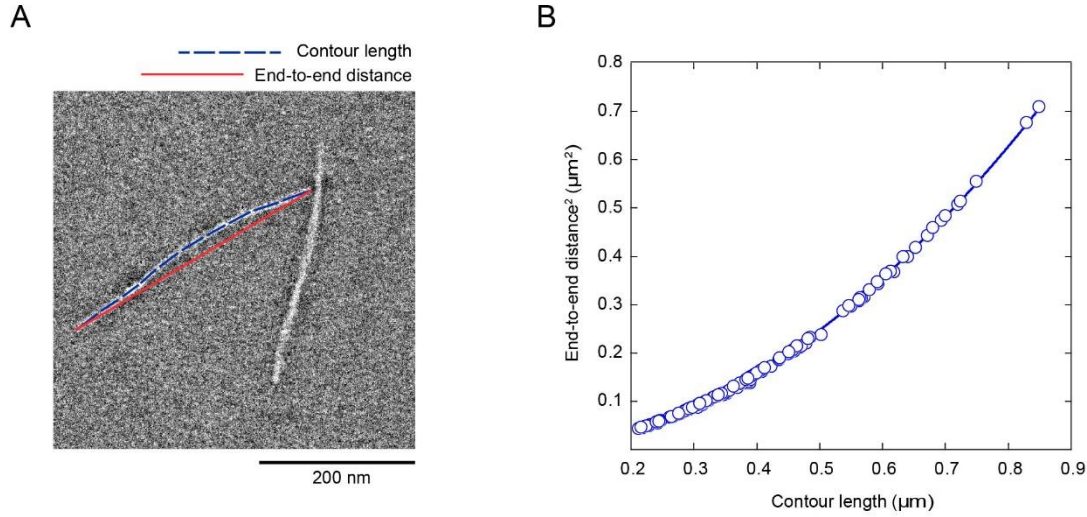


Supplementary Information

Cryo-EM structure of a light chain-derived amyloid fibril from a patient with systemic AL amyloidosis

L. Rademaker et al.

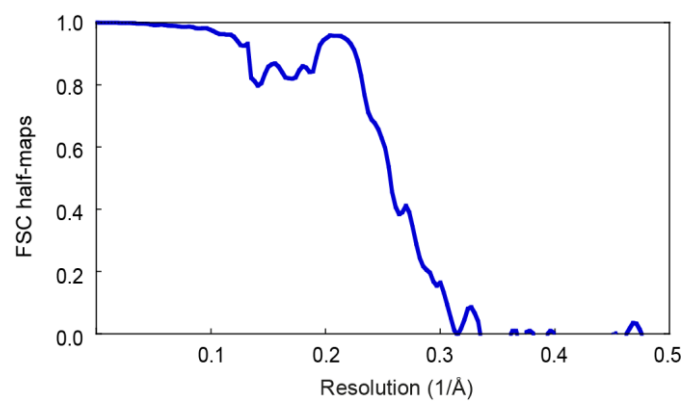
Supplementary Figure 1



Quantification of the fibril bending rigidity

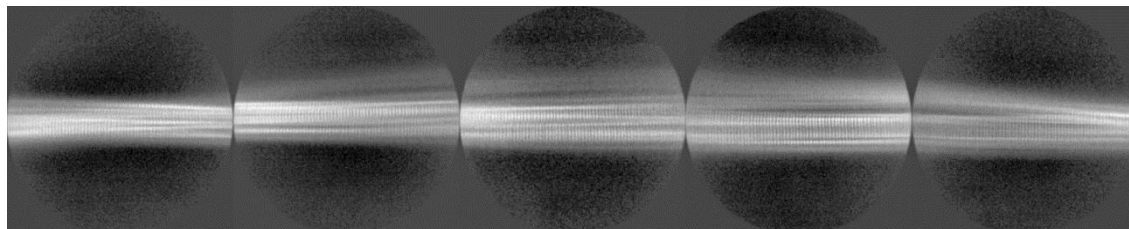
(a) Representative negatively stained TEM image of the analyzed fibrils showing the contour length and the end-to-end distance. (b) Plot of the squared end-to-end distance versus the contour length for 124 fibrils, fitted with a formula as described in the methods to obtain the fibril persistence length. The fit produced a value of $6.7 \pm 0.5 \mu\text{m}$ for the persistence length and of $2.78 \pm 0.21 \cdot 10^{-26} \text{ Nm}^2$ for the bending rigidity ($R^2 = 0.9995$, errors refer to standard deviation).

Supplementary Figure 2



FSC curve of the reconstructed density

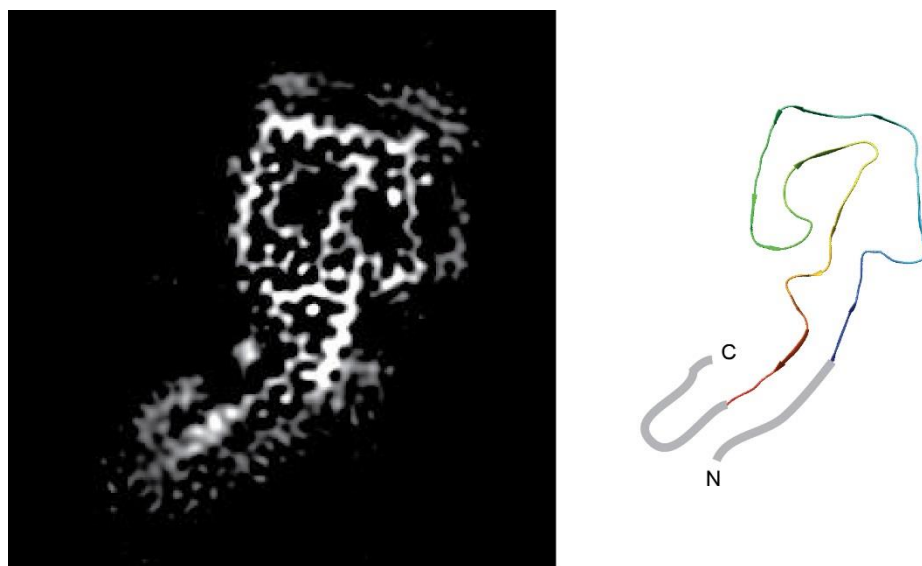
Supplementary Figure 3



2D class averages

Selection of 2D class averages showing five classes which roughly cover one cross-over distance.

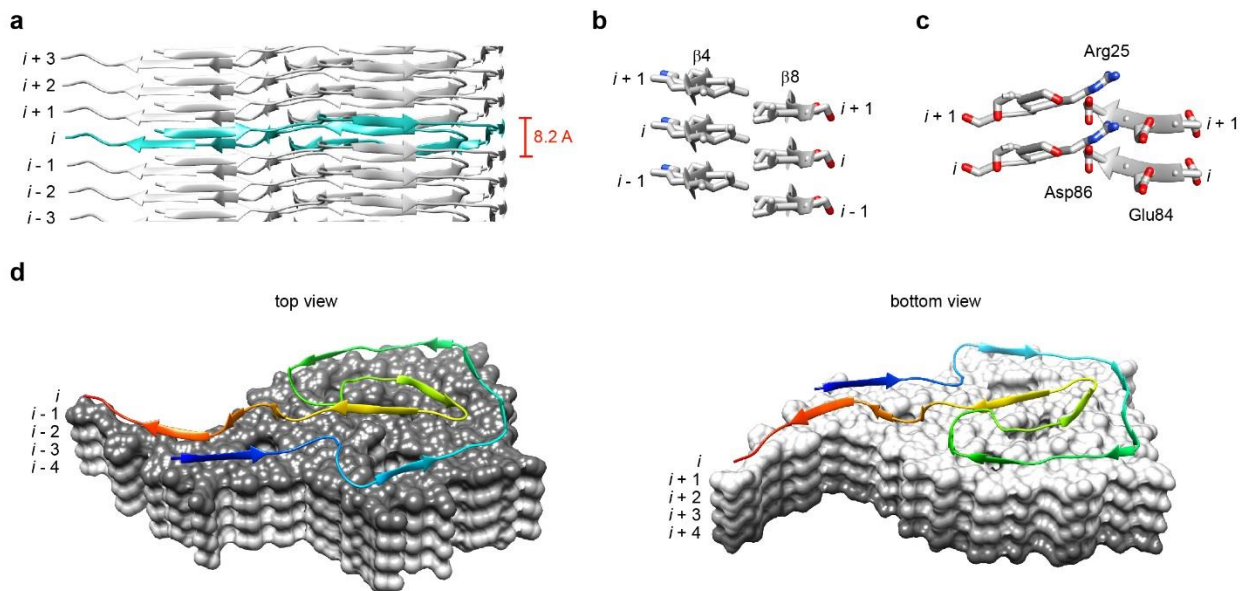
Supplementary Figure 4



Presence of ordered and disordered regions in the fibril structure

Left: A 29 Å thick cross-sectional slice of the unmasked 3D map of the AL fibril. Right: Ribbon diagrams of one fibril molecule with a schematic drawing of the disordered C-terminus (grey). The drawing of the C-terminus corresponds to some of the diffuse density in the 3D map. Additional diffuse density of uncertain origin can be seen, similar to other *ex vivo* fibrils^{1,2,3}.

Supplementary Figure 5



Intermolecular interactions along the fibril axis

(a) The height change of the fibril protein (8.2 Å) was determined between the C α atom of Asn28 (highest point) and the C α of Ala72 (lowest point). (b) Staggering of sheet $\beta 4$ relative to sheet $\beta 8$. Sheet $\beta 4$ from layer i interacts with sheets $\beta 8$ in layers i and $i+1$. (c) Interaction of Arg 25 from layer i with Glu84 and Asp86 in layer $i+1$. (d) Different structural topology of the two fibril tips (left/right). Four layers are shown in gray scale (spacefill). The terminal layer is shown as a ribbon diagram in rainbow color from N (blue) to C (red).

Supplementary Table 1

Patient characteristics

Parameter	At AL diagnosis	At heart transplantation
Karnofsky Index / New York Heart Association cardiac stage	80% / III	70% / III-IV
Difference free LC value	137 mg/l	40 mg/l
Concentration of λ -LC in the urine	36 mg/d	Not determined
N-terminal pro brain natriuretic peptide concentration in the plasma	8,300 ng/l	19,800 ng/l
High sensitive troponin T concentration in the plasma	53 pg/ml	136 pg/ml
Cardiac stage	III A	III B
Septum thickness	18 mm	19 mm
Estimated glomerular filtration rate	94 ml/min	56 ml/min

Supplementary Table 2

Modeling parameters

Model resolution (Å)	
FSC threshold 0.143	3.3
FSC threshold 0.5	3.9
Model resolution range (Å)	330-3.3
Map sharpening <i>B</i> factor (Å ²)	-119.6
Model composition	
Non-hydrogen atoms	5472
Protein residues	728
Ligands	-
<i>B</i> factors (Å ²)	
Protein	111.43
Ligand	-
R.m.s. deviations	
Bond lengths (Å)	0.010
Bond angles (°)	1.257
Validation	
MolProbity score	2.29
Clashscore	9.22
Poor rotamers (%)	1.4
Ramachandran plot	
Favored (%)	83.1
Allowed (%)	16.9
Disallowed (%)	0

Supplementary Table 3

Analysis of the aggregation score for residues Val3-Ser118. Please refer to the Methods section for details. Hits are presented in bold print, and for AmylPred as +

Sequence	WALTZ	TANGO	Fold amyloid	Aggrescan	AmylPred	Score
V	0.00	0.00	23.00	-0.10	–	0
L	0.00	0.00	22.10	-0.10	–	0
T	0.00	0.00	21.20	-0.10	–	0
Q	0.00	0.00	19.90	0.09	–	0
P	0.00	0.00	18.40	-0.14	–	0
P	0.00	0.00	18.40	-0.38	–	0
S	0.00	0.00	18.20	-0.44	–	0
A	0.00	0.00	18.20	-0.28	–	0
S	0.00	0.00	18.60	-0.28	–	0
G	0.00	0.00	18.50	-0.31	–	0
T	0.00	0.00	17.90	-0.45	–	0
P	0.00	0.00	18.10	-0.62	–	0
G	0.00	0.00	18.90	-0.35	–	0
Q	87.96	0.00	19.70	-0.30	–	1
R	87.96	0.00	20.20	-0.01	–	2
V	87.96	0.00	21.90	-0.01	–	2
T	87.96	0.00	21.70	0.16	–	2
I	87.96	0.00	22.20	0.29	–	2
S	87.96	0.00	21.10	0.39	–	2
C	0.00	0.00	20.50	-0.01	–	1
S	0.00	0.00	19.60	-0.03	–	0
G	0.00	0.00	19.60	-0.34	–	0
R	80.60	0.00	18.50	-0.48	–	1
S	80.60	0.00	18.60	-0.31	–	1
S	80.60	0.00	20.30	-0.34	–	1
N	80.60	0.00	19.50	-0.44	–	1
I	80.60	0.00	20.10	-0.45	–	1
G	80.60	0.00	20.20	-0.21	–	1
R	80.60	0.00	21.50	0.06	–	2
N	91.97	0.00	21.20	0.11	–	2
L	91.97	0.00	21.30	0.00	–	2
V	91.97	0.00	22.80	0.24	–	3
K	91.97	0.00	24.30	0.24	–	3
W	79.93	0.00	23.00	0.25	–	3
Y	79.93	0.00	22.10	0.31	–	3

Q	79.93	0.00	24.00	0.03	–	3
Q	79.93	0.00	21.80	0.09	–	3
F	79.93	0.00	20.00	-0.08	–	1
P	79.93	0.00	20.20	-0.25	–	1
G	0.00	0.00	20.30	-0.13	–	0
T	0.00	0.00	18.30	-0.08	–	0
A	0.00	0.00	18.40	-0.14	–	0
P	79.93	0.00	20.00	0.11	–	2
K	97.99	0.00	21.10	0.45	–	2
L	87.29	27.12	22.30	0.63	+	4
L	87.29	27.30	24.00	0.60	+	4
I	87.29	27.30	24.10	0.46	+	4
Y	87.29	27.30	22.70	0.33	+	4
S	87.29	27.30	21.10	-0.04	+	3
N	87.29	12.36	19.90	-0.42	–	2
D	0.00	0.00	18.90	-0.73	–	0
Q	0.00	0.00	18.70	-0.93	–	0
R	0.00	0.00	18.70	-0.97	–	0
P	0.00	0.00	18.60	-0.55	–	0
S	0.00	0.00	19.50	-0.34	–	0
G	0.00	0.00	18.80	-0.43	–	0
V	0.00	0.00	18.80	-0.43	–	0
P	0.00	0.00	19.40	-0.13	–	0
D	0.00	0.00	21.40	-0.13	–	0
R	0.00	0.00	20.20	-0.13	–	0
F	0.00	0.00	20.20	-0.40	–	0
S	0.00	0.00	20.30	-0.48	–	0
G	0.00	0.00	19.70	-0.26	–	0
S	0.00	0.00	17.90	-0.16	–	0
K	0.00	0.00	17.70	-0.44	–	0
S	0.00	0.00	18.20	-0.44	–	0
G	0.00	0.00	18.20	-0.36	–	0
T	0.00	0.00	18.60	-0.36	–	0
S	0.00	0.00	18.60	-0.03	–	0
A	0.00	0.40	20.30	0.00	–	2
S	0.00	0.40	20.30	0.31	–	2
L	0.00	0.64	21.50	0.29	–	2
A	0.00	0.64	21.10	0.25	–	2
V	0.00	0.64	20.90	0.46	–	2
S	0.00	0.24	20.90	0.32	–	2
G	0.00	0.24	20.80	0.08	–	2

L	0.00	0.24	19.60	-0.11	–	1
Q	0.00	0.00	19.50	-0.60	–	0
S	0.00	0.00	19.50	-0.76	–	0
E	0.00	0.00	18.00	-0.69	–	0
D	0.00	0.00	18.10	-1.15	–	0
E	0.00	0.00	17.90	-0.81	–	0
A	79.93	0.00	19.60	-0.60	–	1
D	79.93	0.00	21.30	-0.31	+	2
Y	79.93	0.39	22.50	-0.06	+	4
Y	80.60	0.39	22.50	0.14	+	4
C	80.60	0.39	23.00	0.29	+	4
A	80.60	0.39	23.50	0.29	+	4
A	80.60	0.39	21.80	0.12	+	4
W	79.93	0.39	21.10	-0.07	–	2
D	79.93	0.00	21.10	0.05	–	2
A	79.93	12.73	22.20	-0.14	–	2
T	88.63	28.85	20.20	-0.14	–	2
L	88.63	11.30	20.70	-0.14	+	3
N	93.98	12.67	22.40	0.35	+	5
A	93.98	15.72	23.20	0.61	+	5
W	93.98	16.02	23.60	0.56	+	5
V	93.98	16.02	23.30	0.28	+	5
F	93.98	15.35	22.80	0.39	+	5
G	93.98	43.39	20.50	0.37	–	3
G	93.98	0.55	19.70	0.09	–	3
G	0.00	0.00	17.80	0.06	–	1
T	0.00	0.00	19.40	-0.21	–	0
K	0.00	0.00	20.00	0.09	–	1
L	82.61	0.63	21.30	0.37	–	3
T	82.61	0.63	22.40	0.40	–	3
V	82.61	0.63	22.50	0.25	–	3
L	82.61	0.63	21.30	0.33	–	3
S	82.61	0.63	20.80	0.00	–	3
Q	82.61	0.00	19.60	0.02	–	3
P	0.00	0.00	18.50	-0.21	–	0
K	0.00	0.00	18.80	-0.46	–	0
A	0.00	0.00	18.50	-0.46	–	0
A	0.00	0.00	18.60	-0.44	–	0
P	0.00	0.00	18.90	-0.44	–	0
S	0.00	0.00	18.50	-0.44	–	0

Supplementary References

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