Physikalische Ansätze zur Diagnostik und Therapie von Tumoren

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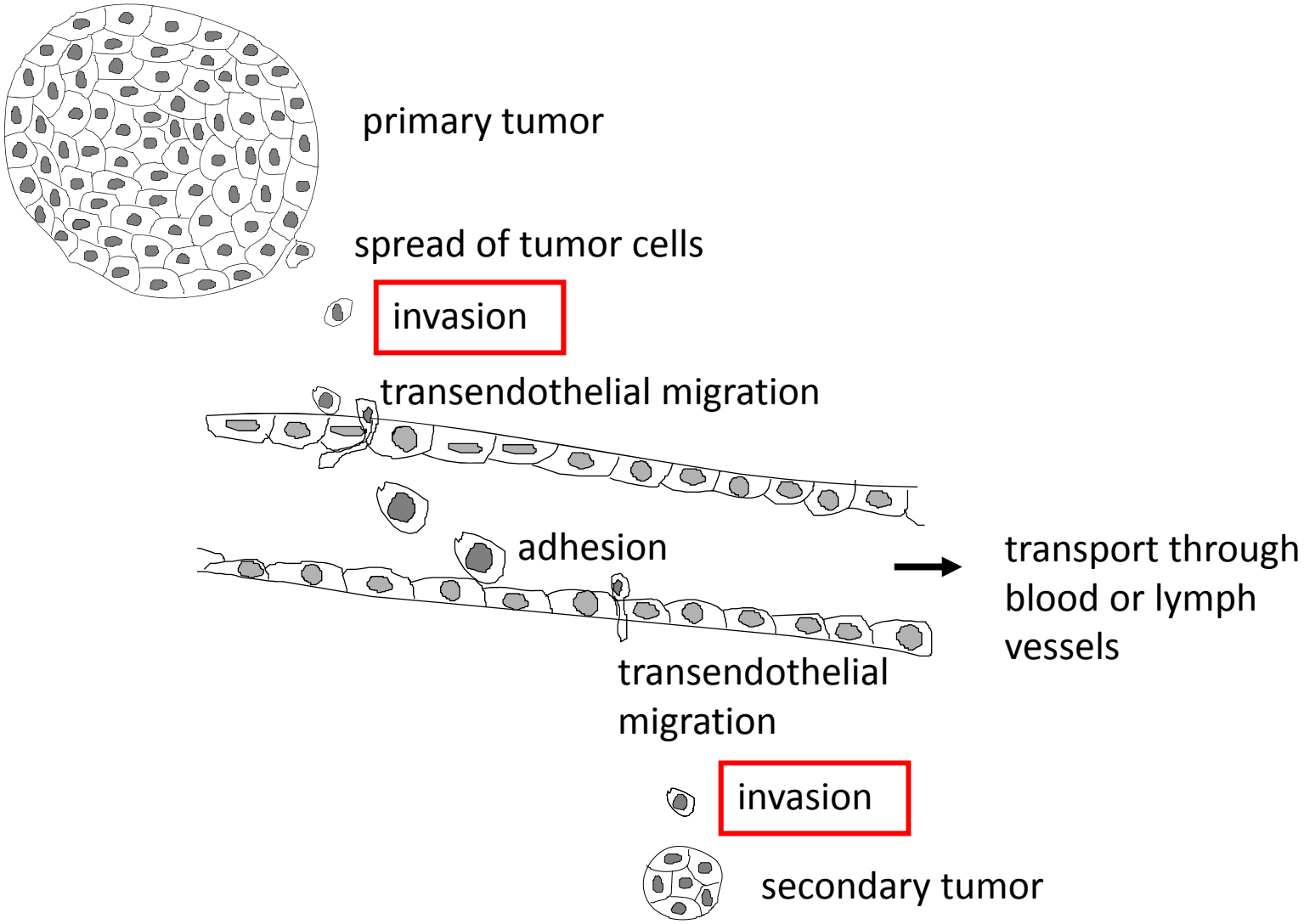
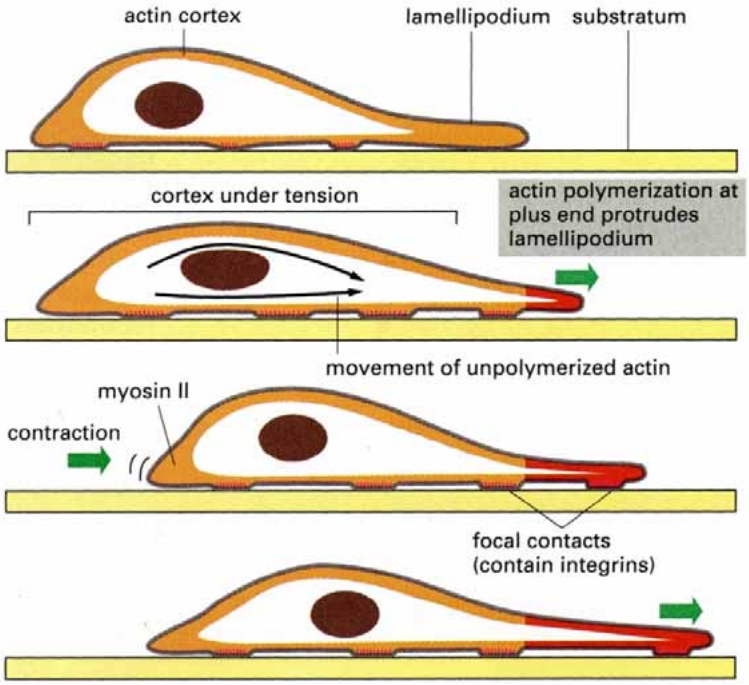
Metastasis

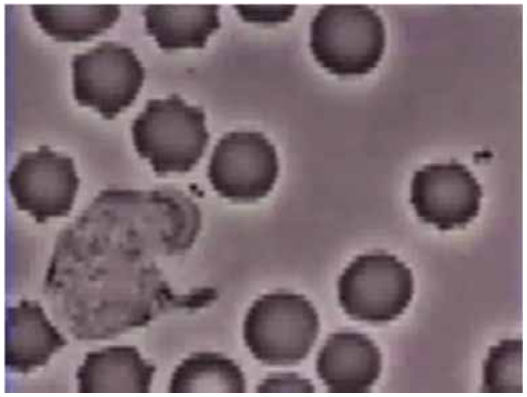

primary tumor
spread of tumor cells
invasion
transendothelial migration
adhesion
transport through blood or lymph vessels
transendothelial migration
invasion
secondary tumor

Cell crawling and migration in 2-D



(Alberts B. *et al.*, Molecular Biology of the Cell)

- CSK dynamics
- adhesion
- de-adhesion



Crawling Neutrophil
Chasing a Bacterium
(D Rogers)

Resisting forces of the surroundings = zero

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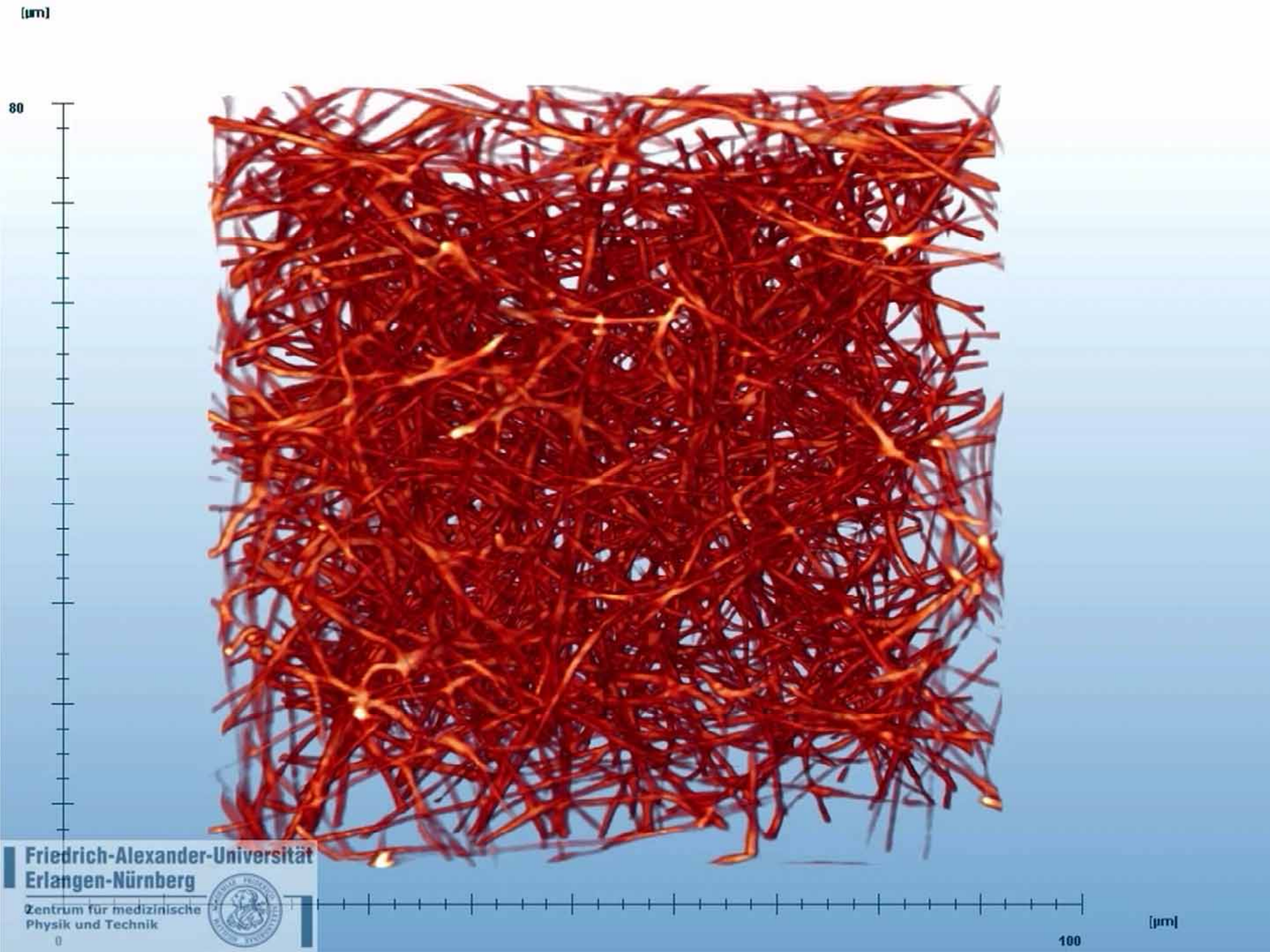
[µm]
80
[µm]
100
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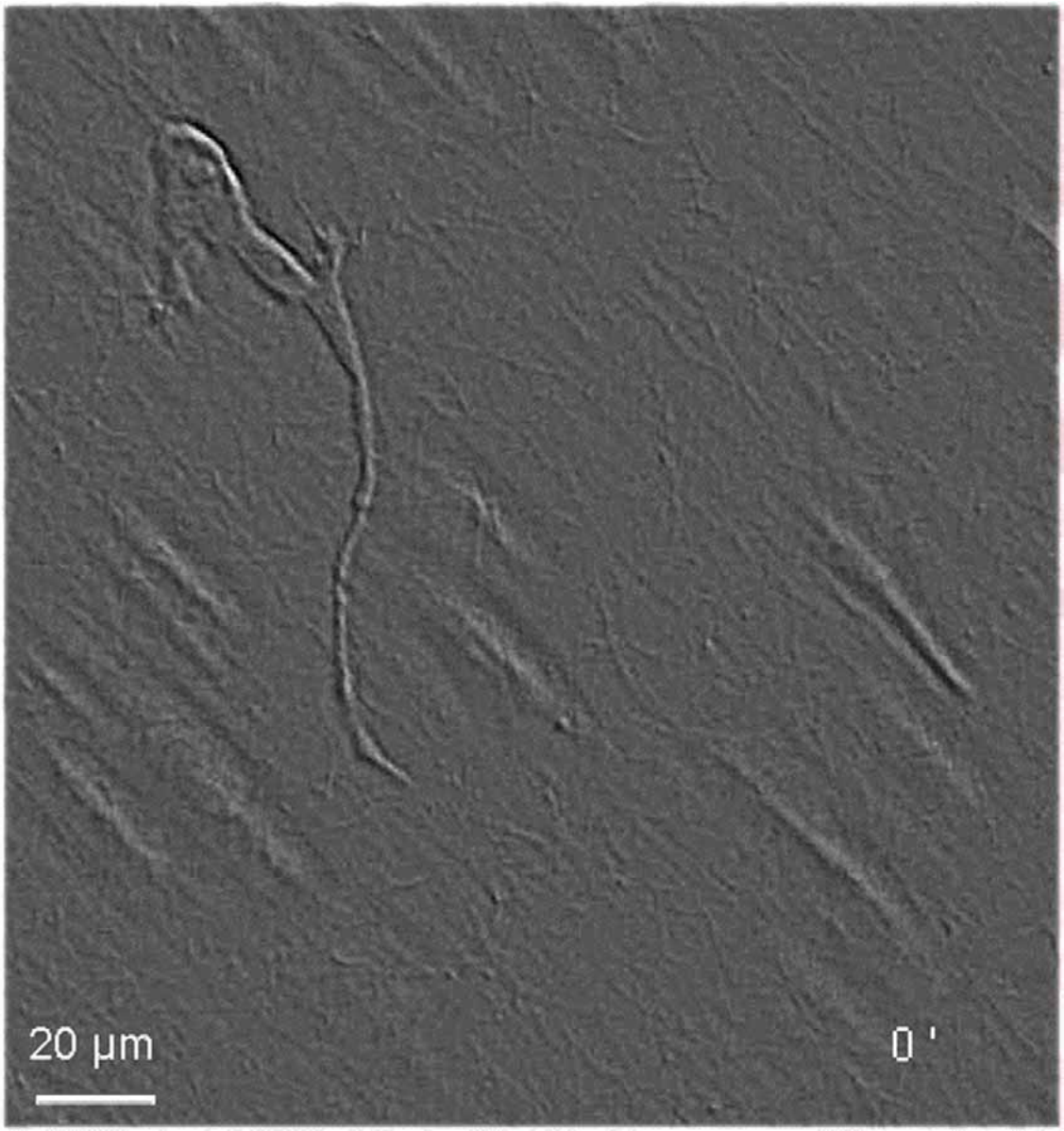
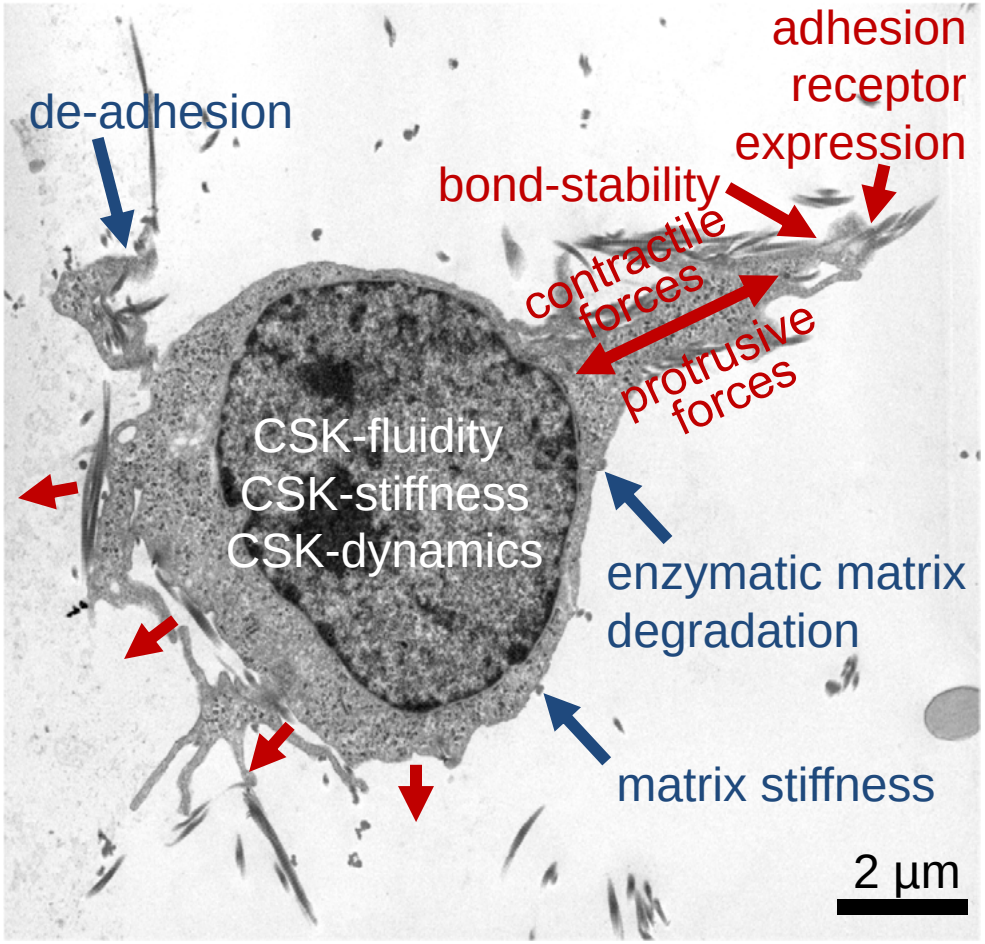
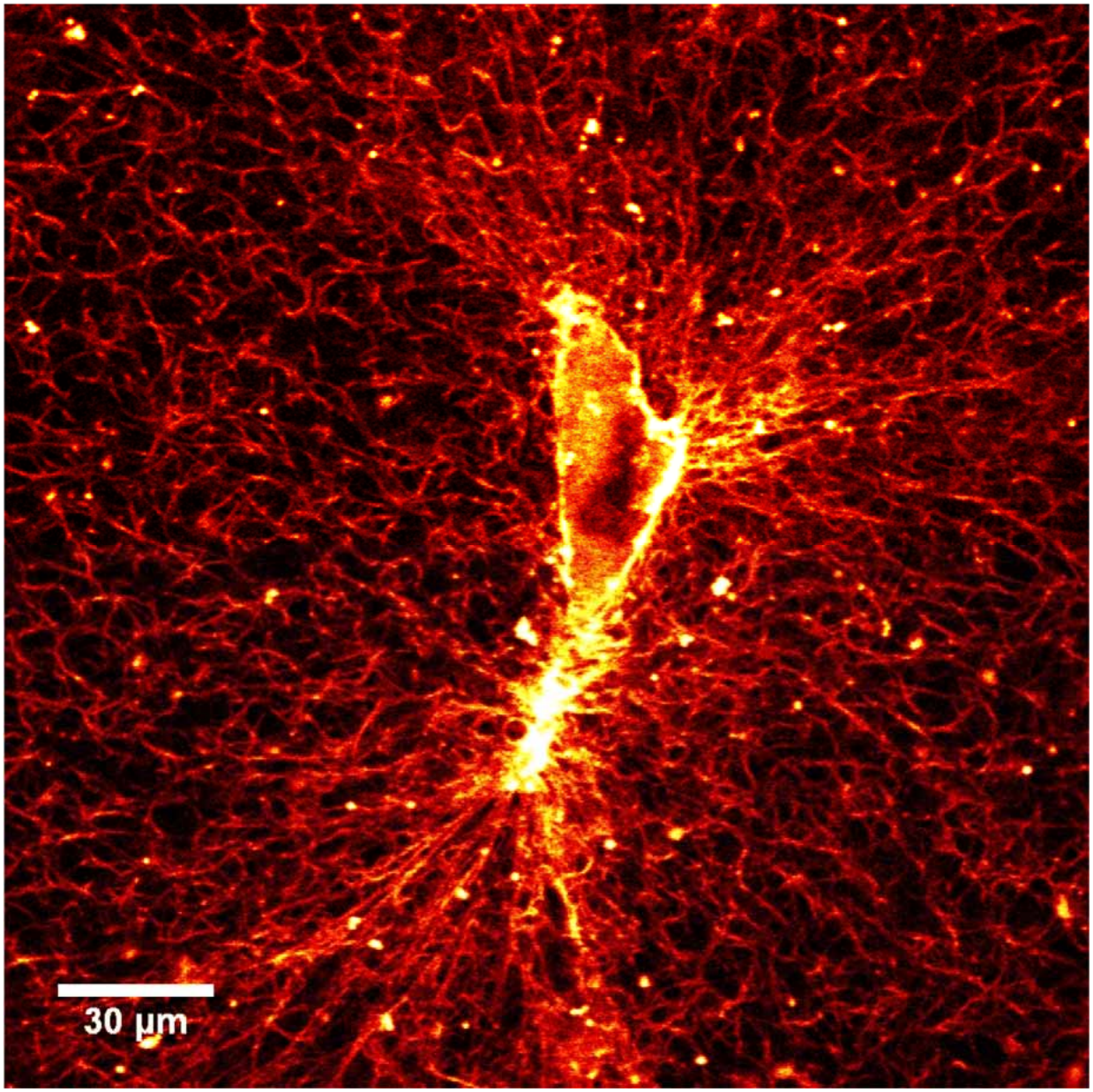

20 µm
0 '

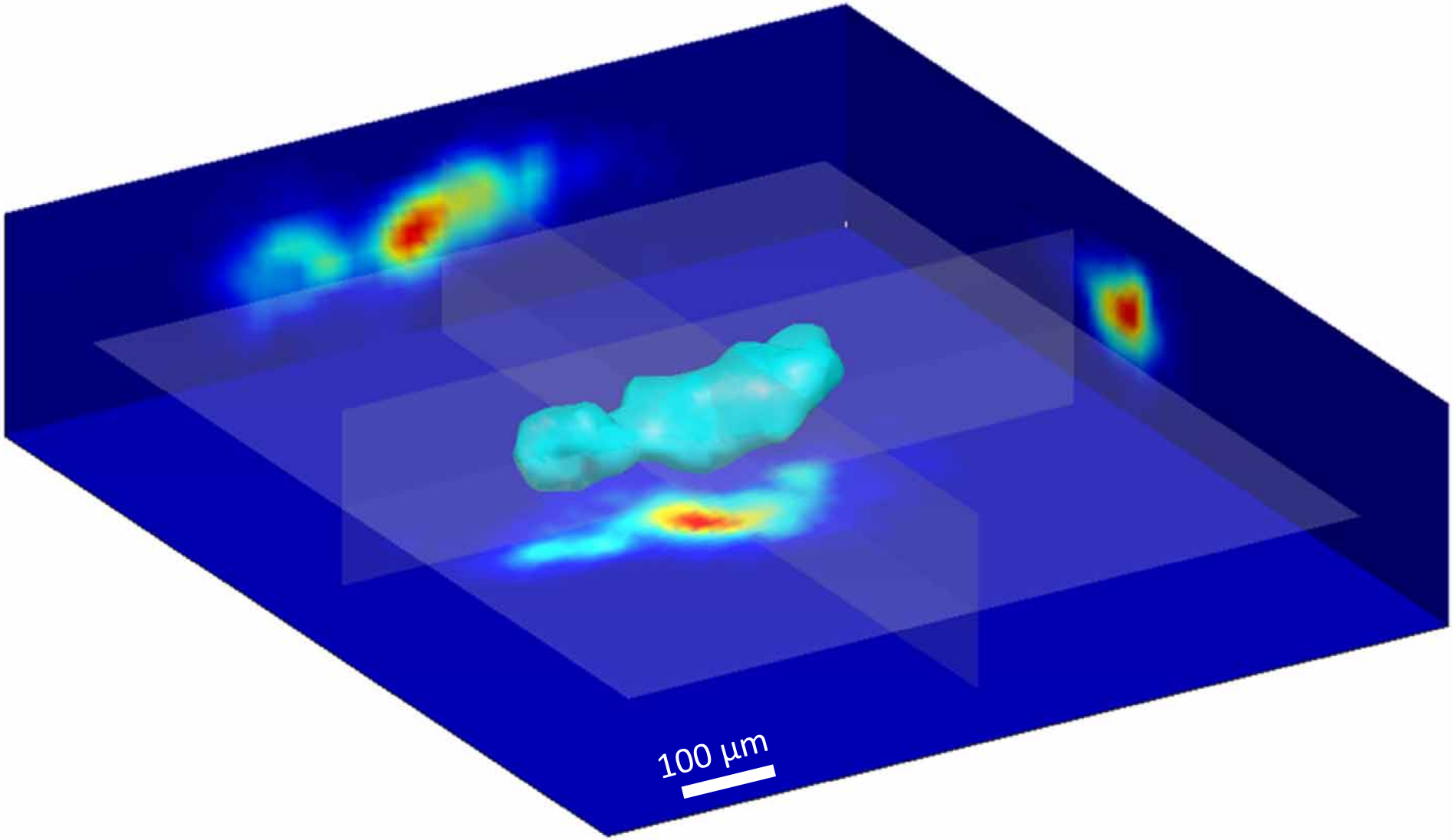
Cell invasion is governed by a force balance



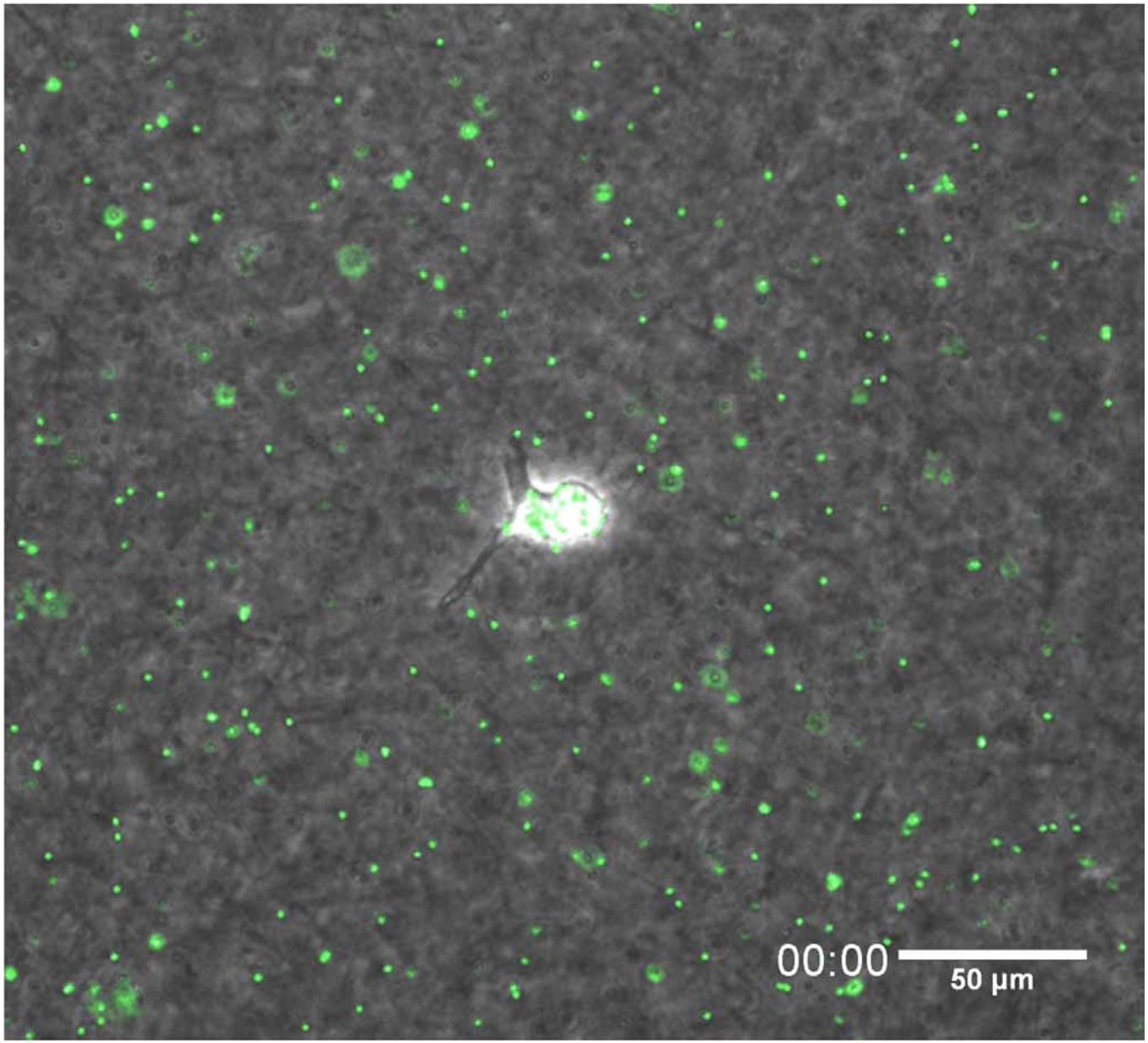
- protrusive forces
- traction forces
- CSK resistive forces
- matrix resistive forces

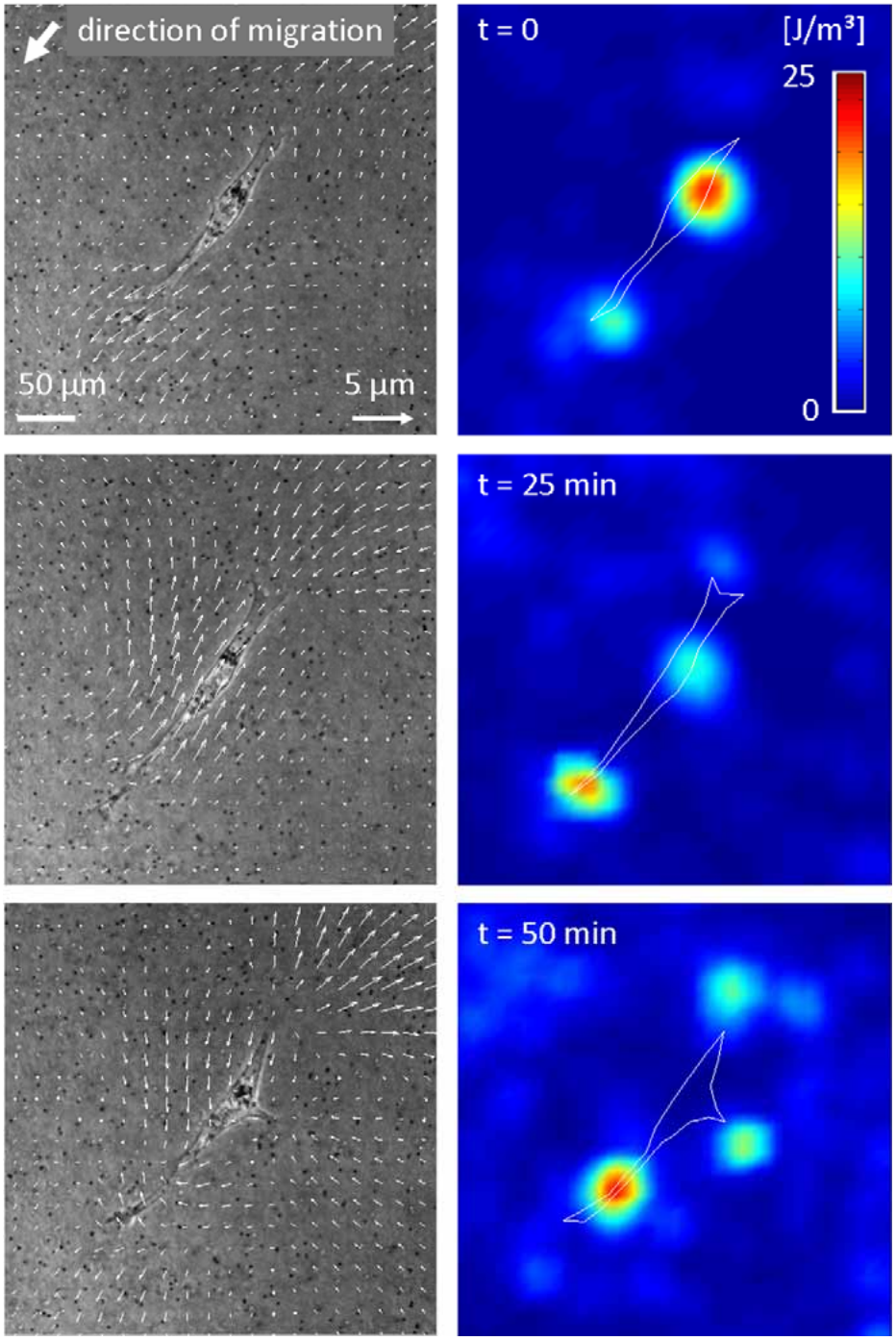

30 µm

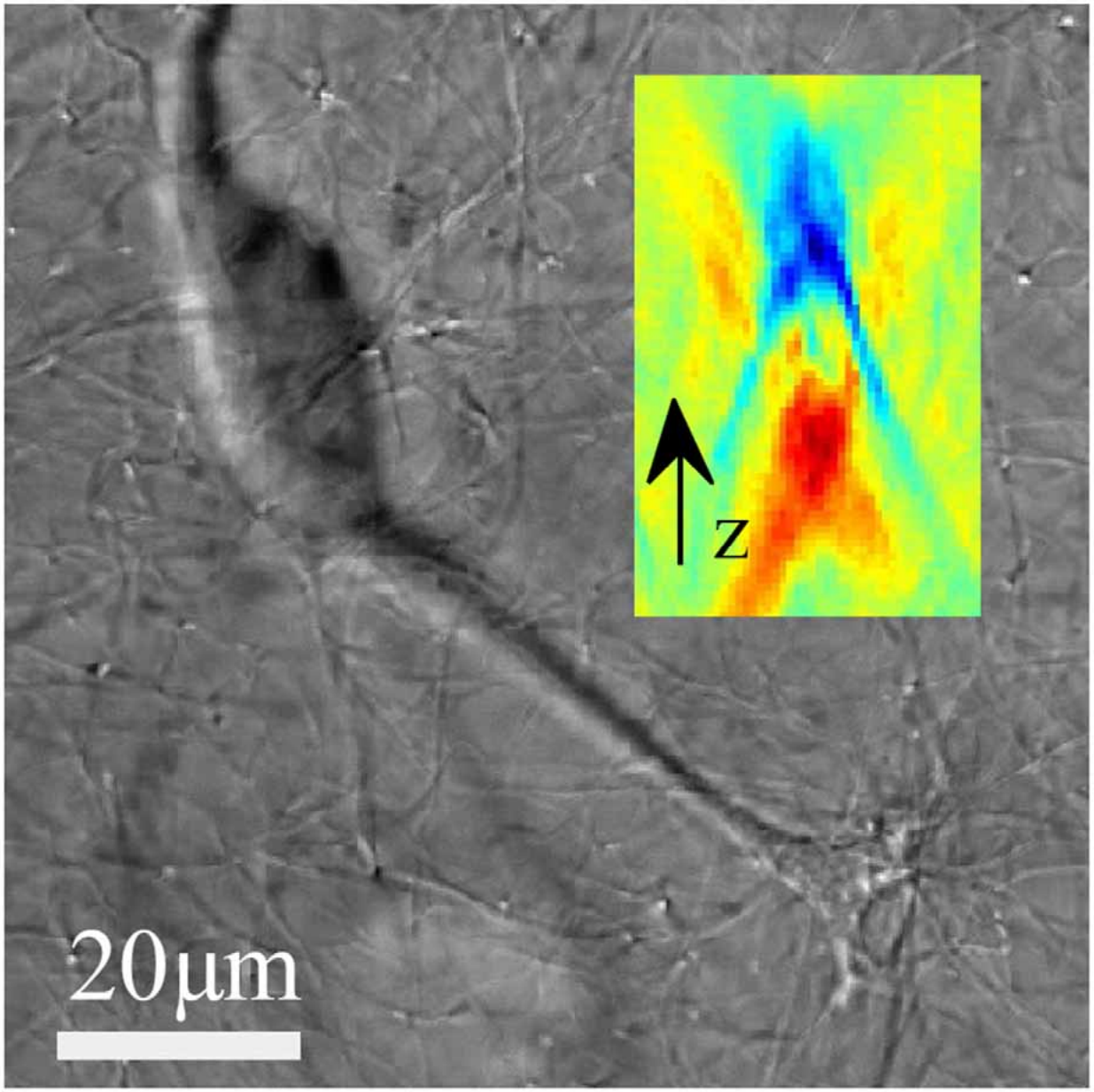
Strain energy around an invaded MDA-MB-231 cell

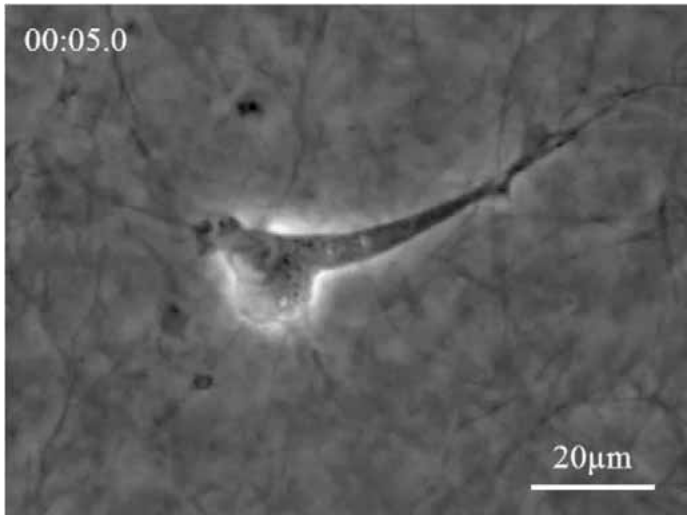


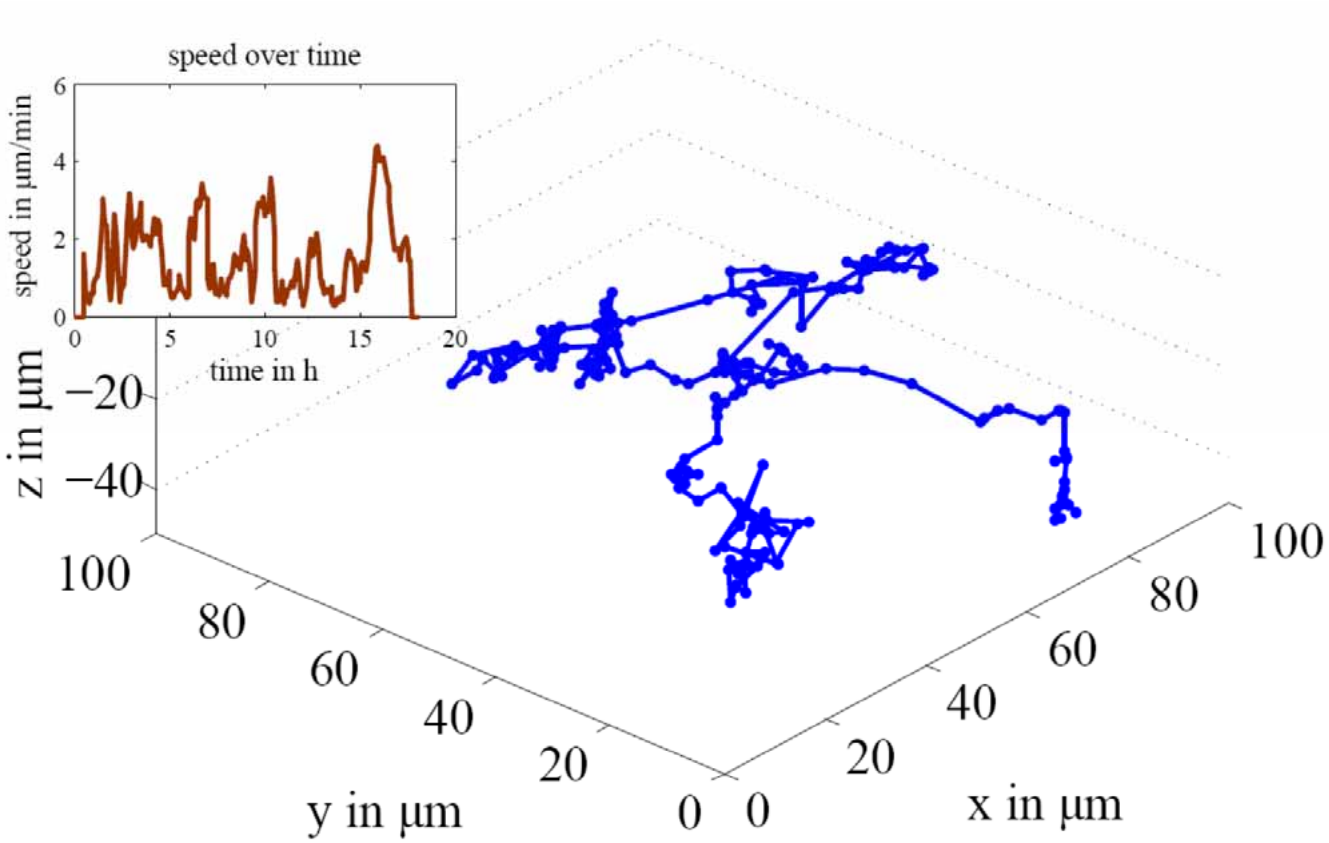
0 3.5 fJ/(10 µm)³


00:00
50 µm

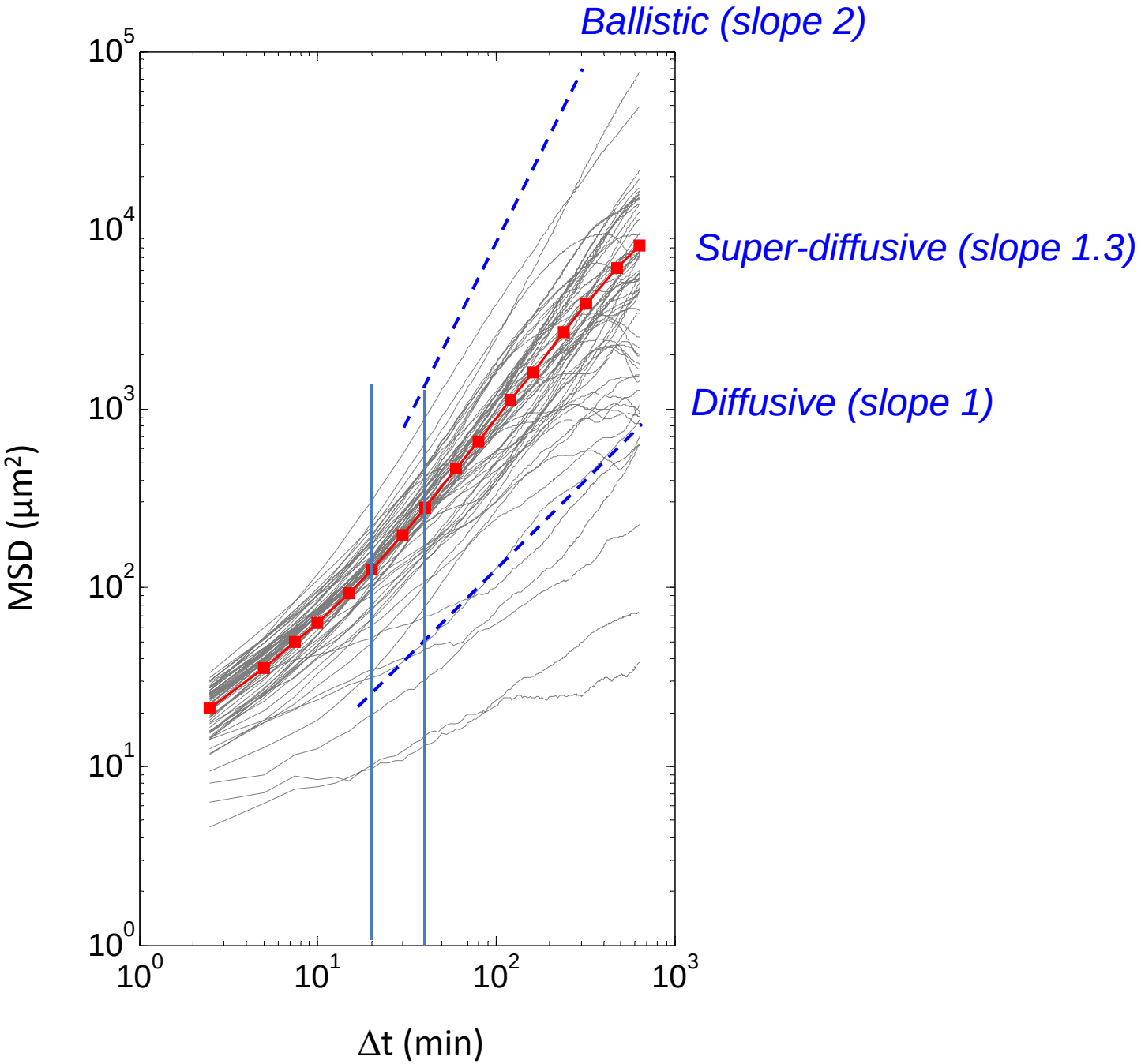

direction of migration
50 µm
5 µm
t = 0
[J/m³]
25
0
t = 25 min
t = 50 min


z
20μm

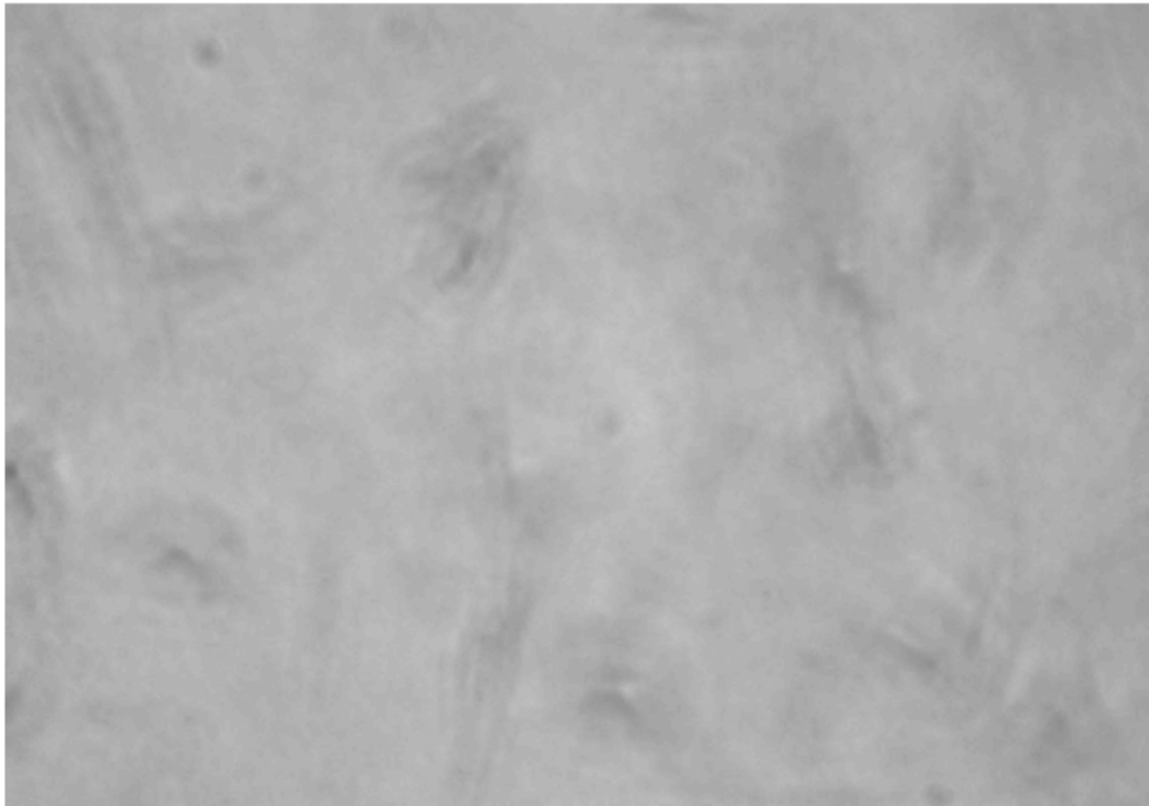

00:05.0
20μm


speed over time
speed in µm/min
time in h
z in µm
y in µm
x in µm

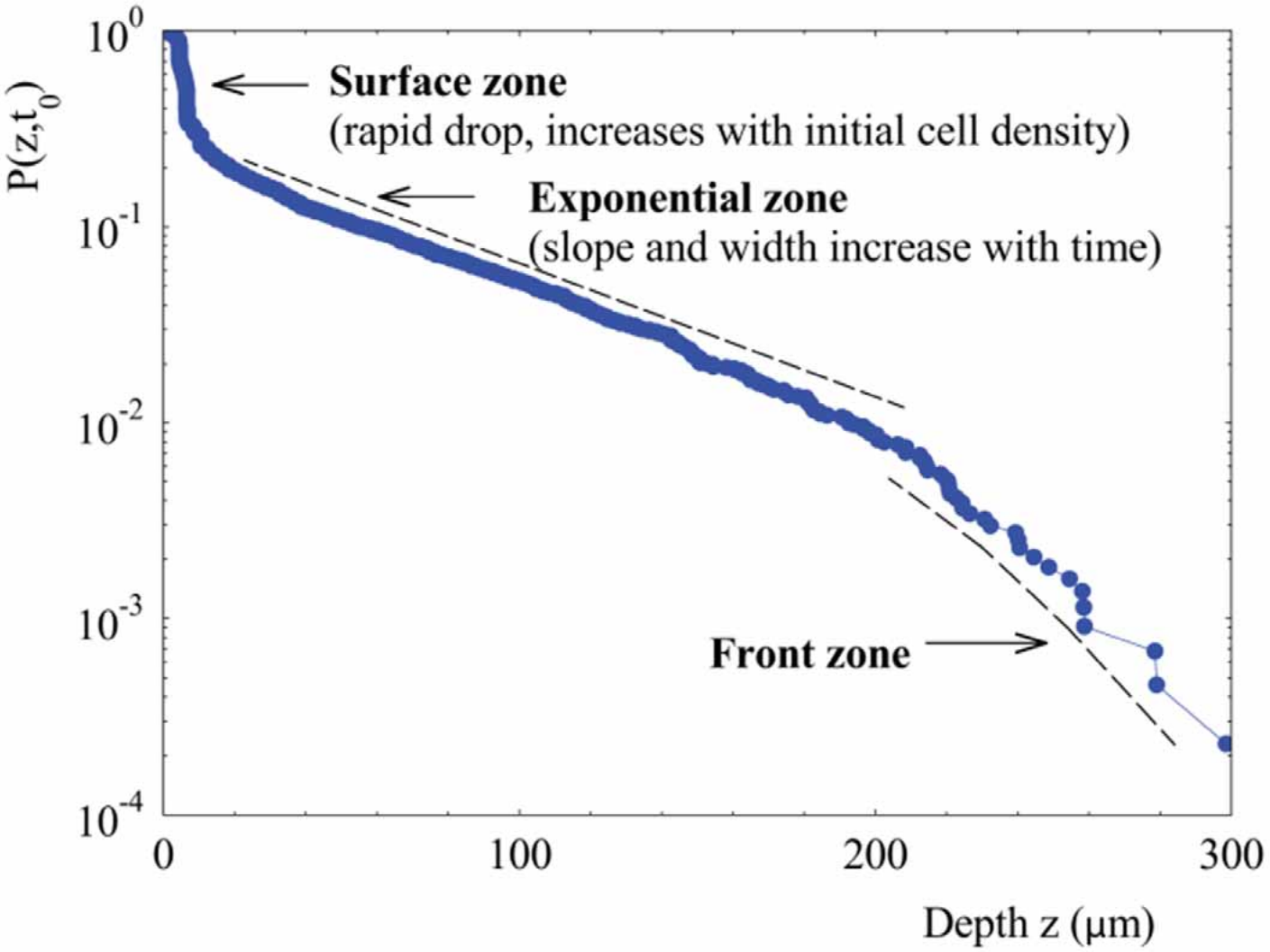
Mean Squared Displacement



Automatic measurement of the invasion profile



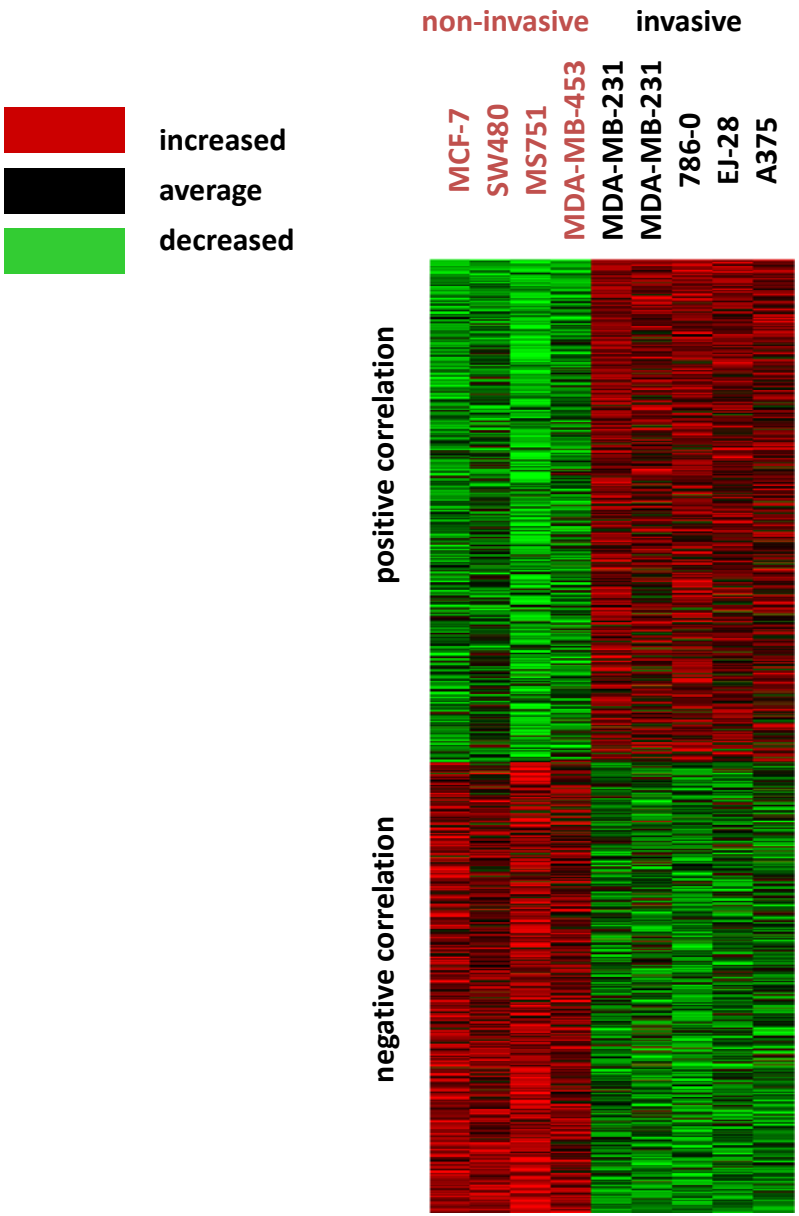
General characteristic features of the invasion profile



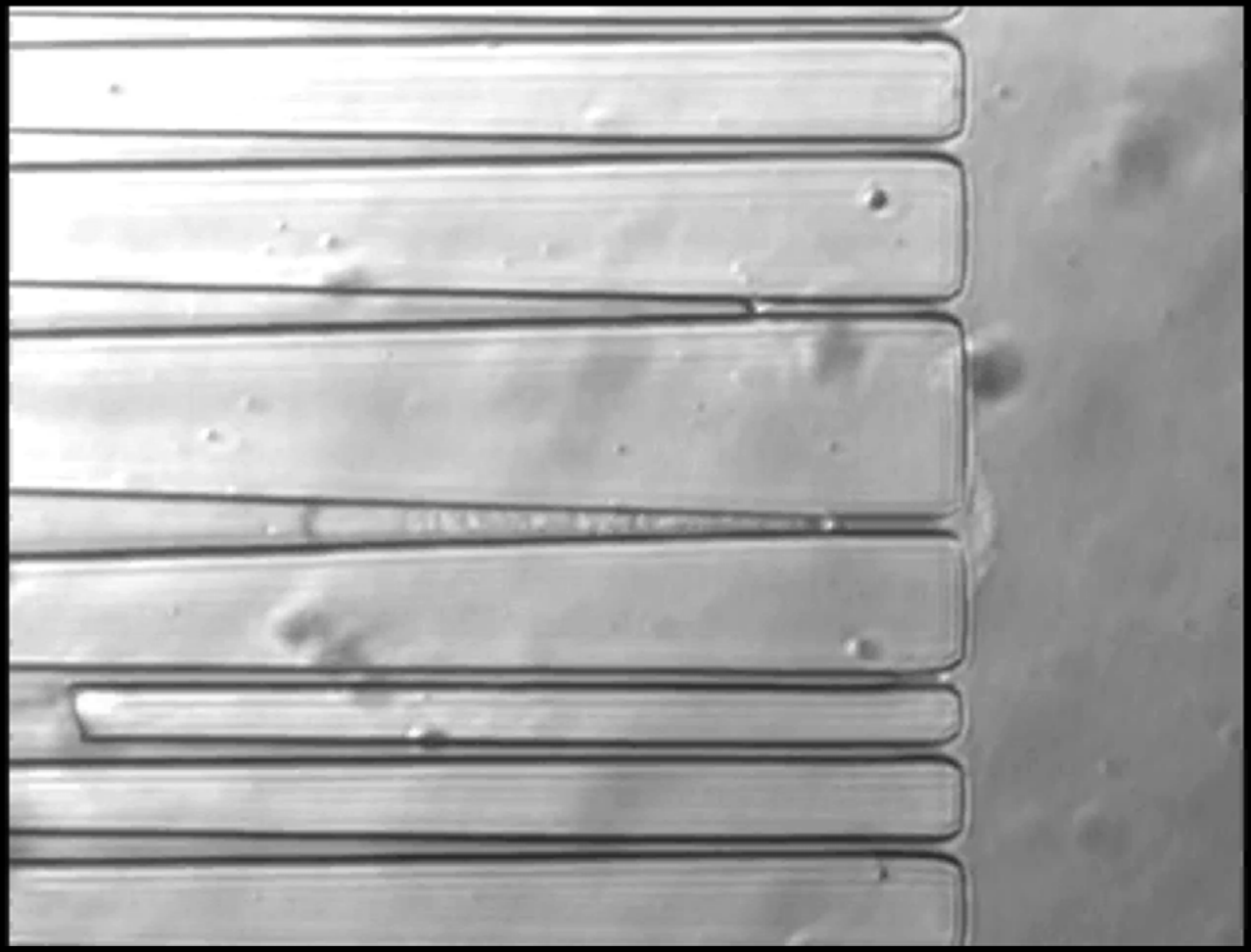
Classification of tumor cell lines

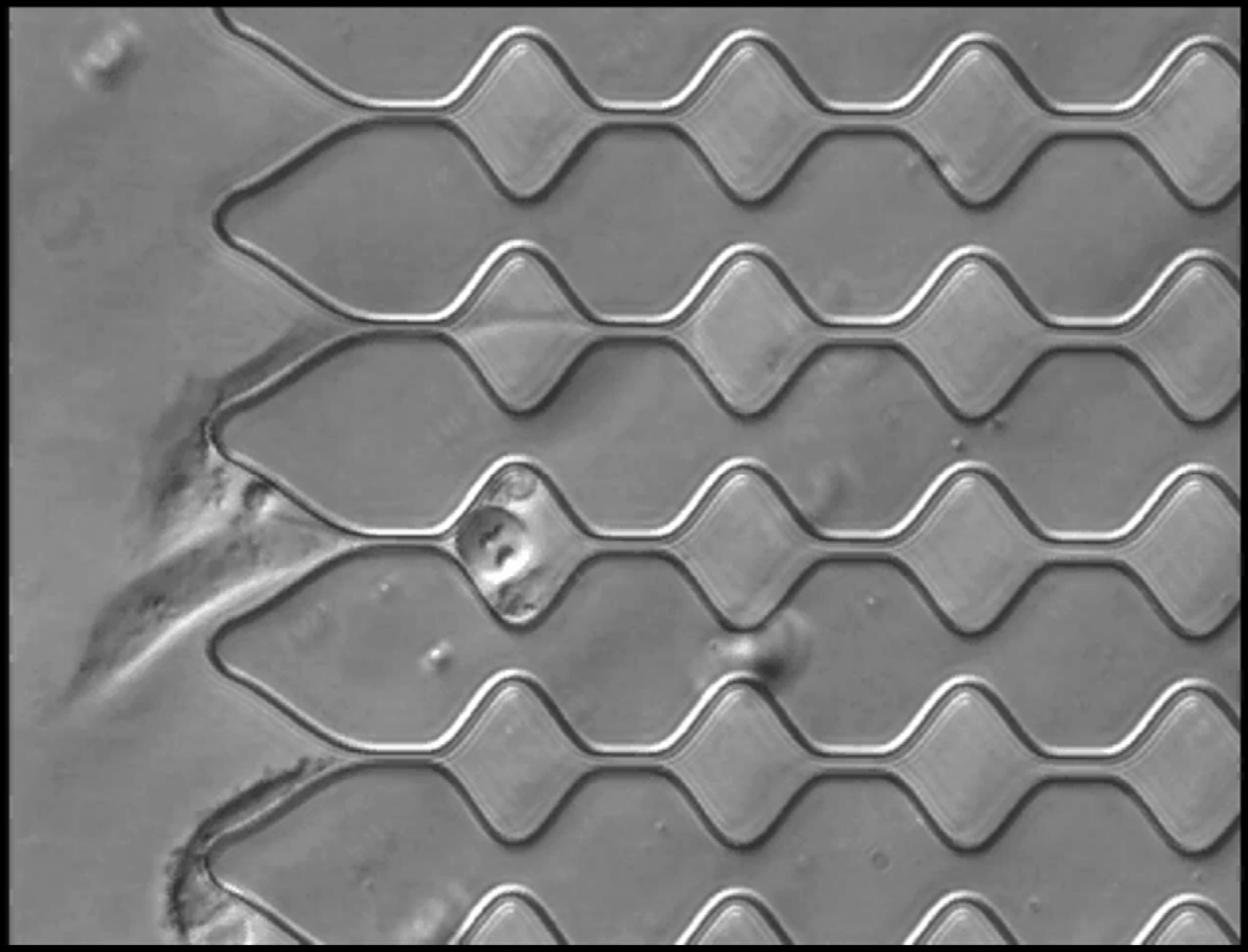
	Effect of HUVEC	cell line	tissue	invasion score w/o HUVEC	invasion score with HUVEC
non-invasive	unchanged	Colo205	colon	0.05 ± 0.02	0 ± 0
		BT-20	breast	0 ± 0	0 ± 0
		Caco-2	colon	0 ± 0	0 ± 0
		CX1	colon	0 ± 0	0 ± 0
		KS	breast	0 ± 0	0 ± 0
		MDA-MB-453	breast	0 ± 0	0 ± 0
		MDA-MB-468	breast	0 ± 0	0 ± 0
		HCT116	colon	0.01 ± 0.01	0.01 ± 0
		MCF-7	breast	0.08 ± 0.02	0.08 ± 0.02
		Capanl	colon	0 ± 0	0.01 ± 0.01
		SW948	colon	0 ± 0	0.01 ± 0.01
		HS578T	breast	0.04 ± 0.01	0.06 ± 0.01
		A431	lung	0 ± 0	0.02 ± 0.01
		Colo201	colon	0.03 ± 0.01	0.05 ± 0.01
		A427	lung	0 ± 0	0.37 ± 0.09
		DLD-1	colon	0.07 ± 0.02	0.14 ± 0.03
	induction of invasion	SW48	colon	0 ± 0	0.05 ± 0.01
		CX-2	colon	0 ± 0	0.06 ± 0.03
		LX-1	colon	0 ± 0	0.13 ± 0.03
		T47D	breast	0 ± 0	0.14 ± 0.03
		HT-29	colon	0 ± 0	0.15 ± 0.02
		A549	lung	0 ± 0	0.48 ± 0.09
		SW620	colon	0.01 ± 0	0.08 ± 0.02
		SW480	colon	0.02 ± 0.01	0.06 ± 0.02
		MS751	cervix	0.02 ± 0.01	0.07 ± 0.01
		A172	brain	0.02 ± 0.01	0.1 ± 0.01
		Mia-Paca-II	pancreas	0.04 ± 0.01	0.16 ± 0.03
invasive	decreased invasion	BT549	breast	5.69 ± 0.20	0.52 ± 0.10
		MDA-MB-436	breast	5.05 ± 0.60	0.96 ± 0.19
		Mewo	skin	3.04 ± 0.32	0.02 ± 0.01
		PC-3	prostate	6.13 ± 0.66	3.86 ± 0.4
		SKBR3	breast	3.02 ± 0.44	1.30 ± 0.13
		Hacat	colon	0.98 ± 0.18	0.04 ± 0.01
		Hela	skin	1.01 ± 0.10	0.34 ± 0.09
		Me180	cervix	1.38 ± 0.49	0.76 ± 0.20
		DANG	pancreas	0.86 ± 0.11	0.26 ± 0.03
	unchanged	C33A	colon	0.53 ± 0.06	0.39 ± 0.08
		MDA-MB-361	breast	0.24 ± 0.03	0.18 ± 0.02
		A875	skin	0.35 ± 0.06	0.31 ± 0.05
		RT112	bladder	0.32 ± 0.06	0.34 ± 0.07
		CAKI-1	kidney	0.11 ± 0.03	0.21 ± 0.04
		MDA-MB-435	breast	1.09 ± 0.15	1.23 ± 0.2
		786-0	kidney	0.29 ± 0.04	0.59 ± 0.14
		FaDu	pharynx	0.65 ± 0.13	1.39 ± 0.28
		A125	lung	3.15 ± 0.29	3.38 ± 0.28
	increased invasion	A375	skin	0.55 ± 0.09	2.49 ± 0.34
		DU145	prostate	0.67 ± 0.05	2.89 ± 0.25
		1205Lu	breast	0.82 ± 0.20	1.52 ± 0.36
		T24	skin	2.04 ± 0.12	3.98 ± 0.51
		MDA-MB-231	breast	2.52 ± 0.12	8.05 ± 0.55
		EJ-28	bladder	3.84 ± 0.42	9.01 ± 1.00

Gene expression profiles



Bauer et al, Int J Cancer 2007





Cell invasion assay

- Effect of drugs
- Influence of gene expression profile
- Cell types

- Understand the mechanism of metastasis formation
  - Adhesion receptors
  - Matrix proteinases
  - Forces / cell contractility
  - Cytoskeletal mechanics and dynamics