Supplementary Figure 1. (a) Distribution of # animals across 436 wells from 64 tested conditions (bars). Normalized distribution of animals across wells corresponds to the efficacy of worm loading setup (dashed line). The total # of worms tested for each condition is normalized to $n \times 11$ worms distributed across $n$ wells. (b) % detection success decreases with increasing # worms per well, due to greater likelihood of animals overlapping and therefore being censored. n=436 wells totaling 4660 worms. (c) Re-analyzing videos-snapshot comparison test from Figure 2c using only Coiled postures. The Snapshots Automated panels includes curling data for rounds 1, 2, and 3 and rounds 4, 5, and 6, respectively. All rounds of snapshots are captured within a 60min window after transfer to liquid. n = 5 wells totaling 50 worms for control videos, 7 wells totaling 73 worms for bcat-1 videos, 6 wells totaling 71 worms for control snapshots, 6 wells totaling 41 worms for bcat-1 snapshots. (d) Illustration of geometric model for C. elegans body. Two-tailed t-tests. *p<0.05, ***p<0.001. Box plot show minimum, 25th percentile, median, 75th percentile, maximum. Mean of bcat-1(RNAi) divided by mean of control RNAi is abbreviated as mean ratio.
Supplementary Figure 2. (a) New analyses in SnapMachine can be simply initiated after loading raw data and a trained neural network. CurlNet performance in identifying target classes of worm postures in front of a noisy background (b) and in wells with debris and bacterial chunks (c). Scale bar, 1mm.
**Supplementary Figure 3.** CurlNet performance in identifying target classes of worm postures (a) in an out-of-focus photograph of a well, (b) in an image distorted due to non-uniform meniscus, and (c) in the presence of a bubble and off-centered well. Scale bar, 1mm.
Supplementary Figure 4. (a) Disease indications of the 50 drugs selected for the screen, with number of drugs in parentheses. (b) Targets/mechanisms of action of the 50 drugs, with percentage of drugs in parentheses. (c) High-throughput screen result of 50 FDA-approved drugs utilizing Coiled + Curled postures. Vehicle-treated level of bcat-1(RNAi) worm curling was set to 100%, and color indicates curling level relative to vehicle. Blank wells are those that had <3 worms and were excluded. (d) Post screen validation of three negative drugs, riluzole, linagliptin, and milnacipran. Vehicle-treated level of bcat-1(RNAi) worm curling was set to 100%, and color indicates % Coiled relative to vehicle. Blank wells are those that had <3 worms and were excluded. (e) bcat-1 worms were moved to dcr-1 RNAi on day 5 to disrupt RNAi machinery and curling was manually measured on day 8. n = 119 worms for L4440=>L4440, 90 worms for L4440=>dcr-1, 133 worms for bcat-1=>bcat-1, 110 worms for bcat-1=>dcr-1. Data are mean±s.e.m. One-way ANOVA with Tukey’s post-hoc. ns, not significant. ****p<0.0001. Box plot shows minimum, 25th percentile, median, 75th percentile, maximum.