- **File S1: Primers for amplicon sequencing of highly cold-induced editing sites and cytochrome c oxidase I (for species identification). Related to Figures 3 and 6.**

- Cytoplasmic_dynein_1_heavy_chain_1 (Ocbimv22033392m)
  - Editing site(s):
    - 2384 (Δ37% editing in RNASeq-based analysis)
  - Fwd: CGCAATTTACGATGGCTGGG
  - Rev & Sanger: ATTCCACATCAAGCCCCACC
  - Amplicon size: 634 bp

- Kinesin_heavy_chain_isoform_5A (Ocbimv22000619m)
  - Editing site(s):
    - 845 (Δ29% editing)
      - Genomic coordinate: Scaffold10378:107063
  - Fwd: GTTAAGGGAGCAACAGAGAG
  - Rev & Sanger: CGTGCCAATGTAGCCTTC
  - Amplicon size: 590 bp

- Synaptotagmin-1 (Ocbimv22021175m)
  - Editing site(s):
    - 741 (Δ25% editing)
    - 742 (Δ24% editing)
      - Genomic coordinate: Scaffold311:554700
  - Fwd: CGTCAAAGTCTATCTAATGCCCG
  - Rev & Sanger: ATTCTTCTCGGGCACTTC
  - Amplicon size: 712 bp

- Titin-like (Ocbimv22028814m)
  - Segment 1
    - Editing site(s):
      - 3635 (Δ28% editing)
      - 3636 (Δ31% editing)
      - 3646 (Δ28% editing)
      - 3647 (Δ14% editing)
      - 3660 (Δ16% editing)
    - Fwd: CGGACCCTAAAGATAAGGC
    - Rev & Sanger: CTAGTTGTGTCTGAAGGC
    - Amplicon size: 636 bp
  - Segment 2
    - Editing site(s):
      - 6350 (Δ11% editing)
      - 6598 (Δ26% editing)
      - 6664 (Δ17% editing)
    - Fwd: GCATAGTGAACTGACTGAAGGG
    - Rev & Sanger: GGTTGTTGGCTCTTTGAAGGG
    - Amplicon size: 810 bp
  - Segment 3
    - Editing site(s):
      - 8774 (Δ23% editing)
      - 8784 (Δ35% editing)
      - 8934 (Δ17% editing)

    - Fwd: TAATAACGGCTGCGAAGG
    - Rev & Sanger: GGAAGATAAACGTTCCGCTC
    - Amplicon size: 665 bp
  - Segment 4
    - Editing site(s):
      - 15116 (Δ14% editing)
      - 15330 (Δ26% editing)
      - 15432 (Δ13% editing)
    - Fwd: GATGCTCATTCCGGTTCAGC
    - Rev & Sanger: GGTGTGACCCACAGTACCA
    - Amplicon size: 660 bp

- Cytochrome c oxidase I
  - Fwd: TTCGAACAGAATTAGGTCAAC
  - Rev & Sanger: AATTTCGATCAGTTAAAAGTATTG
  - Amplicon size: 534 bp

Table S5: Pairwise comparisons of the change in editing level (EL) among all 18 sites at each timepoint during the warm-to-cold and cold-to-warm timelapse experiments. Related to Figure 3.

Warm-to-cold (24° →14°)

Time 1*	Time 2*	Average ΔEL	P-value	Bonferroni-adjusted p-value
-20	24	9.17500762	9.94E-05	0.00029811
24	48	6.00995749	0.009358025	0.028074076
48	96	5.416140318	0.001088504	0.003265513

Cold-to-warm (14° →24°)

Time 1*	Time 2*	Average ΔEL	P-value	Bonferroni-adjusted p-value
-20	0	-4.42390715	0.000304709	0.001218836
0	8	-0.29464479	0.73539669	1
8	24	-5.35957329	0.00010478	0.000419122
24	96	-12.7316026	3.94E-06	1.58E-05

* All time comparisons are expressed in hours relative to the end of the temperature change. Temperature was changed at 0.5°C per hour for 20 hours, so "-20" is immediately before the start of the change and "0" is immediately at the end of the change.

Table S6: Statistics for wild-type and I248V edited *Octopus* synaptotagmin-1 crystal structures. Related to Figure 5.

	***Octopus* Syt1 C2A (wild type)**	***Octopus* Syt1 C2A (I248V)**
Wavelength (Å)	1.5418	1.5418
Resolution Range (Å)	33.4 – 1.85 (1.92 – 1.85)	41.5 – 1.95 (2.02 – 1.95)
Space Group	$P2_12_12_1$	$P2_1$
Unit Cell (Å, °)	28.73, 54.94, 84.14, 90°,90°,90°	43.92, 49.42, 71.71, 90°, 106.278°, 90°
Total Reflections	63769 (2508)	64727 (1993)
Unique Reflections	11556 (878)	20325 (887)
Multiplicity	5.5 (2.8)	3.2 (1.6)
Completeness (%)	96.45 (74.60)	82.93 (40.92)
Mean I/σI	13.09 (0.91)	7.09 (0.90)
Wilson B-factor (Å^2)	34.35	21.99
R_{merge}	0.08502 (0.8457)	0.1118 (0.6204)
R_{meas}	0.09341 (1.004)	0.1324 (0.8148)
R_{pim}	0.03807 (0.5266)	0.07007 (0.5216)
$CC_{1/2}$	0.997 (0.58)	0.995 (0.62)
CC*	0.999 (0.857)	0.999 (0.875)
Reflections used in Refinement	11528 (878)	18036 (879)
Reflections used for R_{free}	0.2210 (0.3895)	1792 (85)
R_{work}	0.1786 (0.4018)	0.1761 (0.3273)
R_{free}	0.2210 (0.3895)	0.2126 (0.3415)
CC_{work}	0.967 (0.745)	0.972 (0.741)
CC_{free}	0.942 (0.867)	0.961 (0.738)
Number of non-Hydrogen atoms	1075	2283
Macromolecules	1043	2135
ligands	0	0
• **solvent**	32	148
• **protein residues**	128 (1 C2A domain in ASU)	260 (2 C2A domains in ASU)
RMS (bonds) (Å)	0.008	0.010
RMS (angles) (°)	0.081	1.17
Ramachandran favored (%)	99.21	97.27
Ramachandran allowed (%)	0.79	2.73
Ramachandran outliers (%)	0.00	0.00
Rotamer outliers (%)	0.00	1.65
Clashscore	5.8	6.60
Average B-factor (Å^2)	45.29	35.36
• **Macromolecule (Å^2)**	45.26	35.17
• **Solvent (Å^2)**	46.30	38.12
Number of TLS groups	7	10