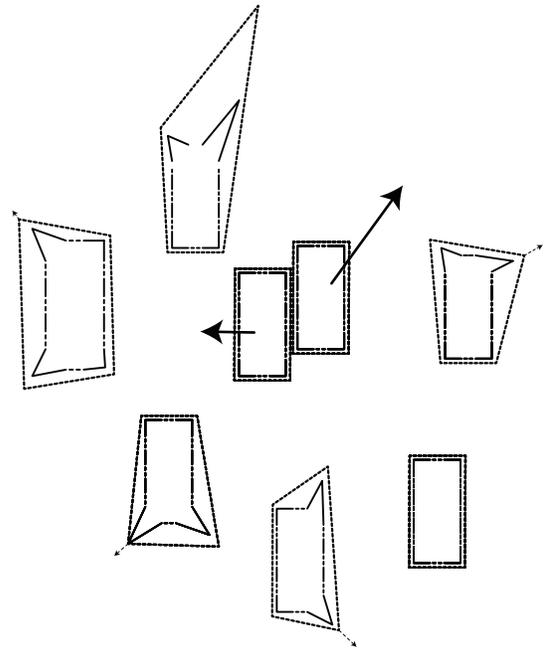
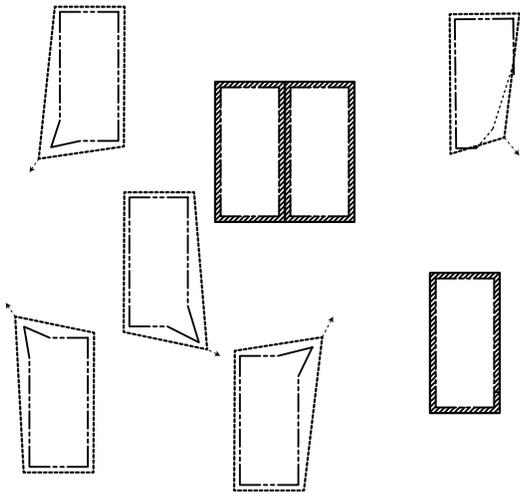
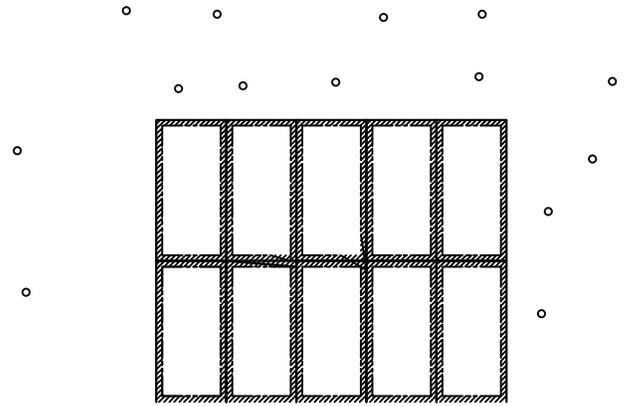
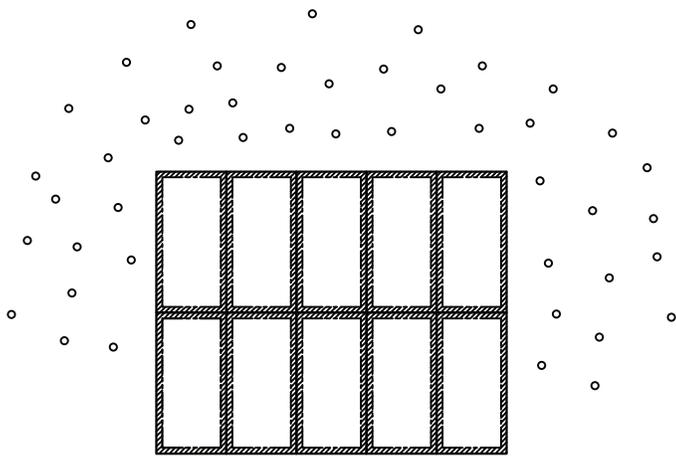
RD systems

Breast cancer is a particularly aggressive form of cancer. Breast cancer cells seem to be the most heterogeneous in terms of how many cells are epithelial, epithelial/mesenchymal, or mesenchymal cells. Here the inducing factors TGF-β and Smad2/3/4 play important roles in transforming epithelial cells to mesenchymal cells.

Photographs of four protein markers for breast cancer (MDA468) removed due to copyright restrictions.

Depicted here are several protein markers on a breast cancer cell line. All of the samples are positive for the respective markers. These are proteins that are both important in epithelial cells and mesenchymal cells, indicating that these breast cancer cells are most likely highly aggressive because they have the ability to form junctions as well as migrate. They have the best of both worlds

Key:
□ Epithelial cells
○ Oxygen



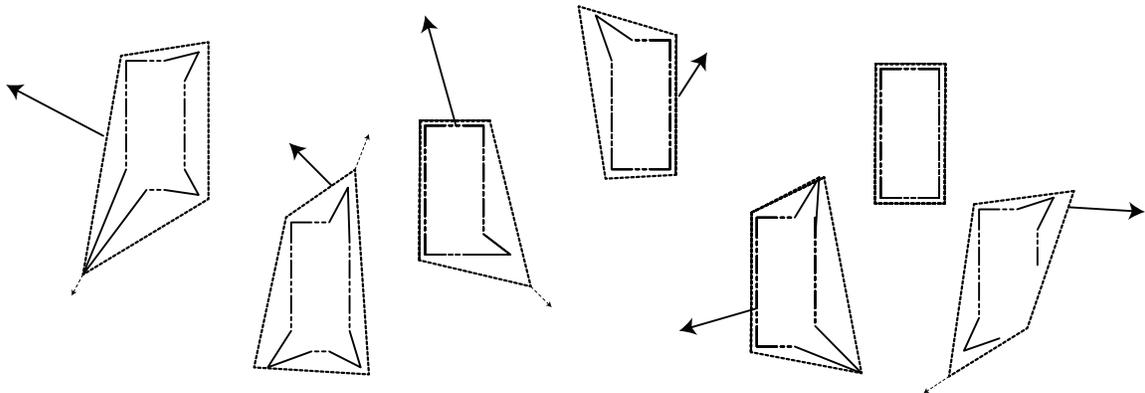
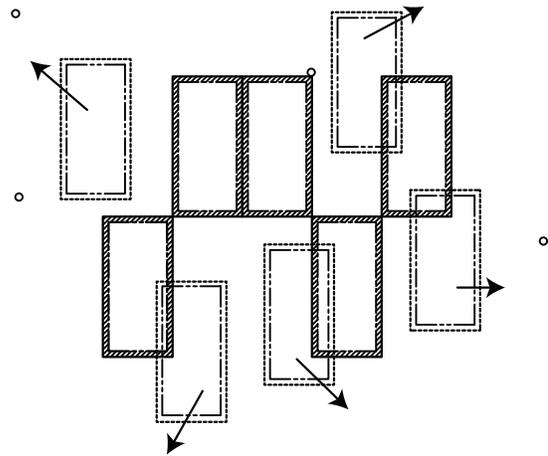
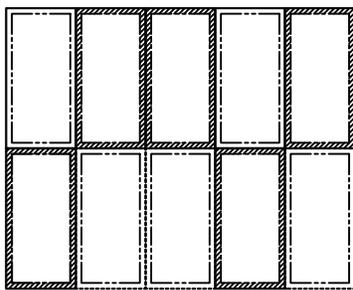
Logic for mesenchymal cells:

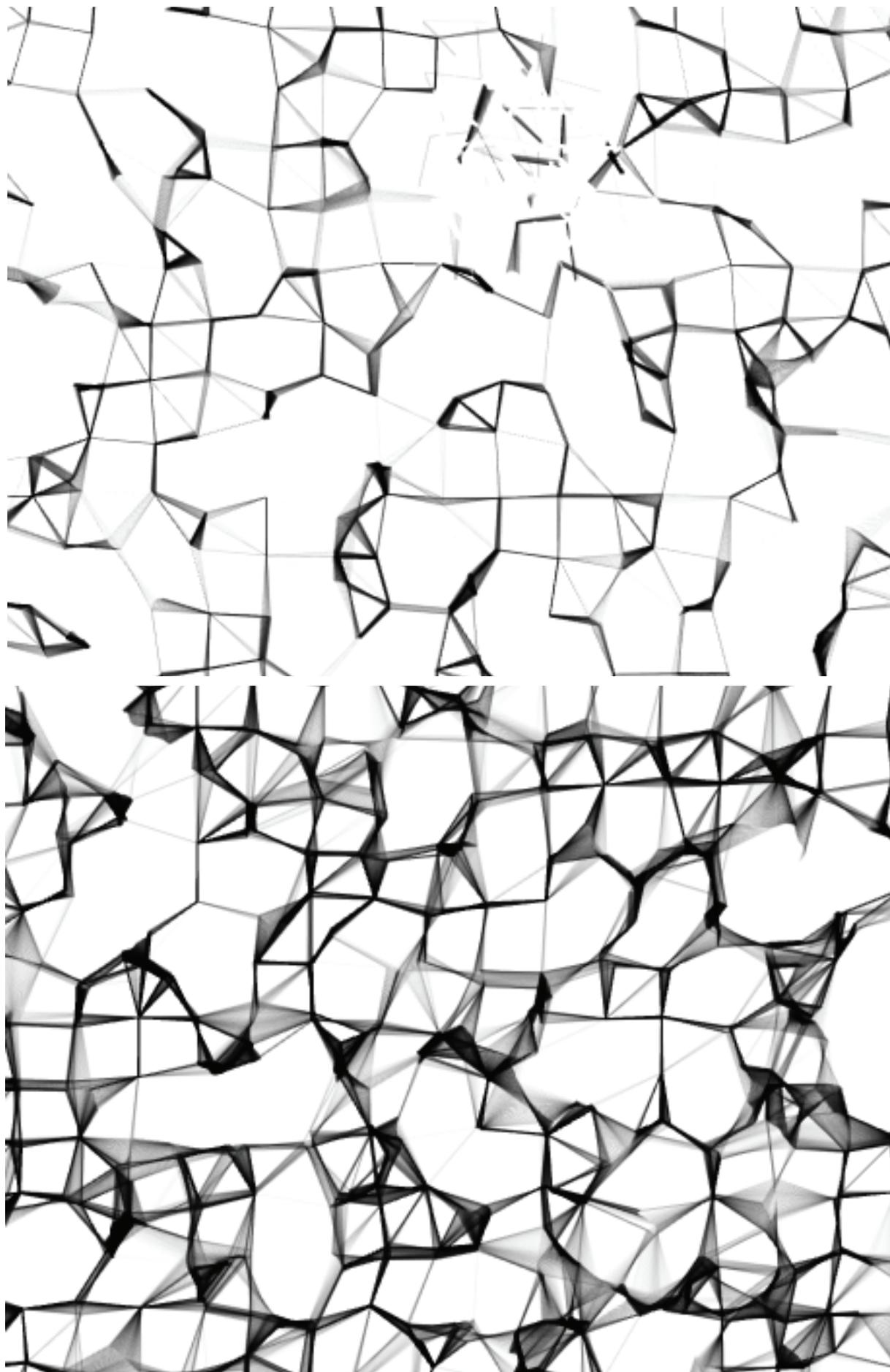
1. Any of the four corners can initially be pulled out

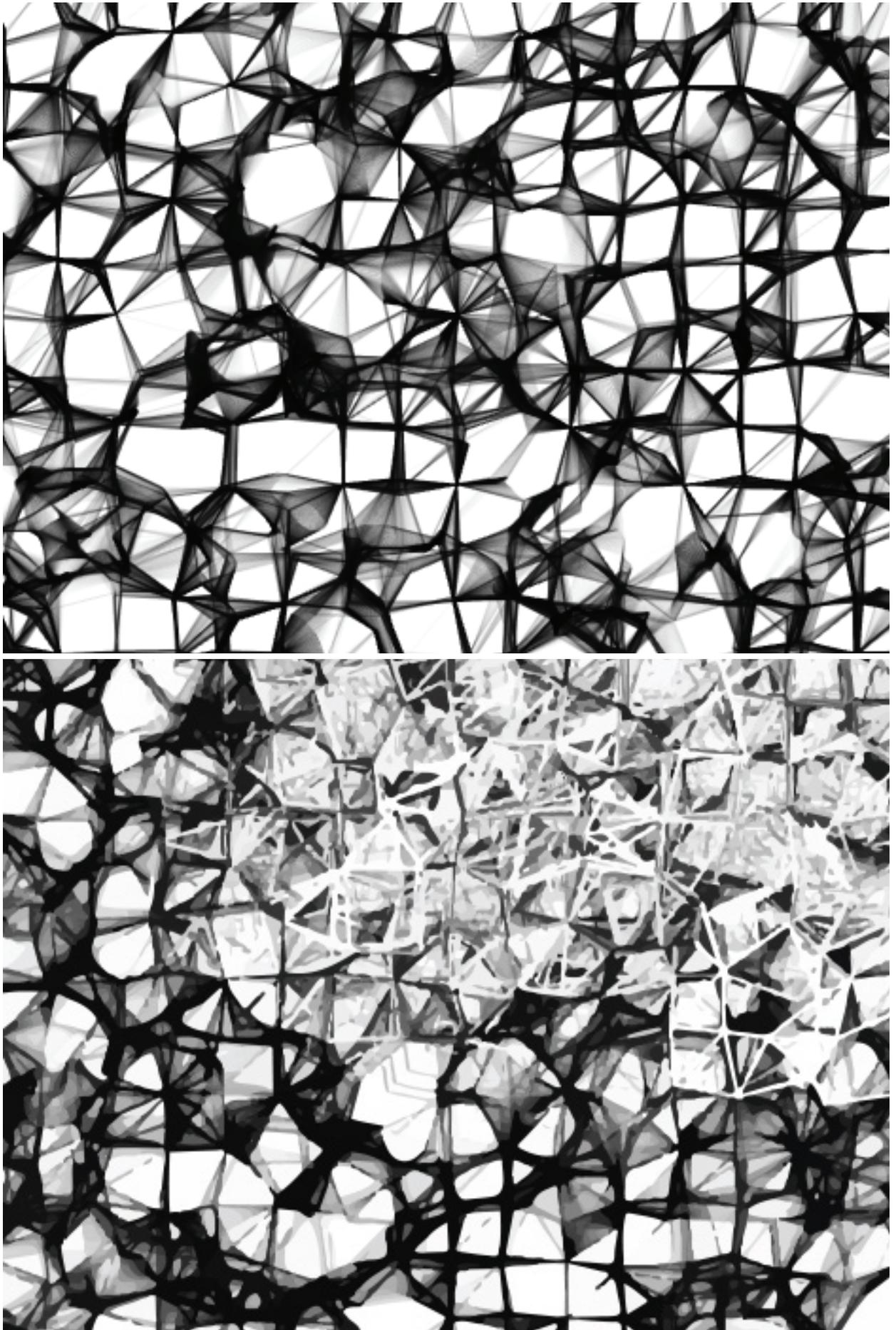
2. Either one of the adjacent corners are pulled out

3. One corner diagonally across is pulled out

*If one or two corners pulled







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